RML Institutional Bio-Safety Committee Minutes

Meeting Date: 2/20/14
Meeting Time: 1:02 PM **Adjourned:** 2:51 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Paul Carlson	☒	☐	Kevin Mora	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Megan Morgan	☒	☐
Becky Anderson (EO)	☒	☐	Frank DeLeo (EO)	☐	☒	Karin Peterson	☒	☐
Alan Applebury	☐	☒	Hideki Ebihara	☒	☐	George Risi	☒	☐
Chris Bosio	☒	☐	Heinz Feldmann (EO)	☐	☒	Dana Scott	☒	☐
Marshall Bloom (EO)	☒	☐	Nancy Hoe	☒	☐	Alexandra Scranton	☐	☒
Teresa Borino	☐	☒	Clay Jarrett	☒	☐			
Jeff Burrows	☒	☐	Josh Kellar (EO)	☐	☒			
Carol Calderwood	☐	☒	Scott Kobayashi	☒	☐			
Harlan Caldwell (EO)	☐	☒	Rachel LaCasse	☐	☒			
Marcie Caldwell (EO)	☒	☐	Alida Merritt	☒	☐			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 12/19/13 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** Action: Meeting minutes were unanimously approved with the following minor modifications: ▪ Sue Priola pointed out that George Risi had informed her he was present at the December meeting, but the minutes did not reflect that. ▪ Sue Priola also noted that the action item on page 3 should be changed from "strain sensitivity" to "strain antibiotic sensitivity". ▪ Bob Heinzen noted at the middle of page 3, a primary lab hazard was listed as viral isolates; it should be corrected to bacterial isolates. **SOP#4-28-24 Removal of Animal Tissues from BSL-4 Tabled at December 19, 2014 IBC Meeting** ▪ Becky Anderson summarized the reasons that SOP#4-28-24 was tabled. The major concern about this SOP was raised by Dana Scott regarding roles and

	responsibilities of RMVB. The SOP was written to state that RMVB was responsible for all tissues removed from the MCL, while RMVB had no oversight over the process. Dana Scott also noted that removal of tissues that do not fit into a tissue cassette are not clearly addressed in the SOP. Dana Scott met with Heinz Feldmann and discussed these concerns. The responsibility for tissue being removed from the MCL is now stated as the user's responsibility. This change in roles reflects how the responsibility is stated in many of the other MCL SOPs. The SOP was also updated to state that any tissue that does not fit into a tissue cassette will be fixed for at least 30 days prior to removal. ▪ Dana Scott added that any mention of fixing carcasses was removed from the SOP as that procedure is not performed. ▪ Karin Peterson stated that a 30 day fixation process is a very long time. Dana Scott agreed, but stated that it is standard for the BSL-4 labs to use this long time frame for larger tissues. ▪ The committee had no additional comments or concerns. Action: The committee unanimously approved SOP#4-28-24 Removal of Animal Tissues from the BSL-4.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans (Renewal) ▪ Bloom (LV) ▪ **HPRD#14-58**: Langat Virus ▪ Becky Anderson presented the risk assessment. The purpose of this study is to examine and characterize changes caused by acute or persistent Langat virus infection in mammalian or tick cells and to determine which specific viral proteins are responsible for morphological changes seen upon infection. The incidence of disease with Langat virus is extremely low; there are no registered naturally occurring cases of human disease. It is a naturally attenuated member of the Tick borne encephalitis virus serogroup. The virus is completely non-virulent for adult mice following subcutaneous or IP inoculation and primates following intracerebral inoculation. In the few encephalitis cases that arose from a live attenuated LGTV based vaccine, the encephalitis was similar to that seen following infection with typical European strains of TBEV. There are currently no specific treatments for Langat virus infection, supportive care is given. The natural route of transmission is through the bite of an infected tick. The primary laboratory hazards include accidental parenteral inoculation, contact with broken skin or mucous membranes, accidental sharps injuries.

	▪ The committee discussed the containment requirements. BSL-2 is appropriate for studies with Langat Virus. ▪ Sue Priola questioned why III-D-1-a was listed from the NIH Guidelines. Becky Anderson informed the committee that the HPRD and RD were combined upon submission. Becky Anderson split the documents, but the HRPD retained some of the RD information. Nancy Hoe added that III-D-1-a can be included because they are working with human cell lines. ▪ No animal work was submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **HPRD#14-58** as written.
Item 2:	Registration of Material (Potentially) Infectious for Humans (Renewal) ▪ Bloom (LV) ▪ **HPRD#14-119**: Sindbis Virus ▪ Becky Anderson presented the risk assessment. This registration is for storage only; no active work will be conducted. Prior to initiation of work, the HRPD will be updated and approved by the IBC. Sindbis virus can cause a self-limiting febrile viral disease. It presents with a sudden onset of fever, rash, arthralgia or arthritis, lassitude, headache and myalgia. A rash may precede or follow joint manifestations by 1-2 days; exanthem on trunk progressing to face, legs, palm, soles and lasts on average 10 days. Signs of jaundice and myocardial damage are reported but rare, quite often, there is no recognized clinical disease manifestations. There currently is no specific treatment for Sindbis virus and supportive care is given. The natural route of transmission is through an infected mosquito bite. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for storage of Sindbis virus. ▪ No animal work was submitted, reviewed, or approved. ▪ The committee had no questions or concerns. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **HPRD#14-119** as written.
Item 3:	Registration of Material (Potentially) Infectious for Humans (New) ▪ Bosio (LICP) ▪ **HPRD#14-157**: *Listeria monocytogenes*

	▪ Becky Anderson presented the risk assessment. The Bosio lab is interested in determining if cells isolated from mice vaccinated against tularemia are able to control replication of an unrelated, intracellular cytosolic bacterium (*Listeria monocytogenes*) in vitro. Although relatively rare, human listeriosis is often severe and mortality rates can approach 50%. Certain factors predispose individuals to infection with *L. monocytogenes*, such as neonates, pregnancy, leukemia, Hodgkin's disease, diabetes mellitus, alcoholism or cirrhosis and immunosuppressive or cytostatic therapy. Most commonly, listeria causes a mild febrile illness however, several types of listeriosis disease manifestations are recognized; for instance, listeriosis in pregnancy, listeriosis of the central nervous system (CNS), febrile gastroenteritis, glandular listeriosis, local listeriosis, typhoid listeriosis, and atypical listeriosis. Listeriosis in pregnancy occurs mostly during the third trimester, and is characterized by a "flu like" illness with symptoms such as fever, chills, malaise, arthralgia, back pain, and diarrhea. In many cases the infection is subclinical or inapparent; however, intrauterine infection of the fetus can lead to fetal death, spontaneous abortion, premature delivery, or the birth of a fetus that dies shortly after birth. No vaccines are currently available; treatment of infection includes ampicillin or amoxicillin together with gentamicin. The recommended course of treatment is ampicillin for 2 to 4 weeks. The infectious dose for healthy persons is 10-100 x 10^6 CFU, but dramatically lower in immunocompromised persons, 0.1-10 x $10^{6.}$ The natural route of transmission is predominately through ingestion of contaminated foods. The primary lab hazards include accidental sharps injuries, ingestion, or inhalation. ▪ The committee discussed the containment requirements. BSL-2 is sufficient for work with *Listeria monocytogenes* with the following additional precautions: Women who are pregnant or thinking of becoming pregnant are encouraged to notify the Lab supervisor and RML OMS Nurse. This is in order to ensure that they are aware of any potential risks to themselves or the fetus and determine if any additional risk reduction measures should be taken. All work with infectious materials is conducted in a BSC; centrifugation of infectious materials must be carried out in sealed safety cups or removable rotors that can be loaded and unloaded in a BSC. ▪ Nancy Hoe added that the recommendation section should include a precaution that immunocompromised persons should be made aware of the risks of working with *Listeria monocytogenes*. ▪ Sue Priola added that the second sentence in the Purpose section should be rewritten to be clearer. ▪ No animal work was submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Chris Bosio abstained) **HPRD#14-157** with minor

	modifications: 1. Add to the recommendation section that immunocompromised persons should be made aware of the risks of working with *Listeria monocytogenes.* 2. The second sentence of the Purpose section should be rewritten to be clearer.
Item 4:	<u>Registration of Material (Potentially) Infectious for Humans (Amend)</u> ▪ Ebihara (LV) ▪ **HPRD#12-123Amend**: Phleboviruses ▪ Becky Anderson presented the description of the amendment to the committee. Hideki Ebihara currently has a Phlebovirus HPRD and an HPRD for Severe Fever with Thrombocytopenia Syndrome Virus (SFTSV). SFTSV was submitted as a separate registration originally so that Biosafety could do a risk assessment and determine a biosafety level because it was such a new virus and there was so little information available. SFTSV is a Phlebovirus so it makes sense to combine it with Hideki Ebihara's Phlebovirus HPRD. This HRPD already contains BSL-2 and BSL-3 agents on it. The amendment that he put together includes the SOPs for working with these viruses at BSL-2 and BSL-3 as well as the original risk assessment for SFTSV. All the previous information associated with the SFTSV is included in this amendment, including animal study proposals. Becky Anderson added that the recommendations section will state that the approval is for BSL-2 and BSL-3 Phleboviruses. ▪ Dana Scott questioned if the "A" in ABSL-4 stood for "Ag". Nancy Hoe clarified that it does not; it is just for "animal". ▪ The committee discussed the containment requirements. BSL-2/ABSL-2 and BSL-3/ABSL-3 are appropriate for specific agents. The table included in the registrations lists the biosafety level for each virus. ▪ Sue Priola questioned the room numbers that were listed on the SOPs. Megan Morgan clarified that there are 2 separate SOPs, one for BSL-2 and one for BSL-3 and that is why the room numbers are different. ▪ Sue Priola also asked if Malsoor virus is going to be handled at BSL-3. Hideki Ebihara stated that it will be even though it has never been isolated from humans; it is genetically close to SFTSV and will therefore be handled at BSL-3. ▪ George Risi pointed out that on page 1 of the attachment, the third paragraph refers to Rift Valley Fever virus and then talks about BSL-2. The statement was confusing and made it sound like Rift Valley Fever Virus was a BSL-2 virus. The committee discussed the wording and agreed that the second sentence of the third paragraph should be deleted because it was causing the confusion. BSL-3 should also be added behind the reference to Rift Valley Fever Virus. Sue Priola added that the first sentence of the third paragraph sounds like a blanket approval for all Phleboviruses, and should be reworded to state, "all

	Phleboviruses listed in Table 1". ▪ Alida Merritt asked if it was standard to reuse disposable gowns at BSL-2 as listed in the SOP. Hideki Ebihara stated that it was for this room, but if it is visibly soiled it is changed. The gowns are also dated and include the employee's name so there is no confusion on use. ▪ Nancy Hoe added that it should be clear in the Description section that BSL-4 and ABSL-4 are being added due to space considerations, not because BSL-4 is a requirement for any of these agents. ▪ Sue Priola reiterated that the recommendations section will be updated to include a statement that both BSL-2 and BSL-3 agents are included in this registration and the tables attached can be referred to for the specific viruses. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved (Hideki Ebihara abstained) **HPRD#12-123Amend** with minor modifications: 1. Add to the recommendations section that both BSL-2 and BSL-2 agents are approved in this registration. 2. Specify in the description section that BSL-4/ABSL-4 is due to space considerations, not a required biosafety level. 3. Paragraph three on the attached information should be updated from "all phleboviruses . . ." to state "all Phleboviruses listed in Table 1". 4. Paragraph three should also have the second sentence deleted. 5. Paragraph three should also have BSL-3 listed after Rift Valley Fever Virus.
Item 5:	<u>Registration of Material (Potentially) Infectious for Humans (Amend)</u> ▪ De Leo (LHBP) ▪ **HPRD#13-1Amend**: Staphylococcus aureus and other BSL-2 agents ▪ Becky Anderson presented the description of the amendment to the committee. The amendment is to add three avirulent, Select Agent exempt phase II strains of *Coxiella burnetii* to the current HPRD. The strains will be obtained from Bob Heinzen at RML. The proposed studies include assessing the ability of *C. burnetii* to alter human neutrophil function in vitro. The phase II strains of *C. burnetii* are attenuated by a 26 kb chromosomal deletion that eliminates multiple genes involved in LPS biosynthesis. The deletion results in a strain that is avirulent for immunocompetent mice and guinea pigs. Pathogenesis in humans is unknown; however, to date there have been no reported infections of humans with the phase II strain.

	▪ The committee discussed the containment requirements. BSL-2 is sufficient for work with *C. burnetii.* ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Scott Kobayashi abstained) **HPRD#13-1Amend** as written.
Item 6:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Bloom (LV) ▪ **RD#14-201**: Characterization of Langat virus infection in mammalian and tick cells ▪ Reviewers: Hideki Ebihara, Karin Peterson ▪ **Summary:** The RD describes determining which specific viral proteins from Langat virus are responsible for the morphological changes seen during infection. ▪ Hideki Ebihara summarized the registration. The RD is focused on determining viral protein function from Langat virus. They will clone viral genes in expression plasmids and express in eukaryotic cells, including 293, Vero, MNB, ISE6, or mouse primary cells. All appropriate cloning maps are attached. The NIH Guidelines listed are appropriate and there were no dual use concerns marked on the questionnaire and no additional dual use concerns noticed. ▪ Karin Peterson questioned Marshall Bloom if his lab would infect cells with Langat virus and transfect at the same time. Marshall Bloom responded that they might want to do that at a later date. Karin Peterson recommended changing the "or" in the first sentence in the Eukaryotic Cells Section to "and/or" so that Marshall Bloom does not need to amend the registration at a later date. ▪ No animal studies were proposed, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved **RD#14-201** with the following minor modifications: 1. Change the "or" in the first sentence in the Research Using Eukaryotic Section to "and/or". Research using prokaryotic hosts is approved at BSL-2 under sections III-D-2-a and III-E-1 of the NIH Guidelines. Research using eukaryotic cells will be performed at BSL-2 and is approved under Sections III-D-1-a of the NIH Guidelines.

Item 7:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Gherardini (LZP) ▪ **RD#14-319**: To understand and characterize the infectious cycle of the Lyme Disease pathogen, *Borrelia burgdorferi* ▪ Reviewers: Bob Heinzen, Clay Jarrett ▪ **Summary:** The goal of these studies is to investigate how *B. burgdorferi* survives and proliferates in both an arthropod vector and various mammalian hosts. ▪ Bob Heinzen summarized the registration. This registration describes work with *B. burgdorferi* which causes Lyme disease. They will use basic bacterial genetics to make mutants. They will run the mutants through microarray analysis and generate beta-galactosidase gene fusion reporter constructs to study the mutants. The antibiotics used for selection include streptomycin, kanamycin, chloramphenicol, and gentamicin. None of these antibiotics are clinically useful for treatment of Lyme disease. Bob Heinzen also pointed out that he had no concerns with the registration and did not identify any dual use concerns. ▪ George Risi pointed out that gentamicin was spelled incorrectly and should be fixed. ▪ Clay Jarrett pointed out that the list of antibiotics used for selection included four drugs, but the sentence stated "three", that number should be clarified with Frank Gherardini. Clay Jarrett also informed the committee that a suicide vector, pCRScriptCAM was described, but the map was not attached. The map needs to be attached. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved **RD#14-319** with the following minor modifications: 1. Correct the spelling for gentamicin in the Research Using Prokaryotic Host section. 2. Clarify if there are three or four antibiotics that will be used in the Research Using Prokaryotic Host section. 3. Attach the suicide vector map for pCRScriptCAM. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-1-a and III-D-2-a of the NIH Guidelines.

Item 8:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Heinzen (LICP) ▪ **RD#14-106**: ▪ Reviewers: Chris Bosio, Scott Kobayashi ▪ **Summary:** The research described in this registration focuses on understanding the molecular mechanisms of intracellular survival and virulence by *C. burnetii*. ▪ Chris Bosio summarized the registration. The antibiotic resistance genes proposed are not used clinically for the treatment of Q Fever. It was a very well written registration and Chris Bosio had no concerns with the research outlined in the proposal. Chris Bosio did not find any dual use concerns in the proposal. ▪ Nancy Hoe added that Bob Heinzen already has DSAT authorization to use the listed antibiotics. ▪ Scott Kobayashi had nothing to add, and no additional concerns with the registration. ▪ Animal studies with guinea pigs were proposed. ▪ Sue Priola pointed out that the dual use form needs the very last box checked to indicate no overall dual use concerns. Bob Heinzen also needs to sign the dual use form and initial page 2. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Bob Heinzen abstained) **RD#14-106** with the following minor modifications: 1. Bob Heinzen needs to initial page 2, sign the dual use form, and check the final dual use question "no". Research using prokaryotic hosts is approved at BSL-2 under sections III-D-1-a, III-D-1-b, and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells will be performed at BSL-2 and is approved under Sections III-D-1-a and Appendix G-II-C of the NIH Guidelines.
Item 9:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Ebihara (LV) ▪ **RD#14-431**: ▪ Reviewers: Rachel LaCasse, Sue Priola ▪ **Summary:** The goal of the studies described in this RD is to characterize the roles that viral proteins play in the viral replication cycle and pathogenesis using *in vitro* systems.

	▪ Sue Priola summarized the registration. This RD covers cloning ORFs from a lot of different viruses. They plan to clone and express individual proteins in eukaryotic cell lines to look at their function. This registration does not include any live virus work, just expression of viral or host proteins. The listed sections of the NIH Guidelines are appropriate. III-E-1 is listed because they are handling individual ORFs so this comprises less than 2/3 of the genome. ▪ Sue Priola noted that the dual use form has two questions marked yes. The first is question A6 because they will expand the host range by transiently expressing the receptor for MERS in mice. There is no concern with this because it is a transient expression in an experimental group of mice and they are not altering the agent in any way. Sue Priola noted that question B was also marked yes for the synthetic biology techniques; however it does not need to be checked yes. The entire question reads if you are using synthetic biology techniques to construct a "pathogen, toxin or potentially harmful product. . ." Hideki Ebihara will only be using synthetic biology for the ORFs, not creating a whole virus. The committee agreed that question B should be changed from yes to no. ▪ Sue Priola also noted that the table, "List of the representative RNA viruses and their ORFs to be used for experiments" has an asterisk at the end that states they will add other viruses in the species/genus dependent on the experiment. This statement should be clarified that new viruses will be added after consultation/approval from the IBC. ▪ Rachel LaCasse was not in attendance, but had informed Sue Priola in advance that she had no questions or concerns with the registration. ▪ No animal studies were proposed, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. Question A6 is correctly marked and question B will be changed from yes to no. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Hideki Ebihara abstained) **RD#14-431** with the following minor modifications: 1. Change question B on the dual use form from yes to no. 2. Update the asterisk statement at the end of the first table to state that new viruses will be added after consultation/approval from the IBC. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-2-a of the NIH Guidelines. Research using eukaryotic cells will be performed at BSL-2 and is approved under Sections III-D-2-a and III-E-1 of the NIH Guidelines.
Item 10:	**Standard Operating Procedure: SOP#4-28-54 Operation of the FACS Canto II (NEW)** ▪ Becky Anderson informed the committee that this SOP was a new SOP for the

	use of a FACS Canto analyzer at BSL-4. ▪ Paul Carlson pointed out that when Aaron Carmody aligns the lasers for maintenance, he will have to wear safety glasses. A statement that refers to the laser safety SOP would be appropriate to include in the box on page 1. Paul Carlson will send a copy of the SOP to Becky Anderson. ▪ Sue Priola questioned if the cells were live or fixed that would be run on the flow cytometer. Becky Anderson clarified that all cells would be treated with 4% paraformaldehyde (PFA) for 20 minutes prior to running on the cytometer. Becky Anderson stated that if they wanted to bring cells out of the BSL-4, they would have to do a fixation step that lasts overnight, which is hard on the fluorochromes and makes it difficult to get clear results on some studies. Sue Priola questioned if 20 minutes is sufficient to inactivate all the viruses used in the BSL-4. Karin Peterson added that they only do a 10 minute fixation step at BSL-2 and that is sufficient. Sue Priola stated that it is important to include the details of how the cells are treated with PFA prior to running them on the FACS Canto II. It also would be beneficial to add any references about the effectiveness of using PFA for enveloped viruses. ▪ Sue Priola also pointed out that 10,000 ml should be changed to 10 Liters in section 6.1.3.4. ▪ There were no additional concerns with the SOP. Action: The committee unanimously approved **SOP#4-28-54 Operation of the FACS Canto II (NEW)** with the following modification: 1. Add a description of the 20 minute treatment of cells with 4% PFA. 2. Add a reference if available that PFA treatment of cells is an effective method to inactivate enveloped viruses. 3. Change 10,000 mls to 10 Liters in section 6.1.3.4.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Nancy Hoe gave annual IBC training. See attached presentation. ▪ Nancy Hoe informed the committee that the CDC Inspection of the BSL-4 in January went very well. There were many positive comments including: great facilities, skilled staff, best training records and Select Agent Plans they have seen, as well as a good occupation health plan and exposure response program. There were a few issues noted in the exit meeting including: a request to submit a form 3 for a couple of incidents after they reviewed our incident reports for releases or exposures, they asked to view security video footage within the BSL-4 labs- NIH has determined they (CDC DSAT) does not have authority to view this and it was not given to DSAT. This footage can only be requested from NIH Police if there is an investigation for criminal activity.

	▪ See attached BSO report. ▪ Nancy Hoe summarized the mouse bite incident that occurred February 14, 2014. The committee agreed that no further action was necessary. See attached incident report submitted to OBA on February 19, 2014. ▪ The Full Length Cloning Lab Report is ready to submit to OBA, this is done on an annual basis. Megan Morgan and Becky Anderson recently performed the inventory check. ▪ Nancy Hoe also informed the committee that PI Dashboard has been upgraded and PI's she see some new and improved features.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ There was a flood in the log cabin at the entrance to campus. The cabin was not winterized so pipes froze and broke. The cabin has now been properly winterized. ▪ Another pipe broke in (b)(6) and sprayed water and caused a false fire alarm. ▪ Recent winter weather has caused several slips and falls outside. ▪ Motor vehicle accidents are up this year, we have already had 5. ▪ Hazmat has 6 new members; they are halfway through their training. ▪ OSHA 300 report has been posted; it lists injuries and illnesses for the previous year.
Report	**IRF Biosafety Manager Report/Megan Morgan** ▪ The annual shutdown for (b)(6) labs will occur March 14-21. ▪ The annual shutdown for (b)(6) labs will occur March 21-28. ▪ Becky Anderson sent out an email to set up a meeting with the BSL-3 PI's for information and planning of the annual shutdown.
Report	**Associate Director Report/Marshall Bloom** ▪ Marshall Bloom acknowledged the time and effort that RML staff put into preparing for the CDC Inspection in January. The inspection seemed to go very well.
Around the room	▪ Nancy Hoe informed the committee that the Office of Biotechnology Activities will be holding a meeting to discuss primary containment for non-human primates at BSL-4. The agenda includes BSL-4 directors nationally and internationally, biosafety and animal welfare experts. The meeting will be open to the public and may even be webcast.

Other issues	None

Next Meeting:

- Date: 3/20/14
- Place: Bldg A Seminar Room
- Time: 1:00 **PM**

RML Biosafety Committee Meeting
February 20, 2014
Biosafety Officer/Responsible Official Report

1) ***Requests approved by BSO since last meeting:***
   a) *Registrations Inactivated*
      i) *Bloom RD 11-423, 11-424*
      ii) *Feldmann RD 08-401*
      iii) *Schwann HPRD 11-122*
      iv) *Gherardini HPRD 05-2, 05-60, 05-65*
   b) *Heinzen BSL-3 SOP*
      i) *Delete individual procedures as no longer used*
         (a) *BSL-3-Cb-1: Use of C. burnetii, Nine Mile strain, phase II, clone 4*
         (b) *BSL-3-Cb-2: Cloning of C. burnetti using micromanipulation*
   c) *DeLeo HPRD-12-124: H1N1 Influenza*
      i) *Add 2 new isolates of H1N1*
2) ***New requests approved by committee via electronic review:***
   a) *None*
3) ***New requests***
   a) *Registration of Material Potentially Infectious for Humans*
      i) ***Renewal***
         (a) *Bloom (LV)*
            (a) ***HPRD-14-58:*** *Langat virus*
            (b) ***HPRD-14-119****: Sindbis virus (storage only)*
      ii) ***New***
         (a) *Bosio (LICP)*
            (a) ***HPRD-14-157****: Listeria monocytogenes*
      iii) ***Amended***
         (a) *Ebihara (LV)*
            (a) ***HPRD-12-123****: Phleboviruses*
               (i) Consolidate Phlebovirus, SFTSV, and Heartland virus HPRDs
         (b) *DeLeo (LHBP)*
            (a) ***HPRD-13-1****: Staphylococcus aureus et al.*
               (i) Add Coxiella burnetii (exempt)

b) *Registration Documents for Recombinant DNA Experiments*

i) ***Renewals***

(a) *Bloom (LV)*

(a) ***RD-14-201:*** *Characterization of Langat virus infection in mammalian and tick cells*

(b) *Gherardini (LZP)*

(a) ***RD-14-319****: The infectious cycle of Borrelia burgdorferi*

(c) *Heinzen (LICP)*

(a) ***RD-14-106****: Genetic transformation of Coxiella burnetii*

(d) *Ebihara (LV)*

(a) ***RD-14-432****: Characterization of Phlebovirus protein functions in the viral life cycle*

c) *Standard Operating Procedures*

i) ***New***

(a) ***SOP-4-28-54: Operation of the FACS Canto II***

ii) ***Updated***

(a) ***SOP-4-28-24: Removal of Animal Tissues from BSL-4***

(i) Update section on responsibilities and fixation of tissues

4) ***Animal Study Protocols Review***

PI	***Title***	***Associated HPRD***	***Associated RD***	***Reviewer***
(b)(6)	*Assessing T-705 as a post-exposure counter-measure to Lassa virus infection in strain 13 guinea pigs*	*13-94 (Lassa)*	*N/A*	*M. Morgan*
	Determining the protective efficacy of passive transfer of antibodies against lethal CCHFV infection in an established murin model	*13-92 (CCHFV) 13-82 (VSV)*	*13-404 (VSV)*	*B. Anderson*
	Intraperitoneal treatment of scrapie infected mice with anakinra	*N/A Hamster and mouse scrapie*	*N/A*	*B. Anderson*
	Convalescent plasma therapy for the treatment of MERS-CoV	*12-143 (MERS-CoV)*	*N/A*	*B. Anderson*
	Nebulized IFN-b as a therapeutic intervention for MERS-CoV in non-human primates	*12-143 (MERS-CoV)*	*N/A*	*M. Morgan*

RML Biosafety Committee Meeting
February 20, 2014
Biosafety Officer/Responsible Official Report

5) ***Biosafety Training Performed – Megan Morgan, Becky Anderson***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
NIH Police PPE training	***2***	***6***
First Responder PPE training	***2***	***7***
BSL-3 Laboratory Biosafety	***1***	***2***
BSL-4 Laboratory Biosafety	***1***	***2***

6) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
   a) *Biological Incident Report:*
      i) *Bite from mouse infected with Borrelia burgdorferi 2-14-14*

7) ***Select Agent Issues***
   a) *Annual Select Agent inspection of the MCL, January 13-16, 2014*

8) ***Other Issues***
   a) *Full-length cloning laboratory annual report to OBA*
   b) *Dr. Ebihara authorization from OBA*
   c) *PI-Dashboard upgrade*

NIH National Institutes of Health
Office of Management

RML IBC ANNUAL TRAINING

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Division of Occupational Health and Safety, NIH
February 20, 2014

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Training Topics

- Organizational Oversight - OBA
- NIH Guidelines
- IBC Roles and Responsibilities
- IBC Functions
- Reviewing rDNA Research
  - Biosafety Levels
  - Determining Appropriate Biosafety Levels
  - Dual Use Screening
  - Major Actions
- Select Agents
  - Restricted Experiments

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NIH Office of Biotechnology Activities (OBA)

- Partner with IBCs in the oversight of rDNA research
- Within the Office of Science Policy, Office of the Director, NIH
- Oversees rDNA research including human gene transfer
- Manage the Recombinant DNA Advisory Committee (RAC)
- Administer the NIH Guidelines for Research Involving Recombinant DNA Molecules

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NIH Guidelines

- First published in 1976
- Last revisions in November, 2013
- Are not optional-they are a term and condition of NIH funding for rDNA research
- Describe experiments that are exempt, require approval by the IBC and/or RAC review and NIH Director approval
- Describe roles and responsibilities for NIH, Institution, IBC, BSO, PI

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IBC Training

NIH Guidelines Section IV-B-1-h:

- The Institution shall…."Ensure appropriate training for the Institutional Biosafety Committee Chair and members…..The Institutional Biosafety Committee Chair is responsible for ensuring that Institutional Biosafety Committee members are appropriately trained."

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IBC Roles and Responsibilities

- Described under Section IV-B-2
- A responsibility of the Institution is to establish an IBC
- IBC responsibilities need not be restricted to oversight and approval of rDNA research
- RML IBC has a written charter that describes its duties, meetings, and membership

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IBC Roles and Responsibilities

IBC Membership

- No fewer than 5 members
- Members must have collective experience and expertise in rDNA technology
- 2 members not affiliated with the institution
- 1 member with plant expertise if reviewing plant research
- 1 member with animal expertise if animal experiments
- A BSO if performing large scale (>10L) or BSL-3 or BSL-4 research
- Adequate expertise in human research if rDNA involving human research participants

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IBC Roles and Responsibilities

IBC Membership

- Recommended members/consultants:
  - Expertise in biosafety, physical containment
  - Knowledge of institutional policies, applicable law
  - 1 member representing the laboratory technical staff

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IBC Roles and Responsibilities

- **When possible, IBCs are encouraged to open their meetings to the public**
- **Upon request, IBCs will make their minutes available to the public**

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IBC Functions

- **Reviewing rDNA research**
- **Notifying PI of the results of IBC review and approval**
- **Lowering containment levels for certain experiments**
- **Periodically reviewing rDNA research (RML IBC: every 2 years)**
- **Adopting emergency plans covering spills and accidents with rDNA**
- **Reporting violations of the Guidelines and any rDNA research accidents or illnesses to OBA**

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RML IBC Functions

- **Review Human Pathogen Registration Forms (HPRD)**
- **Scientists are required to register:**
  - Human pathogens, blood, body fluids, or tissues
  - Non-human primate blood, body fluids or tissues (if personnel not directly associated with an Animal Study Protocol)
  - Toxins
- **Review BSL-3 and BSL-4 SOPs**

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IBC Functions

- **The IBC may not approve experiments involving recombinant DNA not specifically covered by the Guidelines until NIH (via the RAC) establishes the containment requirements**
- **This is why we reference the sections of the Guidelines on all RDs**

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RML IBC RD Review Process

- **Primary and secondary reviewers will be assigned to each rDNA proposal by BSO/ABSO**
  - Voting member
  - RML scientific and/or technical staff
- **At the meeting, the primary reviewer will present a summary of the proposal and preliminary evaluation of the containment levels proposed**
- **The secondary reviewer will add any comments not mentioned by the first reviewer**
- **The entire committee can comment**
- **The BSO can provide any training records or SOPs as appropriate**
- **IBC must approve risk assessment and containment level and agree with final dual use determination**

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Reviewing rDNA Research

In general, the IBC assesses:

- Conformity with the *NIH Guidelines*
- Potential risk to environment and public health
- Dual Use Research of Concern

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Reviewing rDNA Research

Specifically, the IBC assesses:

- The appropriate containment/biosafety levels per *NIH Guidelines*
- Adequacy of facilities, SOPs, PI and lab personnel training
  - RML Biosafety and Safety staff review protocols prior to meetings for completion of training requirements
- Any Dual Use concerns

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Biosafety Levels

- **Guidelines evolved as a means of protecting workers based on data from**
  - Laboratory-acquired infections
  - Understanding of the risks associated with various manipulations of many agents transmissible by different routes



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Biosafety Levels

- **BSL-1: for work with material not known to consistently cause disease in healthy adults.**
  Example: *Staphylococcus epidermidis*
- **BSL-2: for work with agents of moderate potential hazard to personnel and environment.**
  Example: *Borrelia burgdorferi* (Lyme disease)
- **BSL-3: for work with agents which may cause serious or potentially lethal disease as a result of exposure by the inhalation route.**
- **Example: *Yersinia pestis* (plague)**
- **BSL-4: for work with dangerous and exotic agents that pose a high individual risk of aerosol-transmitted lab infections and life-threatening disease.**
  Example: Ebola virus

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Biosafety Levels

- **Each level consists of combinations of:**
  - Laboratory Practices and Techniques
  - Safety Equipment
    - Primary Barriers (e.g. Biosafety Cabinets (BSCs))
    - Personal Protective Equipment (PPE)
  - Laboratory Facilities
    - Secondary Barriers

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Determining Appropriate Biosafety Levels

Perform Risk Assessment

- **Agent Hazards:**
- Assess risk of biological agent, taking into account:
  - Virulence
  - severity of disease
  - availability of effective treatments
  - route of transmission
  - environmental stability
  - infectious dose
  - Concentration
  - availability of information
- How may these be altered by genetic manipulation or the introduction of antibiotic resistance?

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Determining Appropriate Containment Levels

Perform Risk Assessment

- **Laboratory Procedure Hazards**
  - Will it generate aerosols or splashes?
  - How concentrated is the material?
  - Will it involve the use of sharps?
  - What about exposure to zoonotic diseases of experimental animals?
- **Work Practice Hazards**
  - Are staff adequately trained?
  - Any hazards associated with specific equipment?

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References for Containment Determination

- **Appendices of the NIH Guidelines:**
  - **Appendix B** – Classification of Human Etiological Agents on the Basis of Hazard (Risk Groups) – **Updated in November, 2013**
  - **Appendix G**: Physical Containment
  - **Appendix I**: Biological Containment
  - **Appendix K**: Physical Containment for Large Scale Uses of Organisms Containing Recombinant DNA Molecules
  - **Appendix Q**: Physical and Biological Containment for Recombinant DNA Research Involving Animals
- **Other References**
  - CDC and NIH Biosafety in Microbiological and Biomedical Laboratories (BMBL, 5th ed.)
  - American Biological Safety Association (ABSA):Risk Group Classification for Infectious Agents (Research Tools)

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Dual Use Research

- **Definition: "Research that can be reasonably anticipated to provide knowledge, products, or techniques that could be directly misapplied by others to pose a threat to public health, agriculture, plants, animals, the environment, or materiel"**
  - National Science Advisory Board for Biosecurity (NSABB), "Proposed Framework for the Oversight of Dual Use Life Sciences Research: Strategies for Minimizing the Potential Misuse of Research Information", June 2007

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Dual Use Screening Process at NIH



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Dual Use Screening Survey



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Dual-Use Screening Survey for RDs/HPRDs and all associated amendments

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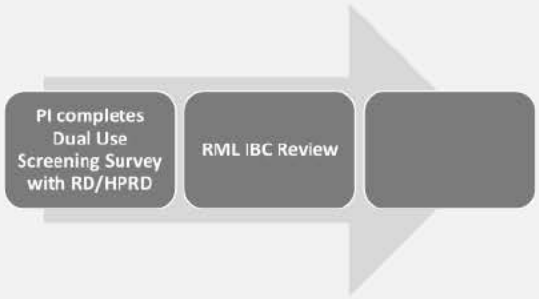
Dual Use Screening Process at NIH



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Dual Use Screening: RML IBC Review

- **IBC evaluates dual use concerns as part of its risk assessment**
- **Meeting discussion provides documented consideration of potential dual use issues at the research proposal stage**
- **If dual use concerns are identified, IBC may table all or part of a proposal pending further review**

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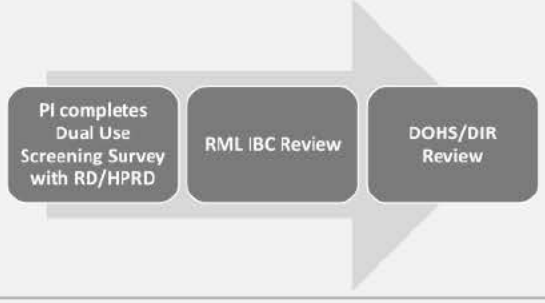
Dual Use Screening Process at NIH



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Dual Use Screening: DOHS/DIR Review

- **If Dual Use concerns identified by the RML IBC, further review by any or all of the following, depending on level of concern:**
  1. Dr. Deborah Wilson, Director DOHS, NIH
  2. Dr. Zoon, Director, DIR, NIAID
  3. Dr. Gottesman, Deputy Director, DIR, NIH
  4. NIH Dual Use Committee

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Major Actions

- **Major Actions are experiments involving rDNA that require review and approval by the RML IBC, the RAC, and the NIH Director prior to initiation**

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Major Actions

- **Section III-A-1**
  - The deliberate transfer of a drug resistance trait to microorganisms that are not known to acquire the trait naturally….if such acquisition could compromise the use of the drug to control disease agents in humans, veterinary medicine, or agriculture, will be reviewed by RAC.

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Criteria

- **A drug is considered to be useful for treatment even if its use is limited to the treatment of a specific patient population (for example, children or immunocompromised individuals), or it is primarily used for treatment outside of the United States (e.g., chloramphenicol)**
- **Even if the drug is not first or second line in the general population of the US it may still have clinical utility and introduction of that drug resistance into an organism may need to be reviewed**

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Major Actions

- **Section III-B-1 of the NIH Guidelines**
  - Deliberate formation of recombinant DNA containing genes for the biosynthesis of toxin molecules lethal for vertebrates at an LD[50] of less than 100 nanograms per kilogram body weight (e.g. microbial toxins such as the botulinum toxins, tetanus toxin, diphtheria toxin, and *Shigella dysenteriae* neurotoxin).

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Major Actions - Procedure

- **PI submits proposal to RML IBC for review**
- **IBC will make determination for RAC review, cannot approve protocol at this stage**
- **In general, justification for the use of ANY antibiotic resistance gene in an organism must be included in the rDNA protocol. References and complete vector maps must be provided.**

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NIH Recombinant DNA Advisory Committee (RAC)

- **Federal advisory committee providing advice and recommendations to the NIH Director regarding rDNA research**
- **Reviews and provides recommendations for experiments that qualify as Major Actions under the NIH Guidelines**
- **Reviews and analyzes clinical gene transfer protocols and safety information**
- **RAC review is NOT an approval process**

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Non-compliance

- **Section I-D**
  - Information concerning noncompliance with the NIH Guidelines may be brought forward by any person. It should be delivered to both NIH/OBA and the relevant institution
  - The institution, generally through the IBC, shall take appropriate action.

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Select Agents

The Centers for Disease Control and Prevention (CDC), HHS, and the Animal and Plant Health Inspection Service (APHIS), USDA, are required to regulate the possession of biological agents and toxins that have the potential to pose a severe threat to public health and safety.

Website: www.selectagents.gov

What are considered Select Agents?

- Bacteria, viruses, fungi, prion agent, and toxins listed on handout
- Any of the listed agents that have been genetically modified
- Nucleic acids that can produce infectious forms of any of the select agent viruses listed (e.g. purified RNA genome from Tick-borne encephalitis virus)
- Recombinant nucleic acids that encode for the functional form(s)of any of the toxins listed if the nucleic acids can be expressed in vivo or in vitro
- any animal infected with a Select Agent (daily census must be kept)

What are NOT Considered Select Agents?

- Any select agent or toxin that is in its naturally occurring environment provided the select agent or toxin has not been intentionally introduced, cultivated, collected, or otherwise extracted from its natural source (e.g. wild sheep infected with *Coxiella burnetii*)
- Non-viable select agents or nonfunctional toxins
- Certain amounts of select agent toxins (e.g. less than 0.5 mg of Botulinum neurotoxins)- see handout

What are NOT Considered Select Agents?

- Specific attenuated strains of select agents (e.g. *Yersinia pestis* strains lacking the 75kb virulence plasmid) – list of current exclusions included in handout
  - Restoration of virulence to an excluded strain creates a Select Agent that must be regulated as such

Restricted Experiments

- Restricted Experiments are experiments with Select Agents that require authorization from the CDC Division of Select Agents and Toxins (via the ISATTAC*), and the RML IBC prior to initiation

*Intragovernmental Select Agents and Toxins Technical Advisory Committee

Restricted Experiments

- Definition used in CDC/USDA Select Agent regulations (42 CFR, § 73.13)
  - "Experiments utilizing recombinant DNA that involve the deliberate transfer of a drug resistance trait to select agents that are not known to acquire the trait naturally, if such acquisition could compromise the use of the drug to control disease agents in humans, veterinary medicine, or agriculture"
  - Experiments involving the deliberate formation of recombinant DNA containing genes for the biosynthesis of select toxins lethal for vertebrates at an LD[50] <100ng/kg body weight.

Select Agents: Antibiotic Resistance

- Approval for the introduction of any antibiotic resistance gene into a Select Agent (even if an intermediate in construction of final strain) requires the approval of:
  - The RML Institutional Biosafety Committee (IBC)

    AND
  - The CDC Division of Select Agents and Toxins
- Introduction of any antibiotic resistance that is not approved is a violation of both the NIH Guidelines for rDNA Research and the Select Agent regulations!

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Select Agents: Non-compliance

- **Regarding Restricted Experiments**
  - "The HHS Secretary my revoke approval to conduct any of the experiments in paragraph (b) of this section, or revoke or suspend a certificate of registration, if the individual or entity fails to comply with the requirements of this part."

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Any Questions?

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Template for Reporting Incidents Related to Research Subject to the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acids* to the National Institutes of Health (NIH) Office of Biotechnology Activities (OBA)

The *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules* (*NIH Guidelines*) states that "...any significant problems, violations of the *NIH Guidelines*, or any significant research-related accidents and illnesses" must be reported to NIH OBA within 30 days. Certain types of incidents must be reported on a more expedited basis. Spills or accidents occurring in Biosafety Level (BL) 2 laboratories resulting in an overt exposure must be immediately reported to NIH OBA. Spills or accidents occurring in high containment (BL3 or BL4) laboratories resulting in an overt or potential exposure must be immediately reported to NIH OBA.

This template is intended to facilitate the reporting of incidents that occur during the conduct of research subject to the *NIH Guidelines*. This template is also available on the NIH OBA Web pages as a Word document (http://oba.od.nih.gov/oba/ibc/FAQs/Incident_Reporting_Template.doc) in which the fields will expand according to the amount of text entered. Use of this template is not required and other formats for submitting reports may be acceptable.

A separate template for reporting Human Gene Transfer Adverse Events is available at: http://oba.od.nih.gov/oba/rac/Adverse_Event_Template.pdf

Please note that submitting this completed template to NIH OBA does NOT fulfill the reporting requirements of other agencies. You should verify with the other parties to whom you must report whether the use of this template is acceptable.

Completed reports may be sent via U.S. mail, courier service, e-mail, or facsimile to:

Attention: Incident Reports
NIH Office of Biotechnology Activities
6705 Rockledge Drive, Suite 750
Bethesda, Maryland 20892-7985
(For all non-USPS deliveries use Zip Code 20817)
Telephone 301-496-9838
Fax 301-496-9839
E-mail: oba@od.nih.gov

NIH OBA Incident Reporting Template

For reporting Human Gene Transfer Adverse Events a separate template is available at:
http://oba.od.nih.gov/oba/rac/Adverse_Event_Template.pdf

Does this incident involve research subject to the *NIH Guidelines*?	X **YES** NO If no, this incident does not have to be reported to OBA
Institution name:	Rocky Mountain Laboratories/ National Institutes of Health
Date of report:	2/19/14
Reporter name and position:	Nancy P. Hoe, Biosafety Officer
Reporter telephone:	406-363-9334
Reporter email:	nhoe@mail.nih.gov
Reporter mailing address:	903 S. 4th Street Hamilton, MT 59840
Date of incident:	2/14/14
Is this an NIH funded project?	X YES NO
If yes, please provide:	NIH grant or contract number: not applicable
	NIH funding institute or center: Division of Intramural Research, NIAID
	NIH program officer contact information (name, email etc): not applicable
What was the **nature** of incident?	X Personnel exposure Spill Loss of containment Loss of transgenic animal Failure to obtain IBC approval Failure to follow approved containment conditions Other - please describe:

Did the Institutional Biosafety Committee (IBC) approve this research	☐ **YES** ☐ If yes, on what date? 4/20/12
If yes, please provide:	Approval date: 4/20/12
	Approved biosafety level(s) for the research: BSL-2/ABSL-2
	Additional approval requirements: None
What section(s) of the *NIH Guidelines* is the research subject to?	III-D-1-a, III-D-2-a
Has a report of this incident been made to other federal or local agencies? If so please indicate by checking the appropriate box.	☐ CDC ☐ USDA ☐ FDA ☐ EPA **NOT APPLICABLE** ☐ OSHA ☐ Research Funding Agency/Sponsor: (name)_____ ☐ State/Local Public Health ☐ Federal/State/Local Law Enforcement ☐ Other – please describe:
Description of recombinant or synthetic agent or material involved (please indicate strain, attenuation etc. as relevant.)	The mouse that bit the employee was co-infected with a wild type strain of *Borrelia burgdorferi* and a recombinant strain of *Borrelia burgdorferi* called delta BB203. The wild-type version of the interrupted gene is predicted to be a Lambda CII stability-governing protein.

Please provide a narrative of the incident including a timeline of events. The incident should be described in sufficient detail to allow for an understanding of the nature and consequences of the incident. **Include the following information as applicable.**

A description of:

- The incident/violation location (e.g. laboratory biosafety level, vivarium, non-laboratory space).
- Who was involved in the incident/violation, including others present at the incident location? **Note – please do not identify individuals by name. Provide only gender and position titles (e.g., graduate student, post doc, animal care worker, facility maintenance worker)**.
- Actions taken immediately following the incident/violation, and by whom, to limit any health or environmental consequences of the event.
- The training received by the individual(s) involved and the date(s) the training was conducted.
- The institutional or laboratory standard operating procedures (SOPs) for the research and whether there was any deviation from these SOPS at the time of the incident/violation.
- Any deviation from the IBC approved containment level or other IBC approval conditions at the time of the incident/violation.
- The personal protective equipment in use at the time of the incident/violation.
- The occupational health requirements for laboratory personnel involved in the research.
- Any medical advice/treatment/surveillance provided or recommended after the incident.
- Any injury or illness associated with the incident.
- Medical surveillance results (if not available at the time of initial report please indicate when results will be available).
- Equipment failures.

DESCRIPTION OF INCIDENT: (use additional space as necessary)

At approximately noon on Friday 2/14/14, a post-doctoral fellow was working alone and handling a mouse co-infected with wild type and a recombinant strain of *Borrelia burgdorferi* in the ABSL-2 animal facility. The employee was wearing a lab coat, latex gloves, and a surgical mask. She had a cage of 5 mice and was transferring mice to a bell jar. The employee had marked the tails of the mice for the experiment to track individual mice and was grabbing each mouse by the tail, one at a time. The employee picked up one mouse by the tail and was holding it up out of the cage while looking for another mouse to grab when the one in her hand curled up and bit her on the thumb of her right hand. She placed the

mouse back in the cage, secured the cage, removed her latex glove and expressed the wound and washed it with soap and water.

The employee then reported the incident to the Principal Investigator and to the RML Occupation Medical Services (OMS) at approximately 12:20pm. OMS applied a topical antibiotic ointment to the wound. No oral antibiotics were given as OMS determined it to be a low risk exposure. The risk was assessed and determined in consultation with the Principal Investigator. This decision was based on the fact that there is no evidence that *Borrelia burgdorferi* is secreted through mouse saliva; instead, it is found in tissues such as the joints, skin, and bladder. The employee was given contact information to report over the weekend if there were any signs or symptoms of illness or infection and a follow-up visit with OMS was scheduled for 2/18/14. OMS contacted the Biosafety Officer at 12:45 pm 2/14/14 of the incident. A summary of the incident was taken at that time. The employee left early that day due to other commitments and was not available for immediate debriefing. The employee met with the RML Associate Biosafety Officer on 2-19-14.

The occupational health requirements for employees working at BSL-2 are a pre-placement medical evaluation that includes informing the employee to report all occupational injuries/illnesses to their supervisor and OMS. The employee has not exhibited any signs of infection since the incident. OBA will be notified immediately if the employee exhibits any signs or symptoms of infection or if they receive any additional medical treatment.

Notifications made after the incident included the Principal Investigator, the Laboratory Chief, the RML Associate Director, the Director, Division of Occupational Health and Safety, the Chairperson of the RML IBC and the Senior Veterinary Officer, RML, DIR.

The employee has been at RML for a little over a year. She received initial health and safety training on 1/7/13 and emergency evacuation training on 7/15/13.

An incident report will be reviewed by the Rocky Mountain Laboratories IBC on 2/20/14.

Has the IBC reviewed this incident?	□ YES x□ NO If yes, please provide a copy the minutes of the IBC meeting in which the incident was reviewed. The RML IBC will review the incident on 2/20/14. Minutes from the meeting will be provided once they are finalized at the 3/20/14 IBC meeting.
Has a root cause for this incident been identified?	x□ YES □ NO If yes please describe: The employee was distracted while handling the mouse. They have been reminded of proper mouse handling techniques.
Describe measures taken by the institution to mitigate any problems identified. For measures identified but not yet taken, please include a timeline for their implementation: (use additional space as necessary) This is a specific incident. The employee was distracted while handling the mice. She has been advised of proper handling of animals.	

- **Please provide copies of any documents referenced in this report.**
- **Additional information may be requested by OBA after review of this report depending on the nature of the incident.**

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 3/20/14
Meeting Time: 1:01 PM **Adjourned:** 1:53 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Paul Carlson	☒	☐	Kevin Mora	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Megan Morgan	☒	☐
Becky Anderson (EO)	☒	☐	Frank DeLeo (EO)	☐	☒	Karin Peterson	☒	☐
Alan Applebury	☒	☐	Hideki Ebihara	☒	☐	George Risi	☒	☐
Chris Bosio	☒	☐	Heinz Feldmann (EO)	☐	☒	Dana Scott	☐	☒
Marshall Bloom (EO)	☒	☐	Nancy Hoe	☒	☐	Alexandra Scranton	☐	☒
Teresa Borino	☒	☐	Clay Jarrett	☒	☐			
Jeff Burrows	☒	☐	Josh Kellar (EO)	☐	☒			
Carol Calderwood	☐	☒	Scott Kobayashi	☒	☐			
Harlan Caldwell (EO)	☐	☒	Rachel LaCasse	☐	☒			
Marcie Caldwell (EO)	☒	☐	Alida Merritt	☒	☐			

(P=present; A=absent)

Guests: (b)(6)

Minutes: Meeting minutes from 2/20/14 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** Action: Meeting minutes were unanimously approved with the following minor modifications: ▪ Alida Merritt pointed out that she was present at the last meeting and Carol Calderwood was not. ▪ Bob Heinzen noted that in Item 1 on the Bloom RD for Langat virus, the following statement was confusing, "incidence of disease with Langat virus is extremely low; there are no registered cases of human disease." If there are no registered cases, how can incidence be low? Marshall Bloom replied that there are no natural cases registered, but the administration of an attenuated vaccine strain did cause a low incidence of disease. The minutes will be updated to state that there are no "naturally occurring cases". ▪ On page 4, in the description of containment requirements, "assure" in the third sentence should be changed to "ensure".

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans (Amendment) ▪ Peterson (LPVD) ▪ **HPRD#12-103 Amend**: La Crosse Virus (LACV) ▪ Becky Anderson presented the risk assessment. The amendment is to add animal work with non-human primates. La Crosse virus infects many people that end up having no apparent symptoms. Among people who become ill, initial symptoms include fever, headache, nausea, vomiting, and tiredness. Some of those who become ill develop severe neuroinvasive disease (disease that affects the nervous system). Severe LACV disease often involves encephalitis and can include seizures, coma, and paralysis. Severe disease most often occurs in children under the age of 16. In rare cases, long term disability or death can result from La Crosse encephalitis. The case fatality rate is <1%. The natural route of transmission is through a single bite of an infected mosquito. The primary laboratory hazards include sharps injuries, generation of aerosols or splashes and parenteral inoculation. ▪ The committee discussed the containment requirements. BSL-2/ABSL-2 is appropriate for studies with La Crosse virus. The lab is posted that no children under 16 are allowed to enter, (b)(6) should be posted the same; this is where the animals will be housed. The ASP appropriately states that safety glasses or goggles will be worn when performing procedures on non-human primates on tables in (b)(6) ▪ Animal work with non-human primates was proposed. ▪ Nancy Hoe added that OMS should be contacted for all personnel that will be working with non-human primates. Karin Peterson stated that they had already been informed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Karin Peterson abstained) **HPRD#12-103 Amend** as written.
Item 2:	Registration Documents for Recombinant DNA Experiments (New) ▪ Peterson (LPVD)

	▪ **RD#14-221**: ▪ Reviewers: Rachel LaCasse, Sue Priola ▪ **Summary:** The RD describes using lentiviral particles that encode recombinant DNA for specific proteins or protein motifs or shRNA targeting transcripts of these genes. ▪ Rachel LaCasse was not present; Sue Priola read a summary from Rachel LaCasse. This RD is focused on investigating innate immune mediators by producing recombinant lentiviral particles encoding shRNA directed against their transcripts or encoding intact or truncated cDNA homologous to their genes. They will specifically investigate SARM1 to test its effect on viral replication of LaCrosse virus. They will use either plasmid transfer vectors or lentiviral particles obtained from another investigator or from commercial sources. The HIV based lentiviral systems now being used have multiple safety features including separating genes onto different plasmids that cannot regenerate full virus, instead they replicate one time and produce replication incompetent virus. Rachel LaCasse had no dual use or overall concerns. ▪ Sue Priola pointed out that the description section on page 1 was a little confusing as far as what was being obtained from other investigators and what was coming from commercial sources. She spoke with Karin Peterson before the meeting and clarified that these viruses will either be created in the lab or acquired from commercial sources. Sue Priola also pointed out that in the same section, Invitrogen should be changed to ThermoScientific. ▪ Sue Priola noted that the safety features of the lentiviral systems were discussed at the end of the Vector Plasmid DNA/Virus Section within the Prokaryotic host section. The other 3 plasmid lentiviral system described is depicted in Figure 1, that reference should be added to the last sentence in the last paragraph of that section. ▪ Sue Priola informed the committee that III-E-1 of the NIH Guidelines should also be added to both the Prokaryotic Host section and the Eukaryotic Host section. ▪ No animal studies were proposed, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved (Karin Peterson abstained) **RD#14-221** with the following minor modifications: 1. Clarify the description section of the Synopsis on page 1 to state that these viruses will be either created in the lab or acquired from commercial sources. 2. Add the reference to Figure 1 in the last sentence in the last paragraph of the Vector Plasmid DNA/Virus section of the Prokaryotic host section. 3. Add III-E-1 of the NIH Guidelines to both the Prokaryotic Host section and the

	Eukaryotic Host section. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-2-a and III-E-1 of the NIH Guidelines. Research using eukaryotic cells will be performed at BSL-2 and is approved under Sections III-D-2-a and III-E-1 of the NIH Guidelines.
Item 3:	<u>Registration Documents for Recombinant DNA Experiments (Amendment)</u> ▪ Peterson (LPVD) ▪ **RD#13-214 Amend**: ▪ Reviewers: Sue Priola, Hideki Ebihara ▪ **Summary:** The amendment is to add two additional constructs to the proposal. ▪ Sue Priola summarized the registration. The original RD describes examining the impact of specific amino acid residues in the envelope of polytropic murine leukemia viruses. Chimeric viruses will be used to further determine residues that contribute to pathogenesis. The amendment to this RD is to add two constructs, Fr98 with a red fluorescent protein tag and FMuLV57 that has a green fluorescent protein tag. Both of these constructs are risk group 1 viruses because they are mouse pathogens, BSL-1 is the appropriate listed biosafety level. Sue Priola did not identify any dual use concerns and the NIH Guidelines are appropriate. Animal studies attached to the original RD will still be conducted at ABSL-2, because the RML animal facility is ABSL-2. ▪ Hideki Ebihara had no additional comments or concerns. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved (Karin Peterson abstained) **RD#13-214 Amend** as written. Research using prokaryotic hosts is approved at BSL-1 under Appendix C-II of the NIH Guidelines. Research using eukaryotic cells will be performed at BSL-1 and is approved under Sections III-D-1-a of the NIH Guidelines. Animal experiments are approved at ABSL-2.
Item 4:	<u>Registration Documents for Recombinant DNA Experiments (New)</u> ▪ Steele-Mortimer (LICP) ▪ **RD#14-126**: Recombinant attenuated Salmonella Typhimurium vaccine (RASV) for breast cancer. ▪ Reviewers: Scott Kobayashi, Chris Bosio ▪ **Summary:** Recombinant attenuated Salmonella Typhimurium vaccine is a vaccine that can be delivered orally and will be tested as a platform for breast cancer treatment.

	▪ Scott Kobayashi summarized the registration. This is a very detailed RD that describes using an attenuated S. typhimurium vaccine strain to deliver polyoma middle T oncogene and express it in mammalian host cells. The goal is to direct this against breast cancers. Two RASV strains have been developed, one carries a plasmid that allows Salmonella to express the antigen, and the other allows the mammalian host cell to express the antigen. The vaccine strain (RASV) is attenuated by several means described in the RD. The strain lyses in the host and only goes through a few rounds of division inside the host cell. Scott Kobayashi added that this is a unique system in that they do not use antibiotic resistance for selection; instead they utilize a plasmid retention system whereby an essential gene is deleted from the chromosome of the Salmonella and added to the multi-copy expression plasmid. Loss of the plasmid would result in a non-viable carrier vaccine. ▪ Scott Kobayashi thought the NIH Guidelines listed were appropriate and did not identify any dual use concerns. ▪ Chris Bosio pointed out that there was a redundant insertion in the Prokaryotic Host Section, Vector Plasmid DNA/Virus section. The redundancy can be deleted. Chris Bosio did not have any additional comments or concerns. ▪ Sue Priola pointed out that inserting an oncogene (Polyoma middle T antigen) can make cells cancerous but this one is inactivated so it is not a biosafety concern. ▪ Sue Priola also added that the base plasmid, pVAX does encode for kanamycin even though they do not use it for selection in this RD. Kanamycin is not used for treatment of Salmonella so it is fine if it is in the pVAX backbone. ▪ George Risi asked if the RASV could even replicate. Typically they do not treat people with Salmonella infections clinically, but it may be necessary if someone is immunocompromised. It would be useful if the RD included information on the antibiotic sensitivity of the strain listed in the RD. ▪ No animal studies were proposed, reviewed, or approved. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved **RD#14-126** with the following minor modifications: 1. Delete the redundant insertion in the Prokaryotic Host Section, Vector Plasmid DNA/Virus section. 2. Add the antibiotic sensitivity of the RASV strain to the BSO recommendations section. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-1-a of the NIH Guidelines. Research using eukaryotic cells will be performed at BSL-2 and

	is approved under Sections III-D-1-a of the NIH Guidelines.
Item 5:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Steele-Mortimer (LICP) ▪ **RD#12-108 Amend**: Salmonella-host cell interactions ▪ Reviewers: Dana Scott, Clay Jarrett ▪ **Summary:** The amendment is to add animal studies with mice. ▪ Dana Scott was not present so Clay Jarrett summarized the registration. The amendment is to add mice to the registration as they want to understand how Salmonella typhimurium crosses the blood brain barrier in neuroinvasive disease. They hypothesize that younger mice may be more susceptible and will be comparing weanlings to adult mice. This work will be performed in (b)(6) (b)(6) Clay Jarrett did not identify any dual use concerns and all the vector maps and antibiotics utilized were provided and remained unchanged from the original RD. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved **RD#12-108 Amend** as written. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-2-a and III-D-1-a of the NIH Guidelines. Research using eukaryotic cells will be performed at BSL-2 and is approved under Sections III-D-1-a of the NIH Guidelines. Animal studies with mice are approved at ABSL-2.
Item 10:	**Standard Operating Procedure: SOP#3-28-8 Removal of Specimens for Irradiator (NEW)** ▪ Sue Priola informed the committee that this SOP was a new SOP for the (b)(6) BSL-3 located in (b)(6) This SOP will be added to the (b)(6) OSP. ▪ Clay Jarrett asked why and when would specimens be stored at -80C for larger doses of irradiation. Is it because the sample is larger, and how would it be determined if a larger dose was needed. (b)(6) answered that stock viruses would use the highest dose to inactivate them, while serum samples from animals that recovered from infection could use lower doses. The doses were not specified because they wanted flexibility for the different types of samples. The doses are determined through previous experience and are

	approved through Heinz Feldmann. ▪ Nancy Hoe stated that some of this wording should be added to the SOP. Karin Peterson suggested adding the statement that "if larger doses are needed, as determined by the Chief Scientist of the MCL . . . ". The committee agreed that wording should be sufficient and could be added to 5.10. ▪ Paul Carlson added that Section 4.0 Equipment should be specific for the Class II biosafety cabinet and should read, "Class II, Type A2 BSC." ▪ There were no additional concerns with the SOP. Action: The committee unanimously approved **SOP#3-28-8 Removal of Specimens for Irradiator (NEW)** with the following modification: 1. Add the statement to section 5.10, "if larger doses are needed, as determined by the Chief Scientist of the MCL . . . " 2. In Section 4.0, change Class II BSC to Class II, Type A2.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ See attached BSO report. ▪ Nancy Hoe informed the committee that she had received a close-out letter from OBA regarding the mouse bite an employee received from an animal infected with recombinant *Borrelia burgdorferi.*
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ There are lots of construction activities going on now, so employees are reminded to pay attention when walking and driving on campus.
Report	**IRF Biosafety Manager Report/Megan Morgan** ▪ The BSL-4 (b)(6) annual shutdown is now underway. ▪ The annual shutdown for (b)(6) labs is nearly finished this week. ▪ The annual shutdown for (b)(6) labs will occur next week, March 21-28. ▪ SEA will be onsite April 7-11 for annual testing of (b)(6)
Report	**Associate Director Report/Marshall Bloom** ▪ Marshall Bloom is working with the OMS Nurses to determine why the individual that received the mouse bite with *Borrelia burgdorferi* was not enrolled in the animal exposure surveillance program. This person was also not included on the animal study proposal. They are working out a process to fix the problem.

Around the room	▪ None

Other issues	▪ None

Next Meeting:

- Date: 4/17/14
- Place: Bldg A Seminar Room
- Time: 1:00 PM

RML Biosafety Committee Meeting
March 20, 2014
Biosafety Officer/Responsible Official Report

1) ***Requests approved by BSO since last meeting:***
    i) *None*
2) ***New requests approved by committee via electronic review:***
    a) *None*
3) ***New requests***
    a) *Registration of Material Potentially Infectious for Humans*
        i) ***Amend***
            (a) *Peterson (LPVD)*
                (a) ***HPRD-12-103:*** *La Cross Virus Pathogenesis*
                    (i) Add cynomologus macaques as an animal model
    b) *Registration Documents for Recombinant DNA Experiments*
        i) ***New***
            (a) *Peterson (LPVD)*
                (a) ***RD-14-221:*** *Use of lentiviral vector transduction of small hairpin RNAs (shRNA) and cDNAs to examine mechanisms of La Crosse Virus infection and cell death*
            (b) *Steele-Mortimer (LICP)*
                (a) ***RD-14-126****: Salmonella cancer vaccine*
        ii) ***Amend***
            (a) *Peterson (LPVD)*
                (a) ***RD-13-214:*** *Recombinant polytropic retroviruses*
                    (i) Addition of 2 constructs: F57-GFP, Fr98-RFP
            (b) *Steele-Mortimer (LICP)*
                (a) ***RD-12-108****: Salmonella-host cell interactions*
                    (i) Addition of mouse studies
    c) *Standard Operating Procedures*
        i) ***New***
            (a) ***SOP-3-28-8:*** *Removal of specimens for Irradiation*

RML Biosafety Committee Meeting
March 20, 2014
Biosafety Officer/Responsible Official Report

4) ***Animal Study Protocols Review***

PI	Title	Associated HPRD	Associated RD	Reviewer
(b)(6)	*Identification of requirements for protective immunity against tularemia in mice*	*13-73 (LVS)*	*N/A*	*N. Hoe*
	Competence of Borrelia burgdorferi variants in the mouse/tick infection cycle	*12-24 (B. burgdorferi)*	*12-308*	*N. Hoe*
	Enhancement of HIV infection in TKO BLT mice	*12-104 (HBBF) 12-55 (HIV)*	*N/A*	*N. Hoe*
	Establishment of latent HIV infection in TKO BLT mice	*12-104 (HBBF) 12-55 (HIV)*	*N/A*	*N. Hoe*
	Temporal analysis of Lassa virus infection and transmission in mastomys natalensis	*13-94 (Lassa virus)*	*N/A*	*B. Anderson*
	Assessment of Spike SynCon DNA vaccine for sever Middle East Respiratory syndrome coronavirus in NHPs	*12-143 (MERS)*	*N/A*	*M. Morgan*
	Defining the effect of unique host genetic backgrounds in mouse-adapted and wild type Zaire Ebolavirus pathogenesis in mice	*13-90 (Ebolavirus)*	*N/A*	*B. Anderson*
	The role of Arterivirus (PRRSV) co-infection in the pathogenesis of Reston ebolavirus	*13-90 (Ebolavirus)*	*N/A*	*M. Morgan*

5) ***Biosafety Training Performed – Megan Morgan, Becky Anderson***

Type of Training	Number of Sessions	Number of Employees Trained
New Security Guard	***1***	***4***
BSL-3 Visitor Training	***2***	***6***
Full Length Clone Lab Refresher	***1***	***12***
Select Agent Initial	***1***	***2***
BSL-3 Laboratory Biosafety	***1***	***2***
BSL-4 Laboratory Biosafety	***1***	***1***

6) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
   a) *Biological Incident Report:*
      i) *None*

7) ***Select Agent Issues***
   a) *None*

8) ***Other Issues***
   a) *OBA closeout of incident "bite from mouse infected with Borrelia burgdorferi 2-14-14"*

National Institutes of Health

U.S. Public Health Service
Bethesda, Maryland 20892

Office of Biotechnology Activities
National Institutes of Health
6705 Rockledge Drive
Suite 750, MSC 7985
Bethesda, MD 20892-7985
(301) 496-9838 (Phone)
(301) 496-9839 (Fax)
http://oba.od.nih.gov/

February 28, 2014

Nancy Hoe, Ph.D., CBSP
Biosafety Officer
Rocky Mountain Laboratories
903 S. 4th Street
Hamilton, MT 59840

Dear Dr. Hoe:

Thank you for your February 19, 2014, correspondence to the National Institutes of Health (NIH) Office of Biotechnology Activities (OBA) describing a February 14, 2014, incident in which a Rocky Mountain Laboratories (RML) researcher was bitten by a mouse that had previously been co-infected with a wild type and a recombinant strain of *Borrelia burgdorferi*.

According to your report, the researcher was in the process of transferring a mouse from its cage to a bell jar when the mouse curled up and bit her on the right hand. Immediately following this incident, the researcher placed the mouse back in its cage, removed her gloves, and washed the wound site with soap and water. The researcher then reported this incident to the laboratory principal investigator and sought medical attention at the RML Occupational Medical Services (OMS). After evaluation, the OMS staff provided a topical antibiotic cream to the researcher. Oral antibiotics were not deemed necessary based on the fact that there is no evidence *Borrelia burgdorferi* is secreted through mouse saliva. To date, the researcher has not shown any symptoms of infection.

In response to this incident, the researcher will be retrained on appropriate animal handling techniques. The RML response to this incident appears appropriate. No further information is requested at this time. Please contact OBA staff by email at oba@od.nih.gov or by telephone at (301) 496-9838 if you have any questions.

Sincerely,

Jacqueline Corrigan-Curay, J.D., M.D.
Acting Director
Office of Biotechnology Activities

Cc: Marshall Bloom, M.D., Associate Director for Science Management, RML
Sue Priola, Ph.D., IBC Chair, RML
RADM Deborah Wilson, Dr. P.H., Director, Division of Occupational Health and Safety, NIH
Amy P. Patterson, M.D., Associate Director for Science Policy, NIH
Allan C. Shipp, Director of Outreach, Office of Biotechnology Activities, NIH
Ryan Bayha, Senior Analyst for Science Policy Outreach, Office of Biotechnology Activities, NIH
Kathryn Harris, Ph.D., RBP, Senior Outreach and Education Specialist (contractor),
Office of Biotechnology Activities, NIH

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 4/17/14
Meeting Time: 1:03 PM **Adjourned:** 1:58 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Paul Carlson	☐	☒	Kevin Mora	☐	☒
Bob Heinzen, Vice Chair	☐	☒	Bruce Chesebro (EO)	☐	☒	Megan Morgan	☐	☒
Becky Anderson (EO)	☒	☐	Frank DeLeo (EO)	☐	☒	Karin Peterson	☒	☐
Alan Applebury	☐	☒	Hideki Ebihara	☒	☐	George Risi	☒	☐
Chris Bosio	☒	☐	Heinz Feldmann (EO)	☐	☒	Dana Scott	☐	☒
Marshall Bloom (EO)	☒	☐	Nancy Hoe	☒	☐	Alexandra Scranton	☐	☒
Teresa Borino	☒	☐	Clay Jarrett	☒	☐			
Jeff Burrows	☐	☒	Josh Kellar (EO)	☐	☒			
Carol Calderwood	☒	☐	Scott Kobayashi	☒	☐			
Harlan Caldwell (EO)	☐	☒	Rachel LaCasse	☒	☐			
Marcie Caldwell (EO)	☒	☐	Alida Merritt	☒	☐			

(P=present; A=absent)

Guests (b)(6)

Minutes: Meeting minutes from 4/17/14 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** Action: Meeting minutes were unanimously approved with the following minor modifications: ▪ Minor typos, recorded by Sue Priola.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans (NEW) ▪ Feldmann (LV) ▪ **HPRD#14-158:** Field Samples ▪ Becky Anderson presented the risk assessment. The proposed studies are to

	obtain and manipulate field samples from various field study sites and from various animal species for assessment of the presence of viruses of interest. Dr. Feldmann submitted an HPRD to cover the collection of field samples; this HPRD has an ASP attached that describes the animal species that will be sampled and sample types to be collected. The HPRD does not describe handling of samples at RML. Dr. Feldmann will be submitting an SOP at a later date to the IBC for review to work with the samples. It is recommended that the HPRD be approved for "storage only" until the IBC can review and approve the field sample SOP. The samples that are proposed include: swabs of mucosal surfaces, blood collection, feces and urine collection, ectoparasite collection, and tissue collection of animals already undergoing necropsy. These may be collected from animals such as: horse, donkey, mule, bovine, goat, sheep, swine, camel, llama, alpaca, deer, rabbit, chicken, duck, goose, turkey, asst. poultry, dog, and cat. The locations that these samples will be collected from are unspecified and likely worldwide, but more specifically they will be from field sites, vet clinics, and sales markets. The risks of collecting these samples include: exposure to potentially infectious material, hazards from splashes, accidental sharps injuries, some aerosol generation, and parenteral inoculation. The PPE listed in the HPRD is minimal and should be expanded to at a minimum include: gloves, mucosal protection (e.g. eye protection, face shield, face mask) and disposable clothing such as apron, Tyvek gown, scrubs, dedicated outer wear, etc. ▪ Becky Anderson also stated that appropriate permits need to be obtained for the samples. Permits for obtaining the samples may be required from Fish and Wildlife in the US or from the Convention on International Trade in Endangered Species (CITES). Permits will also need to be obtained to import the samples into the US. These may include USDA and CDC Import permits. For detailed information, the QPSO office can be contacted. This should be added to the recommendations section. ▪ (b)(6) commented that the animal study is for collection from domestic animals, most of the time the animals will not be showing signs of disease. They want minimal PPE to use at their discretion so they do not scare native people, especially when working in foreign countries. Sue Priola and Becky Anderson commented that the PPE choices offer some flexibility that would allow them to still fit in with the culture. For example coveralls could be worn in western Montana where, dedicated field clothes (like jeans and a shirt) could be worn in other regions. The idea is that the clothes are dedicated to field work only and changed when work is complete. ▪ The committee discussed the containment requirements for handling samples when they are brought back to RML. It was discussed that this will be covered in more detail when the SOP is submitted to the IBC committee in the future. Briefly, there is a dedicated room adjacent to BSL-4 that employees will handle samples at BSL-2, with BSL-3 practices.

	▪ Alida Merritt asked if personnel that collect field samples are given the rabies vaccine and should that be added to the HPRD. Marcie Caldwell stated that employees that go out to perform field work visit OMS and are offered vaccines that include rabies vaccine. ▪ George Risi stated that the HPRD mentions handling the samples, but it is not really relevant until the SOP is approved. Nancy Hoe stated, that is correct, the handling of samples will be covered with the SOP and it is alright for the wording to remain as is because the HPRD is for storage only. ▪ An animal study proposal is attached for the collection of samples from animals. No animal work is proposed with material that is collected from the field samples. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **HPRD#14-158 FOR STORAGE ONLY** with the following minor modifications: 1. Update the PPE listed in the HPRD to state: PPE at a minimum should include: gloves, mucosal protection (e.g. eye protection, face shield, face mask) and disposable clothing such as apron, Tyvek gown, scrubs, dedicated outer wear, etc. 2. Add to the recommendations section information about permits
Item 2:	<u>Registration of Material (Potentially) Infectious for Humans (NEW)</u> ▪ Feldmann (LV) ▪ **HPRD#14-159:** Modified Vaccinia Ankara (MVA) ▪ Becky Anderson presented the risk assessment. The MVA strain will be used to infect cells in comparison with recombinant MVA vaccine strains expressing virus proteins. The recombinant work performed with MVA will be submitted in an RD at a later date. MVA does not cause disease in humans. The attenuated MVA virus was derived from chorioallantoid vaccinia Ankara (CVA), a Turkish smallpox vaccine strain that, after more than 570 passages in primary chicken embryo fibroblast (CEF) cells, became defective for replication in most mammalian cells, including human cells, and avirulent in animal models. During its extended passage in CEF cells, MVA lost nearly 30 kb (or 10%) of genomic information and has multiple deletions and mutations compared with the parental strain, many of them in genes implicated in the modulation of host responses. Toward the end of the smallpox eradication campaign (1968–1980), MVA was inoculated into more than 120,000 individuals in Germany with no reported adverse side effects. Since then, MVA has been evaluated in animal models and human studies under normal or immunosuppressed conditions and was found to be safe and immunogenic without the development of clinical disease. MVA growth is restricted to a few cell types. In cells of human origin,

	MVA produces early and late viral proteins as in permissive cells but there is a block in virion assembly, avoiding the cell- to-cell spread of the virus. The vaccine dose is ~10^8 pfu, and the virus is unable to spread to others because it lacks genes for generating infectious viral particles. BSL-1 is recommended if other human orthopoxviruses are not being used. Vaccination is also not recommended unless other human orthopoxviruses are being used. The listed lab spaces are BSL-2, so the approved biosafety level is BSL-2. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for work with MVA. ▪ No animal studies were proposed, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **HPRD#14-159** as written.
Item 3:	<u>Registration of Material (Potentially) Infectious for Humans (Amendment)</u> ▪ Feldmann (LV) ▪ **HPRD#12-143 Amend:** Coronaviruses ▪ Becky Anderson presented the risk assessment. The amendment to this registration is to add work with sheep and goats. The draft ASP describes establishing sheep and goats as a natural reservoir model for MERS-CoV by infecting the animals intranasally. ▪ The primary hazards of working with sheep and goats (even small or mini's) include: Kicking, head butting, jumping, contamination on surface of suit. To mitigate these hazards, personnel will enter the cage only when necessary, animals will be de-budded, and the cage height will have to be sufficient to hold goats inside. Suit sanitation procedures are carried out when leaving the animal holding rooms and/or procedure spaces. These procedures are described in SOP 4-28-55. ▪ The committee discussed the containment requirements. Work with MERS-CoV is approved at BSL-3/ABSL-3, but these studies with sheep and goats will be conducted at RML at ABSL-4. ▪ Rachel LaCasse stated that there are dwarf goats, but she is unsure of any mini or dwarf sheep. This will have to be researched to figure out the type of sheep and goats that would work best at ABSL-4. Rachel LaCasse also expressed concerns about the current caging (pig cages) that are proposed for use with the sheep and goats. The current caging is only 36" tall and should at least be 4 feet. It is possible that the current caging could be modified, but they will have to verify it does not affect the integrity of the cages. ▪ Sue Priola stated that these are all important concerns; perhaps the committee

	can approve the amendment on the HPRD and then hold the concerns to the SOP that will be reviewed at the end of the meeting. The committee agreed that this would be an appropriate action. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **HPRD#12-143 Amend** as written.
Item 4:	Registration of Material (Potentially) Infectious for Humans (Amendment) ▪ Gherardini (LPVD) ▪ **HPRD#14-03 Amend:** *Borrelia burgdorferi* ▪ Becky Anderson presented the risk assessment. The amendment is to add Borrelia species including: *hermsii, crocidurae, miyamotoi, duttoni, parkeri, coriaceae, turicatae,* and *recurrentis*. Tick borne relapsing fever (TBRF) is caused by Borrelia spp. and is characterized by recurring febrile episodes that last approximately 3 days and are separated by afebrile periods of 7 days. Each febrile episode ends with symptoms known as a "crisis" where patients develop very high fever and may become delirious, agitated, and tachycardic for a duration of 10 to 30 min. This is then followed by a phase called "flush" where they have drenching sweats and a rapid decrease in body temp. Patients that are untreated experience 1 to 4 episodes of fever. TBRF usually has more episodes than Louse borne relapsing fever (LBRF). Mortality is estimated at 5-10% for untreated TBRF patients and 70% for untreated LBRF. Mortality rate for persons treated is less than 1%. Neurologic complications can also occur, more commonly in LBRF and include meningitis, seizures, cranial neuropathies (especially facial palsy) and even coma. Myocarditis can be a fatal complication of either LBRF or TBRF. *B. recurrentis* is the only Borrelia species listed on this registration that can cause LBRF. Treatment for both TBRF and LBRF include penicillin and other beta-lactam antimicrobials, as well as tetracyclines (doxycycline), macrolides, and possibly fluoroquinolones typically for a 10 day course of treatment. LBRF can be treated with a single dose of antibiotics. The natural routes of transmission are either by the bite of an infected tick or by body lice. The primary lab hazards include parenteral contact, accidental sharps injuries and exposure to aerosols. ▪ The committee discussed the containment requirements. BSL-2/ABSL-2 is appropriate for work with Borrelia spp. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **HPRD#14-03 Amend** as written.

Item 5:	Registration of Material (Potentially) Infectious for Humans (Amendment) ▪ Rosa (LPVD) ▪ **HPRD#12-24 Amend:** *Borrelia burgdorferi* ▪ Becky Anderson presented the risk assessment. The amendment is to add animal work with mice. The amendment points out a few administrative changes, but the main update is to add mice. ▪ The committee discussed the containment requirements. ABSL-2 is appropriate for animal studies with *Borrelia burgdorferi*. ▪ Animal work with mice was proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **HPRD#12-24 Amend** as written.
Item 6:	Registration Documents for Recombinant DNA Experiments (NEW) ▪ Munster (LV) ▪ **RD#14-444**: The development of a small animal model for MERS-CoV ▪ Reviewers: Sue Priola, Scott Kobayashi ▪ **Summary:** Generation of DPP4 knockin mouse ▪ Sue Priola summarized the registration. This RD describes making a transgenic mouse that is susceptible to MERS-CoV. Previous work in LV demonstrated that the receptor for MERS-CoV is DPP4. A difference in DPP4 between different species appears to be the driving factor behind the observed species tropism of MERS-CoV. Experiments with transient expression of DPP4 in mouse lungs demonstrated that infection and viral replication were possible in a mouse model. This RD describes expressing human DPP4 via a knockin using the Rosa26 locus. Mice will be generated by a company and breeding and subsequent studies will occur at RML. The initial recombinant work is covered by RD 14-431 from the Ebihara lab in LV. Sue Priola pointed out that the NIH Guideline III-E-3-a should be added for the breeding of the transgenic mice. Dual use question 6 was answered yes, but the explanation is appropriate and does not raise overall dual use concerns. ▪ Dana Scott was not in attendance, but he informed Sue Priola in advance by email that he had no concerns with the registration. ▪ Animal studies with mice were proposed. ▪ The committee discussed the containment requirements. ABSL-4 is appropriate for animal studies that challenge these mice with MERS-CoV. Breeding of DPP4 knockin mice can occur at ABSL-1.

	▪ The committee discussed the dual-use potential of these experiments. As discussed above, dual use question 6 was answered yes, but the committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#14-444** with the following minor modifications: 1. Add III-E-3-a to the NIH Guidelines listed in the Recommendations section. Research generating a DPP4 knockin is approved under III-D-4-a of the NIH Guidelines. Breeding of the DPP4 knockin mice (BL1 transgenic rodent) is exempt from the NIH Guidelines under III-E-3-a and Appendix C-VIII.
Item 7:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Rosa (LPVD) ▪ **RD#14-308**: Identify virulence determinants required for infection by *Borrelia burgdorferi*. ▪ Reviewers: Bob Heinzen, Clay Jarrett ▪ **Summary:** *B. burgdorferi*, the agent of Lyme disease, must adapt to and be transmitted between two very different environments, the tick vector and mammalian host, in order to persist in nature. The broad objective of this project is to use a molecular genetic approach to elucidate the mechanisms of adaptation and variation used by *B. burgdorferi* and thereby gain insight into the virulence determinants required for infection by this pathogen. ▪ Clay Jarrett summarized the registration. This is an RD for general molecular work with *B. burgdorferi.* All the NIH Guidelines listed are appropriate. The antibiotics used for selection are not used clinically and that is clearly stated in the RD. Clay Jarrett pointed out that some of the vector maps are missing and should be attached. ▪ Sue Priola pointed out that zeocin is listed on one of the vector maps but not in the list of antibiotics used for selection, it should be added. ▪ Animal studies with mice and rabbits were proposed. ▪ The committee discussed the containment requirements. BSL-2/ABSL-2 is appropriate for studies with *B. burgdorferi*. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#14-308** with the following minor modifications: 1. Attach missing vector maps. 2. Add zeocin to the list of antibiotics used for selection.

	Research using prokaryotic hosts is approved at BSL-2 under sections III-D-1-a and III-D-2-a of the NIH Guidelines. Animal work with mice and rabbits is approved at ABSL-2.
Item 8:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Feldmann (LV) ▪ **RD#14-402**: Lentiviral vectors ▪ Reviewers: Karin Peterson, Rachel LaCasse ▪ **Summary:** To characterize modification of cellular responses by expression of various viral proteins in target cells using a lentiviral vector system of protein expression. ▪ Karin Peterson summarized the registration. This is a straight forward renewal. They will use lentiviruses to express genes from the list of viruses or host cellular proteins, reporter genes, and siRNAs/shRNAs. The registration lists three different systems, none of the systems generates replication competent virus, they are all very safe systems and the safety mechanisms are listed in the registration. Karin Peterson stated that the NIH Guidelines listed are appropriate. There were three minor typos that should be fixed. ▪ Sue Priola pointed out a typo. ▪ Rachel LaCasse had no comments or concerns. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for studies with Lentiviral vectors. ▪ No animal studies were proposed, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#14-402** with the following minor modifications: 1. Fix the minor typos. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells will be performed at BSL-2 and is approved under Sections III-D-1-a and III-D-3-a of the NIH Guidelines.
Item 9:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Gherardini (LPVD) ▪ **RD#14-319 Amend**: *Borrelia burgdorferi* ▪ Reviewers: Scott Kobayashi, Dana Scott ▪ **Summary:** The amendment is to add *Borrelia hermsii* and a new shuttle vector.

	The amendment also includes adding animal work with *B. hermsii*. ▪ Scott Kobayashi summarized the registration. They already have an approved RD, they want to amend it to add work with *B. hermsii* and conduct the same type of experiments that they describe in the original RD with *B. burgdorferi*. The new vector listed does encode for a different antibiotic resistance gene than what is covered in the original RD, which should be stated in the amendment and as well as some information to describe that zeocin and gentamicin are not used clinically for treatment of Borrelia spp. infections. The NIH Guidelines in the original RD are still appropriate for the amendment and Scott Kobayashi had no dual use concerns. ▪ The animal study proposal that is attached for work with mice does still have Tom Schwann's name on it. Becky Anderson informed the committee that the Gherardini lab is working with the ACUC to transfer everything over to Gherardini as Tom Schwann leaves RML. The attached ASP does allow the committee to understand the type of work they would like to do now in the Gherardini lab. ▪ The committee discussed the containment requirements. BSL-2/ABSL-2 is appropriate for studies with *B. burgdorferi*. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **RD#14-319 Amend** with the following minor modifications: 1. Add zeocin and gentamicin to the amendment description and clearly indicate that neither antibiotic is used clinically to treat Borrelia infections. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-1-a and III-D-2-a of the NIH Guidelines. Animal work with mice is approved at ABSL-2.
Item 10:	<u>Registration Documents for Recombinant DNA Experiments (Renew)</u> ▪ Bloom (LV) ▪ **RD#13-443**: The use of replicons to compare vector-borne Flaviviruses (VBFV) ▪ Reviewers: Hideki Ebihara, Karin Peterson ▪ **Summary:** The amendment to the registration is to include procedures with Powassan virus. ▪ Hideki Ebihara summarized the registration. The Bloom lab would like to amend the current registration to include Powassan virus to their replicon system described in the original RD. This system does not generate infectious virus so it is very safe. They will use it to characterize the UTR region of

	Powassan virus. The NIH Guidelines from the original RD are appropriate for the amendment. Hideki Ebihara did not find any dual use concerns associated with the amendment. ▪ Karin Peterson pointed out that the second paragraph, last sentence should be reworded to state, ". . . use of a POWV replicon will also be relevant." If left unchanged, it will sound like the initial work is no longer relevant. ▪ No animal studies were proposed, reviewed, or approved. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for work with Powassan virus replicons. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#13-443** with the following minor modifications: Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells will be performed at BSL-2 and is approved under Sections III-D-1-a of the NIH Guidelines.
Item 11:	**Standard Operating Procedure: SOP#4-28-55 Husbandry and manipulation of sheep and goats in level 4 biocontainment (NEW)** ▪ Sue Priola informed the committee that this is a new SOP for BSL-4 work with sheep and goats. ▪ Rachel LaCasse reiterated her concerns (as discussed under HPRD 12-143 Amend) about the cage height and the possibility the goats could jump out. She stated that the SOP does not specify the size of animals and she estimates that the caging should be 4 feet tall at a minimum. It is possible to retrofit the current caging, but Rachel LaCasse had concerns that it might affect the integrity of the caging. New caging or retrofitting current caging should be explored. ▪ Nancy Hoe pointed out that there should be a training period for everyone to figure out the details of working with sheep and goats. ▪ Sue Priola asked the committee if they felt the SOP should be tabled until it was determined what appropriate caging would be and if a training period was necessary. The committee agreed the SOP should be tabled on the grounds of proper caging and ensuring a period of training for relevant personnel. Action: The committee unanimously TABLED **SOP#4-28-55 Husbandry and manipulation of sheep and goats in level 4 biocontainment (NEW)** with the following requirements: 1. Current caging is not appropriate as is, either new caging must be procured or

	the current caging must be modified to prevent animals from jumping out. 2. Training with sheep and goats is necessary to figure out details of handling. After completion of a training period, the SOP can be finalized.
Item 12:	**Standard Operating Procedure: BSL-3 POWV-D-6 and 7 Powassan Inactivation SOP and Extraction of POWV RNA, cDNA synthesis (NEW)** ▪ Sue Priola informed the committee that this SOP was for the inactivation of mouse serum and extraction of RNA from Powassan virus in the (b)(6) (b)(6) ▪ Sue Priola stated that references are included for the inactivation, but asked (b)(6) from the Bloom lab if those parameters are effective at inactivating Powassan virus. (b)(6) replied that they are, the Bloom lab has also tested this with Langat Virus and cannot detect any focus forming units after following the outlined procedures. ▪ There were no additional concerns with the SOP. Action: The committee unanimously approved **BSL-3 POWV-D-6 and 7 Powassan Inactivation SOP and Extraction of POWV RNA, cDNA synthesis (NEW)** as written.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ See attached BSO report. ▪ Nancy Hoe informed the committee about a mouse bite. She summarized the attached incident report.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ Not present
Report	**IRF Biosafety Manager Report/Megan Morgan** ▪ Not present
Report	**Associate Director Report/Marshall Bloom** ▪ Nothing to report
Around the room	▪ None

Other issues	▪ None

Next Meeting:

- Date: 5/15/14
- Place: Bldg A Seminar Room
- Time: 1:00 PM

RML Biosafety Committee Meeting
April 17, 2014
Biosafety Officer/Responsible Official Report

1) Requests approved by BSO since last meeting:

a) Summer Student Projects

i) *Hackstadt (Bauler)*

(1) (b) (6) *plasmid transformation systems with an LGV strain of Chlamydia trachomatis*

2) ***New requests approved by committee via electronic review:***

a) *None*

3) ***New requests***

a) *Registration of Material Potentially Infectious for Humans*

i) ***New***

(a) *Feldmann (LV)*

(a) ***HPRD-14-158:*** *Field Samples*

(b) ***HPRD-14-159****: Modified Vaccinia virus Ankara (MVA)*

ii) ***Amend***

(a) *Feldmann (LV)*

(a) ***HPRD-12-143:*** *Characterization of a novel betacoronavirus (MERS-CoV)*

(i) Add sheep and goats as animal models

(b) *Gherardini (LZP)*

(a) ***HPRD-14-03****: The infectious cycle of Borrelia burgdorferi*

(i) Add strains of relapsing fever Borrelia spp.

(c) *Rosa (LZP)*

(a) ***HPRD-12-24****: Molecular genetic investigation of the infectious cycle of Borrelia burgdorferi*

(i) Add mice as an animal model

b) *Registration Documents for Recombinant DNA Experiments*

i) ***New***

(a) *Munster (LV)*

(a) ***RD-14-444:*** *Mouse DPP4 knock-in*

ii) ***Renew***

(a) *Rosa (LZP)*

(a) ***RD-14-308:*** *Molecular genetic approaches to elucidate the mechansism of adaptation and variation used by B. burgdorferi*

(b) *Feldmann (LV)*

(a) ***RD-14-402:*** *Lentiviral vectors*

iii) ***Amend***

(a) ***Gherardini (LZP)***

(a) ***RD-14-319:*** *The infectious cycle of Borrelia burgdorferi*

(i) Addition of Borrelia hermsii

(ii) Addition of pBHSV2 vector

(b) ***Bloom (LV)***

(a) ***RD-13-443****: The use of replicons to compare vector-borne flaviviruses*

(i) Addition of Powassan virus

c) <u>*Standard Operating Procedures*</u>

i) ***New***

(a) ***SOP-4-28-55:*** *Husbandry and manipulation of sheep and goats in level 4 biocontainment*

(b) ***BSL3-POWV-D-6****: Powassan Inactivation*

(c) ***BSL3-POWV-D-7****: Extraction of POWVRNA, cDNA synthesis*

4) ***Animal Study Protocols Review***

PI	***Title***	***Associated HPRD***	***Associated RD***	***Reviewer***
(b)(6)	*Acute CD4+ T cell depletion in TK0 BLT mice*	*12-104 (HBBF) 12-55 (HIV)*	*N/A*	*B. Anderson*
	Regulatory and effector T-cell responses to a murine retrovirus in APOBEC3 knockout mice	*N/A (Friend virus)*	*N/A*	*B. Anderson*
	Evaluation of macrophage subpopulations during LDV infection of mice	*N/A (Lactate-dehydrogenase-elevating virus)*	*N/A*	*B. Anderson*
	Evaluation of superantigen requirement for Friend virus-induced Treg responses in mice	*N/A (Friend virus)*	*N/A*	*B. Anderson*
	Determining the role of gammadeltaT17 cells in control of Y. pestis infection	*11-66 (Y. pestis exempt)*	*12-320*	*M. Morgan*

RML Biosafety Committee Meeting
April 17, 2014
Biosafety Officer/Responsible Official Report

5) ***Biosafety Training Performed – Megan Morgan, Becky Anderson***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
Select Agent Initial	***1***	***1***
BSL-3 Laboratory Biosafety	***1***	***2***
BSL-4 Laboratory Biosafety	***2***	***2***

6) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
   a) *Biological Incident Report:*
      i) *Bite from a Mastomys natalensis mouse 4-8-14*

7) ***Select Agent Issues***
   a) *None*

8) ***Other Issues***
   a) *OBA meeting on Primary Containment of Non-human Primates in Biosafety Level 4 Laboratories*

Safety Incident Investigation Report		
Date	**Location**	**Brief Synopsis**
4-8-14	(b)(6)	Employee received a bite from a Mastomys natalensis mouse
Report by:	Nancy Hoe	

Report Detail: *(Provide a description of the incident. This should include a timeline of the incident, the agent/animal worked with, PPE worn, description of procedures conducted at the time of the incident, notifications made, follow-up procedures for decontamination and program improvement, and results of root cause analysis.)*

IBC Report
Description of Incident:
At approximately 11:15AM, an employees was in (b)(6) an ABSL-2 quarantine facility, transferring mice (Mastomys natalensis) into separate caging to transport to the (b)(6) As they removed the cage lid, one of the mice attempted to escape the cage. The employee grabbed the mouse's tail with one hand, but the mouse was able to turn around and bite them on the other hand. They returned the mouse to the cage, closed the cage, and performed wound disinfection (15 mins of treating with a Betadine swab, scrubbing with soap and water, then treating with a Betadine swab). They then reported the incident to their supervisor, who referred them to RML OMS, who then repeated the wound disinfection.

At 11:30AM, their supervisor called RML DOHS to report the incident. They confirmed that the procedure was being performed in a changing station and that the area was disinfected after the incident. They also reported that the mice had been bred for at least 6 or 7 generations from the original wild-caught animals, and had been tested and were negative for Lassa fever virus. Megan Morgan spoke with (b)(6) of LV and he confirmed that the mice were negative by serology and PCR for Lassa and negative by PCR for all of the hantaviruses. The mice had not been tested for monkeypox, but they had been asymptomatic for over 21 days which indicates that they are not infected with the virus. This information was relayed to both RML and NIH OMS.

DOHS debriefed the employee at 3PM. OMS has provided follow up with employee who has not exhibited any signs or symptoms of illness.

Agent present:
Unknown. The mice were not infected with a known agent and are negative for Lassa and hantaviruses.

Employee properly protected:
Yes, employee was wearing scrubs, lab coat, gloves, and filter mask.

Training:
The employee is current on their safety training and attended the Animal Users Course at RML on March 13, 2013 (good for 3 years).

Issues Identified and Follow Up Actions:
RMVB staff has observed that Mastomys natalensis rodents are normally active and jumpy, so a cotton nestlette soaked with isoflurane is added to the cage prior to removing the mice. RMVB has been housing the rodents in hamster-sized cages in case they have a propensity to chew the disposable mouse caging. The larger number of mice (9) that are able to be housed in these cages means that not all the mice are anesthetized to the same extent, increasing the risk that a mouse may try to jump out when the cage lid is removed. To mitigate this risk, RMVB will test house a few mice in a regular mouse-sized disposable cage to see if they are prone to chew those cages. If they are not, RMVB will begin housing fewer mice in the smaller cages. If they are, DOHS

will discuss additional options with RMVB staff.

Conclusion:
The mice had not been infected with a known agent. They are negative by serology and PCR for Lassa and negative by PCR for all of the hantaviruses. They have not been tested for monkeypox, but they have been asymptomatic for over 21 days which indicates that they are not infected with the virus. Therefore, the risk of infection was limited to any unknown agents harbored by the mice, who are asymptomatic. Due to the immediate wound care performed by the employee and then later by OMS, the risk of infection is considered negligible.

☐ No Exposure to Biological Hazards *(No further action)*

☑ Potential Exposure to Biological Hazards *(Complete RML Injury & Exposure Risk Assessment Guide)*

☑ Referred to OMS _____ *(List Department/Office)*

Nancy P. Hoe		4-16-14
DOHS Representative	Signature	Date
OMS Representative	Signature	Date

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 6/19/14
Meeting Time: 1:03 PM **Adjourned:** 2:08 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Paul Carlson	☒	☐	Kevin Mora	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Megan Morgan	☒	☐
Becky Anderson (EO)	☒	☐	Frank DeLeo (EO)	☐	☒	Karin Peterson	☒	☐
Alan Applebury	☐	☒	Hideki Ebihara	☒	☐	George Risi	☒	☐
Chris Bosio	☐	☒	Heinz Feldmann (EO)	☐	☒	Dana Scott	☐	☒
Marshall Bloom (EO)	☒	☐	Nancy Hoe	☐	☒	Alexandra Scranton	☐	☒
Teresa Borino	☒	☐	Clay Jarrett	☒	☐			
Jeff Burrows	☒	☐	Josh Kellar (EO)	☐	☒			
Carol Calderwood	☐	☒	Scott Kobayashi	☒	☐			
Harlan Caldwell (EO)	☐	☒	Rachel LaCasse	☒	☐			
Marcie Caldwell (EO)	☒	☐	Alida Merritt	☐	☒			

(P=present; A=absent)

Guests: (b)(6)

Minutes: Meeting minutes from 4/17/14 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** Action: Meeting minutes were unanimously approved as written.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans (Renew) ▪ Hackstadt (LICP) ▪ **HPRD#14-72:** *Listeria monocytogenes* ▪ Becky Anderson presented the risk assessment. The Hackstadt lab uses *L. monocytogenes* as a control for obligate intracellular pathogens. Although relatively rare, human listeriosis is often severe and mortality rates can

	approach 50%. Certain factors predispose individuals to infection with *L. monocytogenes*, such as neonates, pregnancy, leukemia, Hodgkin's disease, diabetes mellitus, alcoholism or cirrhosis and immunosuppressive or cytostatic therapy. Most commonly, listeria causes a mild febrile illness however, several types of listeriosis disease manifestations are recognized; for instance, listeriosis in pregnancy, listeriosis of the central nervous system (CNS), febrile gastroenteritis, glandular listeriosis, local listeriosis, typhoid listeriosis, and atypical listeriosis. Listeriosis in pregnancy occurs mostly during the third trimester, and is characterized by a "flu like" illness with symptoms such as fever, chills, malaise, arthralgia, back pain, and diarrhea. In many cases the infection is subclinical or unapparent; however, intrauterine infection of the fetus can lead to fetal death, spontaneous abortion, premature delivery, or the birth of a fetus that dies shortly after birth. There are currently no vaccines available, the primary choice of therapy includes ampicillin or amoxicillin together with gentamicin. The recommended course of treatment is ampicillin for 2 to 4 weeks. The addition of gentamicin for 2 weeks is recommended for immunocompromised patients. The infectious dose is 10-100 x 10^6 CFU for healthy persons and 0.1-10 x 10^6 for immunocompromised persons. The natural route of transmission is by ingestion of contaminated food. The primary laboratory hazards include accidental sharps injuries, ingestion, or inhalation of aerosols. ▪ Becky Anderson stated the recommended precautions for working with *L. monocytogenes*: 1. Women who are pregnant or thinking of becoming pregnant are encouraged to notify the Lab supervisor and RML OMS Nurse. This is in order to assure that they are aware of any potential risks to themselves or the fetus and determine if any additional risk reduction measures should be taken. 2. All work with infectious materials is conducted in a BSC, centrifugation of infectious materials must be carried out in sealed safety cups or removable rotors that can be loaded and unloaded in a BSC. 3. Immunocompromised person should be made aware of the risks of working with this material. RML OMS Nurses can help to determine if any additional risk reduction measures should be taken. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for work with *Listeria monocytogenes* with the above stated precautions. ▪ No animal studies were proposed, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **HPRD#14-72** as written.
Item 2:	<u>Registration of Material (Potentially) Infectious for Humans (Renew)</u>

	▪ Hasenkrug (LPVD) ▪ **HPRD#14-114:** *Listeria monocytogenes* ▪ Becky Anderson presented the risk assessment; it is the same as for HPRD 14-72 discussed above. The Hasenkrug lab however, will be working with *L. monocytogenes in vivo*. Specifically, they will co-infect mice with Friend virus and *L. monocytogenes* to determine if FV induced immune suppression is confined to FV primary infections or extends to secondary infections as well. ▪ Becky Anderson stated the recommended precautions for working with *L. monocytogenes*: 1. Women who are pregnant or thinking of becoming pregnant are encouraged to notify the Lab supervisor and RML OMS Nurse. This is in order to assure that they are aware of any potential risks to themselves or the fetus and determine if any additional risk reduction measures should be taken. 2. All work with infectious materials is conducted in a BSC; centrifugation of infectious materials must be carried out in sealed safety cups or removable rotors that can be loaded and unloaded in a BSC. 3. Immunocompromised person should be made aware of the risks of working with this material. RML OMS Nurses can help to determine if any additional risk reduction measures should be taken. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for work with *Listeria monocytogenes* with the above stated precautions. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **HPRD#14-114** as written.
Item 3:	<u>Registration of Material (Potentially) Infectious for Humans (Renew)</u> ▪ Hackstadt (LICP) ▪ **HPRD#14-38:** Rickettsia spp. ▪ Becky Anderson presented the risk assessment. The focus of the Hackstadt lab is to study the differences between virulent and avirulent strains of rickettsiae through comparative genomics and directed knockout and complementation studies of suspected virulence determinants. Specific genes/proteins will be deleted or complemented and differences in virulence determined. These specific studies will be described in the RD reviewed in this meeting. *R. rickettsii* infection causes Rocky Mountain Spotted Fever, a potentially fatal tick-borne disease that normally causes moderate to severe illness. Other Rickettsia spp. can cause spotted fever or Typhus related disease. Spotted fevers can appear as an abrupt onset of fever, malaise, headache, anorexia, nausea,

vomiting, abdominal pain, photophobia, diarrhea and neck stiffness. The characteristic maculopapular rash usually appears 2-5 days after the other symptoms, starting on wrists and ankles before progressing to the rest of the body. Ninety five percent of children and 80% of adults have the rash; however, absence of the rash is more common in fatal cases and cases involving the elderly or African-Americans. The symptoms can last 2 weeks although some patients have neurological sequelae lasting up to one year after disease onset. Twenty percent of untreated cases are fatal compared to 5% of treated cases. Patients with Typhus usually present with a severe, but nonspecific febrile illness that may include: headache, chills, vomiting, nausea, myalgia, and rash. Complications are rare and complete recovery occurs in most cases. Currently there are no vaccines available and the drugs of choice for treatment include: doxycycline, chloramphenicol, or quinolones. The natural route of transmission is typically through blood feeding arthropods for example ticks and fleas. The primary lab hazards include parenteral contact, accidental sharps injuries, and exposure to aerosols.

- Becky Anderson pointed out to the committee that this HPRD has various biosafety levels depending on the agent. Each agent is listed in the recommendations section with the appropriate biosafety level listed.
- The committee discussed the containment requirements. Work with Rickettsia spp. is approved at BSL-2 or BSL-3 depending on the agent. This must be clearly identified on the HPRD.
- Animal studies with guinea pigs were proposed.
- Sue Priola questioned that the recommendations section did not list BSL-2 with -3 precautions for work with large volumes and high concentrations. This is listed on the RD, but not the HPRD. Becky Anderson will correct to make the HRPD and the RD consistent.
- Bob Heinzen questioned why *Wolbachia andersoni* and *Wolbachia persica* were on the BSL-3 list; they do not cause human disease so do not need to be worked with at BSL-3. He further added that *R. tsutsugumushi* is now called *Orientia tsutsugumushi* so that should be updated. Becky Anderson pointed out that the list of Rickettsia species for BSL-3 was generated by Ted Hackstadt. She will follow-up to ensure that Ted Hackstadt works with *Wolbachia andersoni* and *Wolbachia persica* at BSL-3.
- The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.

Action: The committee unanimously approved **HPRD#14-38** with the following minor modifications:

1. Update *Rickettsia tsutsugumushi* to *Orientia tsutsugumushi*.
2. Check with Ted Hackstadt on where he works with *Wolbachia andersoni*

	and *Wolbachia persica.* Update the recommendations section accordingly.
Item 4:	Registration of Material (Potentially) Infectious for Humans (Amendment) ▪ Feldmann (LV) ▪ **HPRD#12-143 Amend:** Coronaviruses ▪ Becky Anderson presented the risk assessment. The amendment is to add swine to the HPRD. The attached animal study proposal describes establishing pigs as an animal model for MERS-CoV by infecting intranasally and intratracheally. The primary lab hazards for working with swine include teeth and hooves, heavy lifting of older swine and contamination on surface of suit or feet (crocs). To mitigate these hazards, the following SOP was developed and is already IBC approved, SOP #4-28-44 Swine husbandry and manipulation. The SOP outlines that, custom-made pig pens with removable metabolism trays are utilized. The pens are modified with catch pans designed to catch solid waste in a filter basket below but allow liquid waste to enter the trench drain and the effluent decontamination system. Additional modifications include a swing gate that allows for isolation of animals at the rear of the cage and a feed hopper that allows for the feed to be added without opening the pen door. Personnel only enter the cage when necessary. Suit and foot sanitation procedures are carried out when leaving the animal holding rooms and/or procedure spaces. For animals over 25 kg, two people are used to lift the animal onto the cart. ▪ The committee discussed the containment requirements. ABSL-3 is appropriate for work with Coronaviruses. The proposed studies with swine will be conducted at RML at ABSL-4. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **HPRD#12-143 Amend** as written.
Item 5:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Hackstadt (LICP) ▪ **RD#14-110:** Virulence determinants of spotted fever group rickettsia ▪ Reviewers: Chris Bosio, Clay Jarrett ▪ **Summary:** The RD outlines specific genes/proteins that will be deleted or complemented to determine differences in virulence of various Rickettsia spp. ▪ Clay Jarrett summarized the registration. This RD is for work with multiple Rickettsia spp. They will use a shuttle vector to introduce mutations by allelic exchange. They will also express epitope tags like Flag, his, CyaA, or myc. As

	specified in the Recommendations section, these experiments will either be performed at BSL-2 or BSL-3, depending on the strain being used. Clay Jarrett questioned if the Prokaryotic Host section should have BSL-2 listed instead of BSL-3. Sue Priola agreed that BSL-2 is appropriate for that work. Clay Jarrett also questioned that on the RD registration, the route of inoculation is listed as subcutaneous, but the animal study proposal lists intradermal. Becky Anderson clarified to the committee that intradermal is not an option on the form and often people classify intradermal as subcutaneous. Clay Jarrett stated that the antibiotic resistance genes used for selection are appropriate and are not used clinically to treat infections. Clay Jarrett also questioned the NIH Guidelines for Eukaryotic cells section, Sue Priola clarified that the listed guidelines are to cover BSL-2 with BSL-3 practices and are appropriate. ▪ Chris Bosio was not in attendance, but informed Clay Jarrett by email that he had no comments or concerns. ▪ Bob Heinzen pointed out that the description in the recombinant DNA section does not mention the vector pMW1650 or the antibiotic resistance marker, kanamycin that it encodes for, although the vector map with this information is attached. This information will be added. ▪ Animal studies with mice were proposed. ▪ Sue Priola added that the recommendations section should list BSL-2 with -3 precautions for work with large volumes and high concentrations of *R. Montana, R. rhipicephali*, and *R. belli*. ▪ The committee discussed the containment requirements. Work with Rickettsia spp. is approved at BSL-2 or BSL-3 depending on the agent. Any experiments introducing *R. rickettsii* genes into less virulent strains will be performed at BSL-3. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#14-110** with the following minor modifications: 1. Add to the recommendations section, work with large volumes and high concentrations of *R. Montana, R. rhipicephali*, and *R. belli* will be performed at BSL-2 with BSL-3 practices. 2. Change the biosafety level from BSL-3 to BSL-2 for the Prokaryotic Host section. 3. Add a description of the vector pMW1650 and kanamycin to the Recombinant DNA section. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-1-a, III-D-1-b, and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells will be performed at BSL-3 and is approved under Appendices G-II-B, and G-II-C of the NIH

	Guidelines.
Item 6:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Hasenkrug (LPVD) ▪ **RD#14-219**: Replication defective Adenovirus 5 vector ▪ Reviewers: Karin Peterson, Sue Priola ▪ **Summary:** Adenovirus 5 vector containing HIV-1 DNA encoding peptides ▪ Karin Peterson summarized the registration. This registration describes vaccinating humanized mice with an Adenovirus 5 vector, followed by infecting them with HIV to see if the adenoviral vectors can provide some level of protection. They are not actually doing any recombinant work, they already have the plasmids that they have received from a collaborator, and this information is provided in the RD. This vector has already been used in human studies, so it is not a concern. Karin Peterson stated that the second to last sentence in the Recombinant DNA section should be removed, "In tabular form below . . . " as this information was copied and pasted from the company website and that table is not included in the registration. ▪ George Risi asked which antiviral drugs are effective against this strain of HIV. Becky Anderson informed the committee that the antiviral information is included in the HPRD and this RD lists the HIV HPRD as an associated registration so it should be easy to track and find the necessary information in the event of a potential exposure to HIV. ▪ Sue Priola had no additional comments or concerns. ▪ Animal studies with mice were proposed. ▪ The committee discussed the containment requirements. BSL-2/ABSL-2 is appropriate for studies with Adenovirus 5. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#14-219** with the following minor modifications: 1. The second to last sentence in the Recombinant DNA section should be removed, "In tabular form below . . . " Research is approved at BSL-2 under sections III-D-4-a of the NIH Guidelines. Animal work with mice is approved at ABSL-2.
Item 7:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Hasenkrug (LPVD)

	▪ **RD#14-218**: Recombinant *Listeria monocytogenes* expressing ovalbumin ▪ Reviewers: Scott Kobayashi, Hideki Ebihara ▪ **Summary:** Ovalbumin expressing *Listeria monocytogenes* ▪ Scott Kobayashi summarized the registration. The registration is for a strain of *L. monocytogenes* that Kim Hasenkrug received from a collaborator that expresses ovalbumin. They will use this strain for co-infection studies with Friend virus to determine if immune suppression induced by Friend virus is confined only to FV specific responses or extends to secondary infections. This strain encodes for resistance to erythromycin which is not used to treat listeriosis so there is no problem with using this marker. ▪ Hideki Ebihara confirmed with Scott Kobayashi that Listeria infections are not treated with erythromycin. Scott Kobayashi agreed that typically they use ampicillin and/or drugs like trimethoprim-sulfamethoxazole, not erythromycin. George Risi also confirmed that erythromycin is not used for treatment. ▪ Hideki Ebihara pointed out that they did not attach a vector map, but they did not create the recombinant strain so it is okay that it is not attached. ▪ The committee discussed the containment requirements. BSL-2/ABSL-2 is appropriate for studies with *L. monocytogenes*. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **RD#14-218** as written. Research is approved at BSL-2 under sections III-D-4-a of the NIH Guidelines. Animal work with mice is approved at ABSL-2.
Item 8:	<u>Registration Documents for Recombinant DNA Experiments (Amendment)</u> ▪ Gherardini (LPVD) ▪ **RD#14-319 Amend**: *Borrelia burgdorferi* ▪ Reviewers: Bob Heinzen, Sue Priola ▪ **Summary:** The amendment is to add procedures to introduce relapsing fever spirochete genes into the Lyme disease agent *B. burgdorferi*. ▪ Bob Heinzen summarized the registration. This amendment is to add relapsing fever spirochetes from Tom Schwan's lab. They want to look at gene function of several Borrelia strains. They will make mutants in *B. burgdorferi* and complement them with homologs from either *B. hermsii* or *B. crocidurae.* This system will allow them to assess gene function in a *B. burgdorferi* model. Bob Heinzen did not see any dual use concerns with cloning strategies outlined in

	the RD. ▪ Sue Priola had no additional comments or concerns. ▪ The committee discussed the containment requirements. BSL-2/ABSL-2 is appropriate for studies with *B. burgdorferi*. ▪ Animal studies with mice were proposed in the original RD submission. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#14-319 Amend** as written. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-1-a and III-D-2-a of the NIH Guidelines. Animal work with mice is approved at ABSL-2.
Item 9:	**Standard Operating Procedure: (b)(6) Coronavirus (excluding SARS-CoV), (b)(6) (b)(6) West Nile Virus, and (b)(6) Powassan (Update)** ▪ Becky Anderson informed the committee that the sample removal section for all three positive strand RNA virus SOPs has been updated to keep the SOPs consistent. The IBC previously approved this type of work with MERS-CoV from the BSL-4 and we are now making all the BSL-3 SOPs reflect the same procedures. ▪ There were no comments or concerns. Action: The committee unanimously approved (b)(6) **Coronavirus (b)(6) West Nile Virus, and (b)(6) Powassan (update)** as written.
Item 10:	**Standard Operating Procedure: (b)(6) Operations and Safety Procedures (OSP) (update)** ▪ Becky Anderson informed the committee that there were minor updates throughout the SOP and the changes were tracked in Word. The biggest update was including the Biosurety Program Description, which was included previously in all the Select Agent BSL-3 OSPs. ▪ Sue Priola questioned what specific life events were in the Biosurety description number 3. Megan Morgan clarified types of events. Sue Priola also questioned if it was required for an employee to submit medical records if they had been deemed not qualified. Marcie Caldwell specified that the employee first has to sign a release to surrender medical records to the Certifying Medical Authority. Action: The committee unanimously approved (b)(6) **Operations and Safety Procedures (update)** as written.
Item 11:	**Standard Operating Procedure: SOP#4-28-53 Husbandry and manipulation procedures for rabbits in level 4 biocontainment (Tabled December 2013)** ▪ Becky Anderson informed the committee that this SOP was tabled at the

	December IBC meeting for concerns regarding which rabbit procedures would require anesthesia. RMVB ordered rabbits for training and performed a training period to practice all the procedures they may perform at BSL-4. The consensus from that training period was that sedation will be dependent on the individual animal and their personality. Some rabbits are at a higher risk for kicking, while others are more docile. The SOP has been written to allow flexibility, so that the rabbits can be handled on a case by case basis. ▪ Rachel LaCasse added that you do not want to sedate the rabbits if it is not necessary as their gut can go static and you can create other health issues. If the rabbits tend to be more aggressive, they will sedate them to be able to safely handle them. They will always wear leather gloves regardless of whether or not the rabbits are sedated. Also, they will try to evaluate the rabbits before they get put into BSL-4 so that they can avoid the use of more aggressive animals at BSL-4. Action: The committee unanimously approved **SOP#4-28-53 Husbandry and manipulation procedures for rabbits in level 4 biocontainment (update)** as written.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ See attached BSO report. Becky Anderson reviewed the BSO report in Nancy Hoe's absence. ▪ Becky Anderson updated the committee on the OBA RAC meeting that took place June 11, 2014 regarding housing of non-human primates at ABSL-4. ▪ Megan Morgan summarized an incident report (see attached).
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ We have completed the Annual Safety Refresher training with 97% compliance. ▪ In May, a drill was conducted with Marcus Daly Memorial Hospital and St. Patrick Hospital. Overall the drill went well; there were a few communications issues that will be corrected. ▪ This summer DOHS will begin conducting lab safety surveys. ▪ Fire drills will be conducted in July.
Report	**IRF Biosafety Manager Report/Megan Morgan** ▪ (b)(6); (b)(3):42 has been re-activated, this is the first time the entire BSL-4 lab at RML has been fully operational and all suites "hot".
Report	**Associate Director Report/Marshall Bloom** ▪ Nothing to report

Around the room	▪ Rachel LaCasse informed the committee that AAALAC will be on site August 5th and 6th for a site visit. These visits occur every 3 years to review the animal program.

Other issues	▪ None

Next Meeting:

- Date: 7/17/14
- Place: Bldg A Seminar Room
- Time: 1:00 PM

RML Biosafety Committee Meeting
June 19, 2014
Biosafety Officer/Responsible Official Report

1) Requests approved by BSO since last meeting:

i) Amend

a) *Best (LV)*

(a) ***HPRD-12-135****: Far Eastern & Central European TBEV*

(i) Addition of personnel

2) ***New requests approved by committee via electronic review:***

a) *None*

3) ***New requests***

a) *Registration of Material Potentially Infectious for Humans*

i) ***New***

(a) *Hackstadt (LICP)*

(a) ***HPRD-14-72:*** *Listeria monocytogenes*

(b) ***HPRD-14-38****: Rickettsia spp.*

(b) *Hasenkrug*

(a) ***HPRD 14-114:*** *Listeria monocytogenes*

ii) ***Amend***

(a) *Feldmann (LV)*

(a) ***HPRD-12-143:*** *Characterization of a novel betacoronavirus (MERS-CoV)*

(i) Add pigs as animal models

b) *Registration Documents for Recombinant DNA Experiments*

i) ***New***

(a) *Hackstadt (LICP)*

(a) ***RD-14-110:*** *Virulence determinants of spotted fever group Rickettsia*

(b) *Hasenkrug (LPVD)*

(a) ***RD-14-219:*** *Adenovirus Type 5*

(b) ***RD-14-218****: Ovalbumin expressing Listeria monocytogenes*

ii) ***Amend***

(a) ***Gherardini (LZP)***

(a) ***RD-14-319:*** *The infectious cycle of Borrelia burgdorferi*

(i) Introducing genes from B. hermsii or B. crocidurae into B. burgdorferi

c) *Standard Operating Procedures*

i) ***Update***

(a) ***SOP-(b)(6)*** *Coronavirus, Powassan, and West Nile virus SOP(s) inactivation procedures*

(b) (b)(6) ***Operations and Safety Procedures:*** *minor updates throughout*

(c) ***SOP 4-28-53 Husbandry and Manipulation procedures for rabbits in level 4 biocontainment****: resubmitted, Tabled at 12-19-13 IBC meeting*

4) ***Animal Study Protocols Review***

PI	***Title***	***Associated HPRD***	***Associated RD***	***Reviewer***
(b)(6)	*Laboratory Animal Care & Use Training Program 2014-Rabbits*	*N/A*	*N/A*	*B. Anderson*
	Laboratory Animal Care & Use Training Program 2014-Small Lab Animals	*N/A*	*N/A*	*B. Anderson*
	Immunization of mice w/live Klebsiella pneumonia	*13-1 (Klebsiella pneumonia)*	*N/A*	*B. Anderson*
	Virulence determinants of spotted fever group rickettsia in Guinea pigs	*14-38 (R. rickettsia)*	*14-110*	*B. Anderson*
	A new animal model for MERS-CoV in swine	*11-66 (Y. pestis exempt)*	*12-320*	*B. Anderson*
	Efficacy of mAb treatment against Marburg hemorrhagic fever in a Syrian Golden hamster model	*13-90 (Marburg)*	*N/A*	*B. Anderson*
	Sentinel Animal Surveillance Program	*N/A*	*N/A*	*B. Anderson*
	Lab Animal Care & Use Training Program 2014-NHP	*N/A*	*N/A*	*B. Anderson*
	Lab Animal Breeding Production 2014	*N/A*	*N/A*	*B. Anderson*
	Analysis of C. trachomatis infected cells as possible targets of murine cytotoxic CD8+ T cells	*13-32 (Chlamydia trachomatis)*	*N/A*	*B. Anderson*
	Role of optineurin in immune response to Salmonella infection in mice	*12-44 (Salmonella typhimurium)*	*12-108*	*B. Anderson*
	Competitive indices of mCherry-expressing Salmonella typhimurium in mice	*12-44 (Salmonella typhimurium)*	*12-108*	*B. Anderson*

5) ***Biosafety Training Performed – Megan Morgan, Becky Anderson***

Type of Training	***Number of Sessions***	***Number of Employees Trained***
Select Agent Initial	***3***	***5***
BSL-3 Laboratory Biosafety	***2***	***4***
BSL-4 Laboratory Biosafety	***3***	***5***

6) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
   a) *Biological Incident Report:*
      i) *Escape of rodent outside cage 5-16-14*

7) ***Select Agent Issues***
   a) *None*

8) ***Other Issues***
   a) *OBA RAC meeting on Primary Containment of Non-human Primates in Biosafety Level 4 Laboratories*

Safety Incident Investigation Report		
Date	**Location**	**Brief Synopsis**
5/16/14	(b)(6); (b)(3):42 U.S.C. 262a(h) (Public Heatlh	Escape of rodent outside cage
Report by:	Megan Morgan	

Report Detail: *(Provide a description of the incident. This should include a timeline of the incident, the agent/animal worked with, PPE worn, description of procedures conducted at the time of the incident, notifications made, follow-up procedures for decontamination and program improvement, and results of root cause analysis. Attach additional sheets if necessary.)*

At 11:00 AM on 5/16/14, a Mastomys rodent escaped from (b)(6); (b)(3):42 U.S.C. 262a(h) (Public Heatlh Security and Bioterrorism Preparedness and Response Act) (b)(6); (b)(3):42 U.S.C. 262a(h) while the animals were being prepared for procedures on a backdraft table. The rodent had previously been infected with Lassa virus (strain Z132 from Liberia) 21 days prior. This is the first time that this specific strain of Lassa virus has been infected in the Mastomys rodent at RML. Therefore, scientific and veterinary staff cannot be certain whether the rodent ever became infected after inoculation, and if so, whether there was still virus present at the time of the incident. Another strain of Lassa virus (Soromba strain from Mali) was previously tested in Mastomys rodents at RML and was shown to clear the virus before day 21 post infection. Immediately prior to this incident, the rodents had been anesthetized in the cage and all of the animals appeared to be sufficiently under anesthesia. When the cage lid was opened carefully to remove one animal, another rodent jumped out of the cage and ran down the backdraft table to the floor. It was seen running behind the backdraft table where it then went out of sight. The individuals inside the room did not see it leave this area after that point. They searched in/around the backdraft table and the entire procedure corridor for 1-2 hours and were unable to find the rodent. Live rodent traps containing a food source were placed around the room at designated locations where recapture was most likely to occur. The lights were turned off in the room and a "Do Not Enter" sign was posted on the door to the room. Additionally, a barricade was installed at the bottom of the APR door used to enter the room and was sealed to the floor so that the rodent could not escape when personnel enter/exit. An administrative control was also implemented for personnel to visually make eye contact with the floor surrounding the door to ensure the rodent did not attempt to leave the room as the door was opened/closed. At 3:30 PM that afternoon, scientific program staff re-entered the room and the rodent was not present in any of the traps or visible at that time. It should be noted that there are many hiding places in this room and it is likely that the rodent was hiding due to the high level of personnel traffic, noise levels, and vibrations at the time. The lights remained off and the traps remained set during the night. It was expected that the rodent would emerge sometime during the evening when the room was quiet and the animal began searching for food. There were no other food sources in this room and the food in the traps should attract it into one of the many placed around the room. These rodents are known to be nocturnal animals and it was expected it would re-emerge at night when no one was in the room. Veterinary staff further confirmed that this species of rodent is known to be easily susceptible to trapping with these live traps. BSL-4 personnel entered the suite the next morning and captured the rodent in the necropsy room. The animal was disposed of in accordance with the RML BSL-4 standard operating procedures. Surface decontamination of the animal procedure corridor, necropsy room, and support room was conducted with 5% Microchem. The positive pressure suits for all personnel involved remained intact at all times and there were no breaches in the suits or gloves for anyone entering this room during or after the incident. The IRF Biosafety Manager confirmed with the RML Facility Containment Specialist that there were no facility failures for the BSL-4 at any time during the day. The air handling system (supply and exhaust), HEPA filters, effluent decontamination system, and disinfectant delivery system were all functioning properly to successfully contain any agents. Agent present: Possibly (An infected animal was present outside of the micro-isolator cage and HEPA filtered backdraft table. The animal had been infected with Lassa virus 21 days prior to the incident and exhibited no signs of illness. This is the first time this agent has been inoculated in the Mastomys rodent at RML and it is unknown whether the animal ever became infected and whether the infection would persist to 21 days.) Person(s) appropriately protected: Yes (Respiratory - suits were intact and functioned properly by staying positively pressurized, Skin - the suit remained intact to protect skin from any contact with any agents, Eye/Mucous Membrane - face shield remained intact, Parenteral - no cuts/wounds occurred)face shield remained intact, Parenteral - no cuts/wounds occurred.)

This incident does not meet the definition of an occupational exposure. All of the individuals' suits were intact and functioning properly at all times. We did not think this incident met the definition of a release of a select agent since the CDC/APHIS "Select Agents and Toxins Theft, Loss, or Release Information Document" dated June 8, 2010 states that "the laboratory room may be considered a primary containment barrier in facilities meeting the requirements of BSL-4 or BSL-3Ag as described in the 5th edition of the BMBL." The RML BSL-4 is designed and verified annually to operate in accordance with the BMBL 5th edition and the facility was operating under normal conditions with no alarms or failures at the time. We discovered that this guidance document has since been removed from the NSAR website. Since the rodent could not be immediately recaptured, the ARO reported the incident to the DSAT File Manager with the initial concern that the incident may be considered a loss if the rodent could not be recovered. The DSAT Theft, Loss, and Release Coordinator notified the ARO of receiving the notification and informed the ARO that a Form 3 was required for the "release". Therefore, this incident will be submitted to DSAT as such to let the DSAT make that determination. Even though it was unsuccessful on the first attempt, the procedure for recapturing escaped rodents was followed properly. A thorough review of the procedures for working with Mastomys rodents in the MCL is underway. It is evident that changes are needed to the general rodent husbandry procedures with respect to handling the Mastomys rodents as they behave differently than other rodent species. The following engineering and administrative controls have been proposed and will be evaluated to help prevent this type of incident from happening again in the future: 1) Implementing the use of a Coy glove box or similar flexible film isolator unit when manipulating Mastomys rodents. The cage is placed inside the box where manipulations can be performed inside. 2) Using only the animal holding rooms designed as insectaries (b)(6) for work with Mastomys, as the anteroom also functions as a procedure room, is much smaller and has fewer places for rodents to hide. 3) Developing an anesthesia induction chamber that is compatible with the Mastomys cage units instead of the isoflurane-moistened nestlette method currently in use. 4) A redesigned cage lid for this type of cage has been ordered, which should prevent the rodents from being able to climb closer to the top of the cage. 5) Work closely with the Innovive, Inc. to redesign the disposable cage unit used for these rodents. 6) Work with Carter 2 Systems, Inc. to design a prototype cage specifically for Mastomys. A meeting has been scheduled on Wednesday, May 28th between scientific program, veterinary staff, and the Biosafety staff to review these options and others that are currently being researched to determine the appropriate course of action.

- [x] No Exposure to Biological Hazards *(No further action)*
- [ ] Potential Exposure to Biological Hazards *(See RML Injury & Exposure Risk Assessment Guide)*
- [ ] Referred to _____ *(List Department/Office)*

Megan Morgan	megan.morgan@nih.gov Digitally signed by megan.morgan@nih.gov DN: cn=megan.morgan@nih.gov Date: 2014.05.22 10:24:47 -06'00'	5/22/14
RML IRF Biosafety Manager/ARO	Signature	Date
Rebecca V. Anderson on behalf of Nancy Hoe	rebecca.anderson@nih.gov Digitally signed by rebecca.anderson@nih.gov DN: cn=rebecca.anderson@nih.gov Date: 2014.05.22 10:43:02 -06'00'	5/22/14
RML Biosafety Officer/RO	Signature	Date
(b)(6)	(b)(6)	
RML OMS Nurse	Signature	Date
(b)(6)	(b)(6)	Jun 5, 2014
OMS Physician	Signature	Date

Rocky Mountain Laboratories
Injury and Exposure Risk Assessment Guide

Instructions: Complete the following risk assessment guide, in consultation with the IRF Biosafety Manager or designee and OMS Nurse, following any injury or exposure involving biohazardous agents. Occupational exposure is defined as, "Any event which results in a person not being appropriately protected in the presence of an agent or toxin, including reasonably anticipated skin, eye, mucous membrane, parenteral contact with, or respiratory exposure to infectious agents, blood or other potentially infectious materials that may result from the performance of a person's duties." Both of the following conditions must be met to result in an occupational exposure:

1. An agent or toxin must be present
2. The person must not be appropriately protected from the following routes of exposure: respiratory, skin, eyes, mucous membranes, and parenteral contact

Select the applicable categories below and circle the associated exposure risk classifications in the right column. Assign the final exposure risk classification as the highest level of any of the applicable categories. If there are any factors that increase or mitigate the risk and justifies a different risk classification, provide details in the Notes section. For any minimal, moderate, or high exposure risk classifications, activate the BEAP and notify appropriate personnel and agencies according to procedures outlined in the IRF/Select Agent Emergency Response Plan.

Date: 5/16/14
Time: 11:00 AM
Location: (b)(6); (b)(3):42 U.S.C. 262a(h) (Public Health Security and Bioterrorism

Reference Number: RML049
Agent(s) Involved: Lassa virus
Select Agents Involved: ☑ Yes ☐ No

PERCUTANEOUS (☑ N/A)
**Also complete the Sharps Injury Assessment on page 3.*

Needlestick:	Sharp Instruments or Objects:
☐ Hollow-bore needle *(*May contain more blood/fluid)*	☐ Scalpel
☐ Suture-type needle	☐ Broken Glassware/Lab ware
☐ Other	☐ Other

Injury/Exposure Category	Risk Classification
☐ Sharp had prior contact with solution or culture containing the agent, or prior contact with blood secretions, or tissue of an infected animal that is ill and likely to have organisms in the blood or secretions	HIGH/MODERATE
☐ Sharp had prior contact with blood, secretions, or tissue of an animal infected with an agent, but the animal is not likely to be viremic/bacteremic or shedding organisms (animal is not ill) ** If prior exposure to macaque monkey, consider contamination with Herpes B virus from the skin or mucosal surfaces of the animal.*	MINIMAL
☐ Sharp was sterile (no discernible contact with an infectious agent or an infected animal)	NEGLIGIBLE
☐ Cut occurred near centrifuge or from flasks containing infectious agent(s)	HIGH/MODERATE
☐ Cut resulted from sharp object highly unlikely to be contaminated in a BSL-3 or BSL-4 lab, such as a corner of a desk (no discernible contact with an infectious agent or an infected animal)	NEGLIGIBLE
☐ Injury or breach did NOT occur in the presence of an animal or in a lab with an infectious agent, or resulted in exposure to a substance later determined to be non-infectious	NO RISK
MUCOSAL (☑ N/A)	
☐ Contact of infectious agent with eyes or mucous membranes	HIGH/MODERATE
☐ Contact of body fluids or waste materials of macaque monkeys with eyes or mucous membranes (risk of Herpes B virus)	HIGH/MODERATE
☐ Contact of material unlikely to contain infectious agent with eyes or mucous membranes	MINIMAL
DERMAL (☑ N/A)	
☐ Contact of infectious agent with non-intact skin (abrasions)	HIGH/MODERATE

☐ Contact of infectious agent with intact skin but delay in cleaning the area	HIGH/MODERATE
☐ Contact of body fluids or waste materials of, or contaminated surfaces from, macaque monkeys with non-intact skin (abrasions)	HIGH/MODERATE
☐ Contact of material unlikely to contain infectious agent with non-intact skin (abrasions)	MINIMAL
☐ Direct contact of infectious agent with intact skin and area cleaned immediately	MINIMAL
☐ Injury or breach did NOT occur in the presence of an animal or in a lab with an infectious agent, or resulted in exposure to a substance later determined to be non-infectious	NO RISK
ANIMAL BITE OR SCRATCH (☑ N/A)	
☐ Animal infected with an agent and likely to be viremic or bacteremic (animal ill)	HIGH/MODERATE
☐ Animal infected with an agent but not likely to be viremic/bacteremic or shedding organisms (animal not ill)	MINIMAL
☐ Bite/scratch from a macaque (regardless of infection status)	HIGH/MODERATE
☐ Animal not infected with an agent (*Consider antibiotic prophylaxis against indigenous flora of lab animals.)*	NEGLIGIBLE
AEROSOL (☐ N/A)	
☐ Not wearing respiratory protection:	
☐ Direct splash of infectious agent or aerosolization of dried agent outside the BSC	HIGH/MODERATE
☐ Exposure from centrifuge accident with viable organisms	HIGH/MODERATE
☐ Splash or spill outside BSC of agent unlikely to be viable	MINIMAL
☐ Exposure to equipment/waste that was not adequately decontaminated	HIGH/MODERATE
☐ Exposure to equipment/waste that was decontaminated but did not meet set parameters	NEGLIGIBLE
☐ Break in respiratory protection OR ☐ Compromise of positive pressure suit (In environment <u>with</u> infectious agent or infected animal present)	
☐ Agent likely to be aerosolized	HIGH/MODERATE
☐ Agent unlikely to be aerosolized	MINIMAL
☐ Agent contained in BSC or infected animals unlikely to be shedding organisms	MINIMAL
☑ Positive pressure suit maintained adequate air flow making it unlikely for air to enter (BSL-4 only) *Suit was NOT compromised	NEGLIGIBLE
☐ Break in respiratory protection OR ☐ Compromise of positive pressure suit (In environment <u>without</u> an infectious agent or infected animal)	NO RISK
☐ Exposure to equipment (outside BSC) that may have been exposed to agent when under BSC	MINIMAL
☐ Aerosolized solution or liquid highly unlikely to be infectious	NEGLIGIBLE
☐ No discernible increased risk than would normally occur from entering a biosafety lab (used appropriate personal protective measures and no breaches in laboratory technique)	NO RISK

NOTES/DETAILS
(Attach additional sheets if necessary)

See detailed description of incident above. Even though an infected animal escaped from the micro-isolator cage and HEPA-filtered backdraft table, all personnel in the space were wearing the appropriate PPE and there were no breaches in the suits or gloves. If there were any infectious aerosols present in the room at the time the animal escaped, the suits would protect personnel from exposure and the BSL-4 lab was functioning as designed, which would protect from release of any viral particles outside the BSL-4 containment barrier.

Final Exposure Risk Classification (Highest level of any applicable category above)	☐ High/Moderate	☐ Minimal	☑ Negligible/No Risk
Biological Exposure Assessment Program (BEAP) Activated?	☐ Yes	☑ No	

Megan Morgan RML IRF Biosafety Manager	megan.morgan@nih.gov Digitally signed by megan.morgan@nih.gov DN: cn=megan.morgan@nih.gov Date: 2014.05.22 10:25:31 -06'00' Signature	5/22/14 Date
Rebecca V. Anderson on behalf of Nancy Hoe RML Biosafety Officer	rebecca.anderson@nih.gov Digitally signed by rebecca.anderson@nih.gov DN: cn=rebecca.anderson@nih.gov Date: 2014.05.22 10:43:14 -06'00' Signature	5/22/14 Date
(b)(6) RML OMS Nurse	(b)(6) Signature	Date

NIH OMS Review

Notes:

(b)(6) OMS Physician	(b)(6) Signature	Jun 5, 2014 Date

SHARPS INJURY LOG *(Complete for percutaneous injuries involving sharp devices.)*	
Type/brand name of the device involved in the injury/exposure:	
1. Did the device have engineered sharps injury protection?	☐ Yes ☐ No
2. Was the protective mechanism activated?	☐ Yes ☐ No
3. Did the injury/exposure occur before, during, or after activation of the protective mechanism?	☐ Before ☐ During ☐ After
4. How did the injury/exposure occur?	☐ While using the sharp?
	☐ Between steps of a multi-step procedure?
	☐ After use and before disposal of the sharp?
	☐ While placing sharp into sharps container?
	☐ Sharp left in inappropriate place?
	☐ Overfilled sharps container?
	☐ Disassembling the sharp?
	☐ Other

References:

1. Rusnick, JM et al. Management guidelines for laboratory exposures to agents of bioterrorism. JOEM 46(8):791-800; Aug 2004
2. Risi, G. Management of Laboratory Exposures to CDC Category A Infectious Diseases with Emphasis on Biosafety Level 4 Agents. Developed for Rocky Mountain Laboratories.
3. University of Texas Medical Branch (UTMB) Biological Exposure Evaluation and Risk Assessment documents. Developed by A. Nelson Avery, MD
4. Centers for Disease Control and Prevention and National Institutes of Health. 2009. Biosafety in Microbiological and Biomedical Laboratories, 5th ed. U.S. Government Printing Office, Washington, D.C.

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 7/17/14
Meeting Time: 1:04 PM **Adjourned:** 2:46 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Paul Carlson	☐	☒	Kevin Mora	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Megan Morgan	☒	☐
Becky Anderson (EO)	☒	☐	Frank DeLeo (EO)	☐	☒	Karin Peterson	☐	☒
Alan Applebury	☐	☒	Hideki Ebihara	☐	☒	George Risi	☐	☒
Chris Bosio	☐	☒	Heinz Feldmann (EO)	☐	☒	Dana Scott	☒	☐
Marshall Bloom (EO)	☒	☐	Nancy Hoe	☒	☐	Alexandra Scranton	☐	☒
Teresa Borino	☒	☐	Clay Jarrett	☒	☐			
Jeff Burrows	☐	☒	Josh Kellar (EO)	☐	☒			
Carol Calderwood	☐	☒	Scott Kobayashi	☒	☐			
Harlan Caldwell (EO)	☐	☒	Rachel LaCasse	☒	☐			
Marcie Caldwell (EO)	☒	☐	Alida Merritt	☒	☐			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 6/19/14 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** Action: Meeting minutes were unanimously approved with the following minor modifications: 1. On page 8, 5th bullet, 3rd sentence, change "take" to "make" 2. On page 9, item 9, the SOP title should be changed to state "Coronaviruses (excluding SARS-CoV)".

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans (New) ▪ Feldmann (LV)

	▪ **HPRD#14-160:** *Borrelia crocidurae* ▪ Becky Anderson presented the risk assessment. The goal of this study is to determine the duration of infection of *B. crocidurae* in lab-reared *Mastomys natalensis* with the goal of better defining how long these animals are infectious and capable of transmitting the spirochetes to ticks. Studies in Mali determined that a large number of wild-captured mastomys are infected with or seropositive for *B. crocidurae*. *B. crocidurae* is a spirochete that causes Tick borne relapsing fever and is characterized by recurring febrile episodes that last approx. 3 days and are separated by afebrile periods of 7 days. Each febrile episode ends with symptoms known as a "crisis" where patients develop very high fever and may become delirious, agitated, and tachycardic for a duration of 10 to 30 min. This is then followed by a phase called "flush" where they have drenching sweats and a rapid decrease in body temp. Patients that are untreated experience 1 to 4 episodes of fever. Mortality is estimated at 5-10% for untreated TBRF patients. Mortality rate for persons treated is less than 1%. Infections can be treated with penicillin and other beta lactam antimicrobials and possibly fluoroquinolones. The natural route of transmission is by the bite of an infected tick, however laboratory hazards include parenteral contact, accidental sharps injuries and exposure to aerosols. ▪ The committee discussed the containment requirements. BSL-2/ABSL-2 is appropriate for work *Borrelia crocidurae*. ▪ Animal studies with *Mastomys natelensis* rodents were proposed. ▪ Sue Priola pointed out that the registration number needs to be updated from the default number that PI Dashboard assigns. Also, in the pathogen section, the comments section describes that the organism will not be concentrated, the question should be changed to yes, the organism will be concentrated. ▪ Rachel LaCasse commented that the *Mastomys natelensis* colony should be tested to see if the animals are colonized or have already been exposed to Borrelia spp. The committee agreed that should be an issue brought up with the ACUC committee. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **HPRD#14-160** with the following minor modifications: 1. Update the registration number to HPRD#14-160. 2. In the Pathogen section, Organism Concentration, change Will Not be Concentrated to Will be Concentrated.
Item 2:	<u>Registration of Material (Potentially) Infectious for Humans (Amendment)</u>

	▪ Peterson (LPVD) ▪ **HPRD#12-103 Amend: La Crosse Virus** ▪ Becky Anderson presented the risk assessment. The amendment is to add rabbits to generate polyclonal antibodies to La Crosse virus. The hazards of working with rabbits include scratching of personnel with the hind legs and scratches with claws. To mitigate these hazards the veterinary staff uses proper rabbit restraint where the rabbit is tucked against the body or wrapped with a towel to cover their legs/claws. Lab coats are important for protection and are standard BSL-2 PPE. Claws are clipped as deemed necessary. ▪ The committee discussed the containment requirements. BSL-2/ABSL-2 is appropriate for work with La Crosse virus in rabbits. ▪ Animal studies with rabbits were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **HPRD#12-103 Amend** as written.
Item 3:	<u>Registration Documents for Recombinant DNA Experiments (Renew)</u> ▪ Best (LV) ▪ **RD#14-420:** Mechanisms of Langat virus host evasion ▪ Reviewers: Chris Bosio, Scott Kobayashi ▪ **Summary:** The RD outlines studies to understand the mechanisms that Langat virus uses to evade the host immune response. ▪ Scott Kobayashi summarized the registration. Scott Kobayashi informed the committee that this is a renewal for the registration and no major updates to the projects, just updates to personnel listings. They are studying Langat virus and it's interaction with the host response. They will be performing four types of experiments: 1. Investigate virus replication in both transformed and primary cells, 2. Individual proteins derived from Langat virus cDNA will be expressed in cells and the cells examined for their response to cytokine stimulation, 3. Make mutation in individual amino acids and proteins, examine the recombinant viruses in cell culture and mice to determine the effects of those mutations on virus replication and suppression of the immune response, 4. Perform in vivo experiments with wild type and recombinant viruses in mice to study pathogenesis and suppression of host immune response. The source of cDNA is from a collaborator on main campus. The NIH Guidelines are appropriate and Scott Kobayashi did not identify any dual use concerns associated with the proposed work. ▪ Sue Priola questioned if III-E-1 should be added for less than 2/3 of the genome

	being used. Nancy Hoe agreed that would be appropriate. ▪ Bob Heinzen stated that the way the Recombinant DNA section is written makes it sound like they do not have the clone yet, however this is a renewal so we know they have it. We should change it by removing the word "available". The committee agreed that the word available could be removed. ▪ Animal studies with mice were proposed. ▪ The committee discussed the containment requirements. BSL-2/ABSL-2 is appropriate for work with Langat virus. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#14-420** with the following minor modifications: 1. In the Recombinant DNA section, Description of recombinant molecules being used or created, change "Langat virus is available" to Langat virus from . . ." 2. In the Eukaryote Cells section, add section III-E-1 to the Proposed NIH Guidelines section. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-2-a of the NIH Guidelines. Research using eukaryotic cells will be performed at BSL-2 and is approved under III-D-1-a, III-D-3-a, and III-E-1 of the NIH Guidelines.
Item 4:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Best (LV) ▪ **RD#14-421:** Mechanisms of Flavivirus (Kunjin) virus host evasion ▪ Reviewers: Dana Scott, Bob Heinzen ▪ **Summary:** The RD outlines studies to understand the mechanisms that Flaviviruses (Kunjin) use to evade the host immune response. ▪ Dana Scott summarized the registration. This registration is almost exactly the same of the previous RD, just with a different virus. For this registration, they did include III-E-1, which is appropriate. We should have them remove the word "available" from the recombinant DNA section similar to RD-14-420. ▪ Dana Scott discussed with the committee that all the dual use answers were marked no, however, in the comments section they included a description that supports that their work cannot be readily used for harm. Dana thought it was appropriate to leave the description and keep all the answers marked no. The committee agreed to leave the answers as written. ▪ Bob Heinzen did not have any additional comments. ▪ Animal studies with mice were proposed.

	▪ The committee discussed the containment requirements. BSL-2/ABSL-2 is appropriate for work with Kunjin virus. ▪ The committee discussed the dual-use potential of these experiments. See discussion above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#14-421** with the following minor modifications: 1. In the Recombinant DNA section, Description of recombinant molecules being used or created, change "Kunjin virus is available" to "Kunjin virus from . . ." Research using prokaryotic hosts is approved at BSL-2 under sections III-D-1-a and III-E-1 of the NIH Guidelines. Research using eukaryotic cells will be performed at BSL-2 and is approved under III-D-1-a, III-D-3-a, and III-E-1 of the NIH Guidelines.
Item 5:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Best (LV) ▪ **RD#14-422:** Lentiviral systems to deliver RNAs ▪ Reviewers: Rachel LaCasse, Sue Priola ▪ **Summary:** This RD describes using lentiviruses to deliver RNAs to various cell lines and primary cells to induce RNA interference and reduce expression of cellular genes. ▪ Rachel LaCasse summarized the registration. In this registration, they will use commercially available systems to express RNA's for host genes to reduce expression. They will examine the responses to cytokines and viruses and this RD lists Langat virus and West Nile virus. The Eukaryote Cells section states BSL-2, but this is not appropriate for work with West Nile virus. The committee discussed that BSL-2 can stay in the Eukaryote Cell section, but the Recommendations section will be updated to refer personnel to review the appropriate HPRD depending on the virus that they will be using in conjunction with Lentiviruses. ▪ Marshall Bloom pointed out that complementary was spelled incorrectly in the Prokaryote Host section, Nature of Gene Sequence subsection. ▪ No animal studies were submitted, reviewed, or proposed. ▪ Sue Priola did not have any additional comments or concerns. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for work with lentiviruses. However, the appropriate biosafety level should be used when experiments with lentiviruses and infectious viruses are used. See relevant HPRDs for appropriate biosafety levels. ▪ The committee discussed the dual-use potential of these experiments. The

	committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#14-422** with the following minor modifications: 1. Add to the recommendations section the following description: "Experiments with lentiviruses that include infection with other viruses (e.g. Langat or West Nile virus) should refer to the relevant HPRD to determine the appropriate biosafety level. At a minimum, Lentiviral studies will be conducted at BSL-2." 2. In the Prokaryote Host section, the word "complimentary" should be properly spelled as "complementary". Research using prokaryotic hosts is approved at BSL-2 under sections III-D-1-a, and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells will be performed at BSL-2 and is approved under III-D-1-a and III-D-3-a of the NIH Guidelines.
Item 6:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Best (LV) ▪ **RD#14-437:** Reverse Genetics systems of Tick-borne encephalitis virus (TBEV) ▪ Reviewers: Sue Priola, Clay Jarrett ▪ **Summary:** This RD generating a reverse genetics system for TBEV. ▪ Sue Priola summarized the registration. This is a Select Agent RD for TBEV and is another renewal. They will use two plasmids to separate the genome. Seventy eight percent of the genome will be on one, but it is irreversibly defective because the signal sequence is ahead of NS1, so it is not sent to the proper part of the cell. The deleted fragment is on the other plasmid and is less than 2/3 of the genome. They will derive live virus by putting the two plasmids together in the cell. The goal of this work is to mutate different proteins in the virus to disrupt host proteins and determined the effects on virus replication and signaling processes. All the changes are expected to attenuate the viruses. The foreign genes that will be expressed will be fluorescent markers to follow these viruses. ▪ Sue Priola pointed out that Section B should have III-D-4-b removed and replaced by III-D-1-c. ▪ Sue Priola discussed the dual use questionnaire. Sue Priola asked if question B should be marked yes because they will be using synthetic biology techniques. The committee discussed and agreed that they are just using standard techniques here so the dual use form can be left as answered by the PI. ▪ Clay Jarrett did not have any additional comments or concerns. ▪ Animal studies with mice were proposed. ▪ The committee discussed the containment requirements. BSL-2 is appropriate

	for work described in Section A. BSL-4 is appropriate for work described in Section B where infectious virus is produced. ABSL-4 is appropriate for animal studies with recombinant TBEV. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#14-437** with the following minor modifications: 1. Change III-D-4-b in the NIH Guidelines of Section B to III-D-1-c. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells will be performed at BSL-4 and is approved under III-D-3-c, III-D-1-a, and III-D-1-c of the NIH Guidelines.
Item 7:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Best (LV) ▪ **RD#14-439:** Escape of the early immune response of Dengue virus ▪ Reviewers: Scott Kobayashi, Dana Scott ▪ **Summary:** This RD describes evaluating how dengue virus activates and escapes the early immune response. ▪ Scott Kobayashi summarized the registration. This RD is for working with recombinant Dengue viruses, types 1-4. The entire genomes are contained in the pBR3222 backbone and they will make mutations in several proteins from Dengue and test interactions with eukaryotic cells and determine the effects on viral replication. They will clone in *E. coli* and then express in Eukaryotic cells, cell, lines, and primary human cells. The only foreign genes inserted will be fluorescent proteins. ▪ Scott Kobayashi pointed out that there were several spelling errors of Dengue virus that should be fixed. ▪ Sue Priola pointed out that the Nature of the Gene sequence, similar to the other Best RDs should be changed to say "was provided" instead of "will be". III-E-1 also needs to be added to the Eukaryote Cell section. ▪ No animal studies were submitted, reviewed, or proposed. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for work with Dengue virus. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#14-439** with the following minor modifications:

	1. Fix spelling errors of "Dengue" throughout. 2. In the Prokaryote Host section, nature of Gene Sequence, change "will be" to "was" in the first sentence. 3. In the Eukaryote Cell Section, add III-E-1 to the NIH Guidelines. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-3-a and III-D-1-a of the NIH Guidelines. Research using eukaryotic cells will be performed at BSL-2 and is approved under III-D-3-a, III-D-I-a, and III-E-1 of the NIH Guidelines.
Item 8:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Ebihara (LV) ▪ **RD#14-430**: Viral protein expression in Drosophila S2 cells ▪ Reviewers: Bob Heinzen, Chris Bosio ▪ **Summary:** The RD describes establishing a Drosophila S2 system to transiently express viral proteins for molecular biological characterization and the production of antisera. ▪ Bob Heinzen summarized the registration. This RD is to express genes of single proteins for various virus families in Drosophila cells. The proteins will be expressed natively or tagged with affinity tags to help purify the expressed proteins. They will use recombinant expressed protein in neutralization assays to identify proteins involved in host cell interactions, then use tag proteins for affinity approached to identify host cell receptors. All the constructs will be made in E. coli and transfected into Drosophila cells. They have attached an ASP for making antiserum against the proteins. They are only expressing single proteins from each virus so there is no issue with recreating infectious virus. ▪ The committee discussed the containment requirements. BSL-2/ABSL-2 is appropriate for protein expression experiments and antibody production in mice. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#14-440** as written. Research using prokaryotic hosts is approved at BSL-2 under sections III-E-1 and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells will be performed at BSL-2 and is approved under III-D-2-a, and III-E-1 of the NIH Guidelines. Animal work with mice is approved at ABSL-2.
Item 9:	**Standard Operating Procedure: 2/3-28-01 Handling Field Collected Fluid , Blood, and Tissue Samples (NEW)**

	▪ Becky Anderson informed the committee that this SOP is for handling of Field Samples that were described in HPRD-14-158. This SOP describes procedures for handling those samples once they are brought back to RML. ▪ Nancy Hoe stated that this SOP describes handling field samples but that does not include human samples. A definition at the beginning of the SOP could be added to state the "Field Samples" include human samples. a. Change "reception" to "receipt" in the purpose section b. Add more background information on what this applies to from the risk assessment and make it clearer. Perhaps a warning box at the beginning of the SOP could include the Field Samples definition and the assessment information. c. Add restricted access to the description of the field sample room. d. 6.1.c and d- "individual animal" change to "individual or animal" e. 6.1.f add "immediately after use" at the end f. 6.2 change to either (b)(6); (b)(3):42 U.S.C. 262a(h) and/or add room number g. 6.3.d describe use of beaker, add "non-glass beaker" and say what is done with it (emptied, cleaned, re-used) h. 6.4.A.1 – explain where package is opened i. 6.5.a.1 – remove sentence, "include but not limited to" and add "as described in SOP 4-28-32" j. Section 6.5 – add section D to describe use of sealed centrifuge cups/rotors must be used and opened in BSC k. Section 7.0 – change to updated version of illness/injury response paragraph l. Section 9.0 – add reference for gamma irradiator SOP ▪ Alida Merritt stated that they need to clarify what PPE is disposable and update the PPE doffing section how PPE is decon-ed ▪ Sue Priola stated that Section 6.7.b.4 – overt exposure, personal shower should be changed to "will" be taken not "may". <u>Action:</u> The committee unanimously approved **2/3-28-01 Handling Field Collected Fluid , Blood, and Tissue Samples (NEW)** with the following minor modifications**:** 1. All changes summarized above need to be incorporated into the document.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ See attached BSO report ▪ NIH Main campus incident with small pox virus has resulted in the "Clean Sweep" of campus o They are putting together a specific plan for how we are going to

	handle it here and we are currently waiting for information from DOHS in Bethesda for details and the documentation that will be required. ○ The deadline for PI's to finish the clean sweep is September 30th, DOHS will then follow-up with a compliance check.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ Not in attendance.
Report	**IRF Biosafety Manager Report/Megan Morgan** ▪ Nothing to report
Report	**Associate Director Report/Marshall Bloom** ▪ Marshall Bloom gave a brief description of the CDC and NIH incidents that have been in the news over the last couple of weeks.
Around the room	▪ None

Other issues	▪ None

Next Meeting:

- Date: 8/21/14
- Place: Bldg A Seminar Room
- Time: 1:00 PM

RML Biosafety Committee Meeting
April 17, 2014
Biosafety Officer/Responsible Official Report

1) Requests approved by BSO since last meeting:

a) *Registration Documents for Recombinant DNA Experiments*

i) *Ebihara (LV)*

(a) ***RD-14-431 AMEND:***

(a) *add expression of hypothetical gene sequences of ORFs encoding the ancestral proteins of various RNA viruses listed on the original RD*

3) ***New requests approved by committee via electronic review:***

a) *None*

4) ***New requests***

a) *Registration of Material Potentially Infectious for Humans*

i) ***New***

(a) *Feldmann (LV)*

(a) ***HPRD-14-160:*** *Borrelia crocidurae*

ii) ***Amend***

(a) *Peterson (LPVD)*

(a) ***HPRD-12-103: La Crosse virus***

(i) Add rabbits as an animal model

b) *Registration Documents for Recombinant DNA Experiments*

i) ***Renew***

(a) *Best (LV)*

(a) ***RD-14-420:*** *The mechanisms that Langat virus uses to evade the host immune response*

(b) ***RD-14-421****: The mechanisms that flaviviruses (Kunjin virus) use to evade the host immune response.*

(c) ***RD-14-422****: Use of lentiviruses to deliver RNAs (short hairpin or micro RNA) to cells*

(d) ***RD-14-437****: Development of a reverse genetics system for tick-borne encephalitis virus (TBEV) strain Sofjin*

(e) ***RD-14-439:*** *Activation of the host innate immune response by dengue virus*

(b) *Ebihara (LV)*

(a) ***RD-14-430****: establishment of Drosophila S cells as a platform for the transient expression of viral proteins*

c) *Standard Operating Procedures*

i) ***New***

(a) ***SOP-2/3-28-01:*** *Handling Field Collected Fluid Blood and Tissue Samples*

5) ***Animal Study Protocols Review***

PI	***Title***	***Associated HPRD***	***Associated RD***	***Reviewer***
(b)(6)	*Acute CD4+ T cell depletion in TK0 BLT mice*	*12-104 (HBBF) 12-55 (HIV)*	*N/A*	*B. Anderson*
	Regulatory and effector T-cell responses to a murine retrovirus in APOBEC3 knockout mice	*N/A (Friend virus)*	*N/A*	*B. Anderson*
	Evaluation of macrophage subpopulations during LDV infection of mice	*N/A (Lactate-dehydrogenase-elevating virus)*	*N/A*	*B. Anderson*
	Evaluation of superantigen requirement for Friend virus-induced Treg responses in mice	*N/A (Friend virus)*	*N/A*	*B. Anderson*
	Determining the role of gammadeltaT17 cells in control of Y. pestis infection	*11-66 (Y. pestis exempt)*	*12-320*	*M. Morgan*

6) ***Biosafety Training Performed – Megan Morgan, Becky Anderson***

Type of Training	***Number of Sessions***	***Number of Employees Trained***
Select Agent Initial	***1***	***2***
BSL-3 Laboratory Biosafety	***2***	***4***

7) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

a) *Biological Incident Report:*
   i) *None*

8) ***Select Agent Issues***

a) *None*

9) ***Other Issues***

a) *RML Campus-Wide Inventory of Biological Material*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 8/21/14
Meeting Time: 1:04 PM **Adjourned:** 2:33 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Paul Carlson	☒	☐	Kevin Mora	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Megan Morgan	☒	☐
Becky Anderson (EO)	☒	☐	Frank DeLeo (EO)	☐	☒	Karin Peterson	☒	☐
Alan Applebury	☒	☐	Hideki Ebihara	☒	☐	George Risi	☐	☒
Chris Bosio	☒	☐	Heinz Feldmann (EO)	☐	☒	Dana Scott	☐	☒
Marshall Bloom (EO)	☐	☒	Nancy Hoe	☒	☐	Alexandra Scranton	☐	☒
Teresa Borino	☐	☒	Clay Jarrett	☐	☒			
Jeff Burrows	☐	☒	Josh Kellar (EO)	☐	☒			
Carol Calderwood	☐	☒	Scott Kobayashi	☒	☐			
Harlan Caldwell (EO)	☐	☒	Rachel LaCasse	☒	☐			
Marcie Caldwell (EO)	☐	☒	Alida Merritt	☐	☒			

(P=present; A=absent)

Guests: (b)(6)

Minutes: Meeting minutes from 7/17/14 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** Action: Meeting minutes were unanimously approved with the following minor modifications: 1. On page 9, 2nd bullet, first sentence, change "RD" to "SOP". 2. Same bullet as above, last word of paragraph was spelled incorrectly, change to "samples".

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans (New) ▪ Hasenkrug (LPVD)

	▪ **HPRD#14-161:** Diphtheria toxin ▪ Becky Anderson presented the risk assessment. The proposed studies include the use of diphtheria toxin to deplete specific cell types from transgenic mice. These mice express an inducible DTR, treatment of mice with diphtheria toxin ablates specific cell types so they can study how various cell types affect viral pathogenesis. The toxin, when absorbed, affects organs and tissues distant from the site of invasion. The most frequent complications of diphtheria are myocarditis and neuritis. Myocarditis may present as abnormal cardiac rhythms and can occur early in the course of the illness or weeks later, and can lead to heart failure. If myocarditis occurs early, it is often fatal. Neuritis most often affects motor nerves and usually resolves completely. Paralysis of the soft palate is most frequent during the third week of illness. The overall case-fatality rate for diphtheria is 5%–10%, with higher death rates (up to 20%) among persons older than 40 years of age. Treatment with hyperimmune antiserum has been shown to reduce mortality from 7 to 2.5 percent. Antibodies only neutralize toxin before its entry into cells, so rapid treatment is essential. Primary lab hazards include: inhalation of infectious aerosols and droplets; accidental parenteral inoculation; ingestion. Precautions for working with diphtheria toxin include: preparative work with toxin should be conducted in a BSC or chemical fume hood with proper PPE, up to date DTP vaccination, and workers should refer to Appendix I in the BMBL for more specific details on toxin handling. Becky Anderson stated that the up to date DTP vaccination is not listed in the recommendations section and needs to be added. ▪ Nancy Hoe added that in animal rooms, the sharps containers should be labeled "contaminated with toxin" so other personnel present in the room know what is in the waste container. ▪ The committee discussed the containment requirements. BSL-2/ABSL-2 is appropriate for work Diphtheria toxin. ▪ Sue Priola asked if it is a specific BSC that the preparative work should be conducted with the toxin. Nancy Hoe clarified that it needs to be a Class II B2. ▪ Sue Priola also questioned that on page 2, the HPRD states that they will follow ALL guidelines in Appendix I, while not all may be relevant. Rephrase to state that all appropriate guidelines will be followed. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **HPRD#14-161** with the following minor modifications: 1. Specify in the recommendations section that the BSC should be a Class II B2 BSC.

	2. Add to the recommendations section that an up to date DTP vaccine is recommended. 3. Add to the recommendations section that sharps containers in the animal rooms should be labeled, "contaminated with toxin".
Item 2:	Registration of Material (Potentially) Infectious for Humans (Amendment) ▪ Feldmann (LV) ▪ **HPRD#14-158 Amend: Field Samples** ▪ Becky Anderson presented the risk assessment. The amendment is to begin active work with Field samples. Becky Anderson specified to the committee that this HPRD is only for animal samples, human samples will be covered under Dr. Feldmann's Human Blood and Body Fluid HPRD when he updates that registration. This HPRD was approved previously as storage only until the SOP for the handling of field samples at RML was IBC approved. The SOP for handling field samples was approved at the July 17, 2014 meeting, so active work should be able to begin. ▪ Sue Priola stated that to be clear, the word "active" should be added to the type of work for the HPRD in the second sentence of the description. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **HPRD#14-158 Amend** with the following minor modifications: 1. Add the word "active" to the second sentence to describe the type of work.
Item 3:	Registration of Material (Potentially) Infectious for Humans (Amendment) ▪ Feldmann (LV) ▪ **HPRD#12-81 Amend: Hantavirus** ▪ Becky Anderson presented the risk assessment. The amendment is to add rabbits to the HPRD. The ASP is attached to the registration and describes generating polyclonal antibodies to Hantavirus. They will infect rabbits with viable Hantavirus in the ABSL-4 to generate antibodies. The primary hazards include scratching of personnel/suits with hind legs and claws. To mitigate these hazards, RMVB and LV ordered training rabbits earlier this year to determine specific procedures for handling rabbits at ABSL-4. They have developed and updated three SOPs to cover rabbit handling and they are all IBC approved, they include: 4-28-39 ABSL-4 Ferret, rabbit & Chicken anesthesia, sedation and immobilization, 4-25-40 Recapture of escaped Ferrets & Rabbits in Level 4 biocontainment, and 4-28-53 Rabbit Husbandry and Manipulation

	Procedures for Level 4 biocontainment. ▪ The committee discussed the containment requirements. ABSL-4 is appropriate for rabbit studies with Hantavirus. ▪ Animal studies with rabbits were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **HPRD#12-81 Amend** as written.
Item 4:	Registration of Material (Potentially) Infectious for Humans (Amendment) ▪ Best (LV) ▪ **HPRD#12-136 Amend: Kyasanur Forest Disease Virus** ▪ Becky Anderson presented the risk assessment. The amendment is to add mice to the HPRD. The attached ASP describes infecting mice with Kyasanur to develop an animal model to test new drugs to assess inhibition of viral replication. These animal studies will be conducted at ABSL-4. ▪ The committee discussed the containment requirements. ABSL-4 is appropriate for mouse studies with Kyasanur virus. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **HPRD#12-136 Amend** as written.
Item 5:	Registration Documents for Recombinant DNA Experiments (New) ▪ Priola (LV) ▪ **RD#14-222:** Lentiviral systems to deliver RNAs ▪ Reviewers: Hideki Ebihara, Clay Jarrett ▪ **Summary:** This RD describes using lentiviruses to express the mammalian prion protein in established and primary cell lines ▪ Hideki Ebihara summarized the registration. Hideki Ebihara stated that they will use the lentiviral vector system to express prion protein, either wild type or mutant forms of human, mouse or hamster prion protein. They will express prion proteins in primary mouse and hamster cell lines as well as established human and rat cell lines. They want to characterize the various properties to understand the mechanisms of pathogenesis. This is a well defined commercial lentiviral vector system that is safe, the safety features are described in the attached product sheets. Hideki Ebihara commented that the Prokaryotic Host Section should only describe the cloning in *E. coli* part and the additional information should be deleted.

	▪ Clay Jarret was not present, but submitted his comments to Hideki Ebihara, he asked that PrP be defined in the Synopsis section. ▪ No animal studies were submitted, reviewed, or proposed. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for work with lentiviruses. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Sue Priola abstained) **RD#14-222** with the following minor modifications: 1. Define PrP gene in the Synopsis section. 2. In the Prokaryote Host section, just describe cloning in *E. coli*. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-2-a of the NIH Guidelines. Research using eukaryotic cells will be performed at BSL-2 and is approved under III-D-1-a and III-D-3-a of the NIH Guidelines.
Item 6:	Registration Documents for Recombinant DNA Experiments (New) ▪ Bosio (LICP) ▪ **RD#14-127:** Lentiviral vectors for the development of reporter cell lines ▪ Reviewers: Rachel LaCasse, Bob Heinzen ▪ **Summary:** Use of replication deficient lentiviral reporter vectors ▪ Rachel LaCasse summarized the registration. Katy Bosio submitted this registration for lentiviral vectors as an HPRD instead of an RD so some of the relevant RD sections are missing. Sue Priola questioned the committee if they would be comfortable reviewing the information provided during the meeting and then electronically reviewing the remaining sections? The committee agreed that electronic review could be conducted after the additional sections are filled out by Katy Bosio. ▪ Rachel LaCasse then summarized the registration and described that this was another commercially available system that already expresses binding sites for the IRF1 gene that then drives expression of luciferase for a reporter system. This system will be used in conjunction with variants of *Francisella tularensis*. Rachel LaCasse stated that the Eukaryotic cell section, Nature of Experiment description should be updated to allow for some flexibility so that Katy Bosio could use other lentiviral constructs that are listed in the attached product data sheet. State “For example” in front of the IRF1 binding site. ▪ Rachel LaCasse questioned whether the listed guidelines were appropriate. Sue Priola stated that instead, III-D-1-a and III-D-3-a should be listed in the Eukaryotic Cell Section.

	▪ Bob Heinzen questioned whether we should be concerned that Francisella could pick up antibiotic resistance genes from the mammalian cell lines that were transduced with the lentiviral vector system. Bob Heinzen stated that he has never heard of and is not aware of that ever happening, but should we be concerned? Becky Anderson stated that these are quick experiments and they are not isolating any bacteria out of the experiments. Nancy Hoe added that you cannot grow a select agent in the presence of antibotics unless they are approved. Bob Heinzen stated that they could remove all antibiotics prior to infecting cells with *Francisella tularensis*. The committee discussed the concerns and agreed that removal of antibiotics prior to infection should be sufficient. ▪ No animal studies were submitted, reviewed, or proposed. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for work with lentiviruses. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee agreed to review the RD electronically once the additional sections were completed by the PI. The following information should be added and/or changes should be made: 1. Complete the additional sections of the RD registration form. 2. State in the RD that antibiotics will be removed prior to infecting cells with *Francisella tularensis.* 3. Change the guidelines in the Eukaryotic Cell section to III-D-3-a and III-D-1-a. 4. Update the Eukaryotic Cell section to add "for example" in front of the IRF1 binding site in the first sentence of the Nature of Experiment section.
Item 7:	<u>Registration Documents for Recombinant DNA Experiments (Renew)</u> ▪ Ebihara (LV) ▪ **RD#14-432:** Characterization of viral protein functions in the viral life cycle and identification of virulence determinants of Phleboviruses including SFTSV using the replicon/minigenome system and transcription competent virus like particles. ▪ Reviewers: Sue Priola, Chris Bosio ▪ **Summary:** This RD describes generating replicons, mini-genomes and virus like particles to characterize Phlebovirus pathogenesis. ▪ Sue Priola summarized the registration. This is a renewal of the RD, they want to determine Phlebovirus virulence factors with minigenomes and virus like

	particles. They plan on studying the different aspects of viral pathogenesis. They will use standard molecular biology techniques to generate minigenomes and virus like particles. It is a well written and clearly described RD with minimal changes from the last submission. There were some new viruses added to this version of the RD, which are already covered under appropriate HPRDs. The only two comments are: 1. Add III-D-3-a to the Eukaryote Host section of the NIH Guidelines and 2. Delete the first sentence in Attachment 2 under the System Description Section. This is left over from before the RD was split for the IBC committee, that sentence describes doing work with infectious Phleboviruses and that work is not associated with this RD. ▪ Chris Bosio had no additional comments or concerns. ▪ No animal studies were submitted, reviewed, or proposed. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for the described recombinant DNA registration. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved (Hideki Ebihara abstained) **RD#14-432** with the following minor modifications: 1. Add III-D-3-a to the Eukaryote Host Section 2. Delete the first sentence in Attachment 2 under the System Description Section. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-2-a of the NIH Guidelines. Research using eukaryotic cells will be performed at BSL-2 and is approved under III-D-3-a and III-E-1 of the NIH Guidelines.
Item 8:	<u>Registration Documents for Recombinant DNA Experiments (Renew)</u> ▪ Ebihara (LV) ▪ **RD#14-438**: Using reverse genetics technology to characterize viral protein function and identify virulence determinants of tick borne Phleboviruses, including SFTSV. ▪ Reviewers: Karin Peterson, Scott Kobayashi ▪ **Summary:** Development of reverse genetics systems for generation of recombinant tick-borne Phleboviruses from cloned cDNA to advance understanding of viral protein function in the viral life cycle and the molecular basis of pathogenesis. ▪ Karin Peterson summarized the registration. This RD is for the development of a reverse genetics system to Phleboviruses. They have 5 approaches described in this RD for the proposed work: 1. They will generate cDNA clones of each genome segment, 2. Construct helper plasmids, 3. Construct full length RNA

	clone plasmids of each genome segment, 4. Genetic manipulation of full length clones of each RNA genome segment, and 5. Construct chimeric clones of each RNA segment. It is well described that in any combination of a BSL-2 phlebovirus with a BSL-3 phlebovirus, the chimera is handled at BSL-3. Karin Peterson informed the committee that the dual use questionnaire has two questions answered yes by the PI, question A1 and question B. Question A1 is answered yes because they will make chimeric viruses out of BSL-2 (less pathogenic) and BSL-3 viruses (more pathogenic), it is expected that any chimeras with more pathogenic strains like SFTSV will be attenuated. The committee agreed that this was not a dual use concern. Question B was marked yes because of the techniques that they will use to conduct these studies. The committee discussed and agreed that there were no overall dual use concerns of the proposed studies. ▪ Sue Priola pointed out that the Eukaryote Host Section, item number 5 did not include the new viruses (e.g. Malsoor and Heartland) that were described in the prokaryote host section and need to be added. ▪ The committee discussed the containment requirements. BSL-2 phleboviruses and reassortants/chimeric viruses only containing BSL-2 phleboviruses will be rescued and characterized under BSL-2 enhanced conditions (physically separate lab, directional airflow, restricted access, work with all infectious material in a BSC, and PPE includes front cover gown, surgical mask, face shield, shoe covers, and two pairs of gloves). All infectious BSL-3 phleboviruses (Bhanja and SFTSV) rescue experiments and characterization of recombinant infectious virus encoding SFTSV and/or Bhanja virus genes will be conducted at BSL-3. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments above. The committee agreed that there were no overall dual-use concerns with the proposal. Action: The committee approved (Hideki Ebihara abstained) **RD#14-438** with the following minor modifications: 1. Add the new viruses to item 5 in the Eukaryote Host Section. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-2-a of the NIH Guidelines. Research using eukaryotic cells will be performed at BSL-2 or BSL-3 and is approved under III-D-3-a, III-D-3-b and III-E-1 of the NIH Guidelines.
Item 9:	**Exposure Control Plan (Annual Review)** ▪ Sue Priola informed the committee that this was an annual review of the Exposure Control Plan and that there were many changes throughout so the track changes were removed so it was easier to read.

	▪ Nancy Hoe added that she included information to make the document more similar to the main campus NIH plan. Some of the changes include a more stringent description of the clothing worn while working in labs. ▪ Alida Merritt submitted several questions by email: o Is there a supervisor or PI present in the IRF and MCL every day to be able to account for unexplained absences? If not, are coworkers responsible for reporting unexplained absences? Megan Morgan stated that workers and coworkers report to their direct PI's and they can do so even if the PI is not present on site. o Does the Environmental Services staff periodically check the antiseptic hand cleanser to make sure it has not expired? Megan Morgan informed the committee that the OMS Nurses periodically check the hand cleanser stations that are positioned in the common areas on campus. o Are RML employees screened for latex allergies/sensitivities? Paul Carlson stated that yes, RML employees are screened verbally in their meeting with OMS for latex allergies. o Page 23, last paragraph, first line, "work" should be "worn". ▪ Sue Priola pointed out that on page 21, primary barriers section, flaming inoculation loops should be deleted because open flames are not allowed. <u>Action:</u> The committee unanimously approved **Exposure Control Plan (Annual Review)** with the following minor modifications**:** 1. Page 23, last paragraph, first line, "work" should be "worn". 2. Page 21, primary barriers section, flaming inoculation loops should be deleted.
Item 10:	**Standard Operating Procedure: ABSL-3 *Coxiella burnetii* (Update)** ▪ Sue Priola informed the committee that the ABSL-3 Coxiella SOP was updated for general information as it had been a long time since the last update. ▪ Alida Merritt submitted an addition by email, in section 6.3.2, when needles are placed in a sharps container, this should be after the safety device is activated. Sue Priola questioned if they use systems with safety devices and that maybe the statement could be changed to include, "if applicable". ▪ The committee had no additional comments or concerns. <u>Action:</u> The committee approved (Bob Heinzen abstained) **ABSL-3 *Coxiella burnetii* (Update)** with the following minor modifications: 1. Update Section 6.3.2 to include that prior to placing sharps in a puncture resistant sharps container, the safety device is activated if applicable.

Item 11:	**Standard Operating Procedure: SOP#4-28-16 Husbandry Procedures for Rodents in Level 4 Biocontainment (Update)** ▪ Becky Anderson informed the committee that the next three SOPs for BSL-4 have been updated to include procedures for working with a different caging system. ▪ The committee had no additional comments or concerns. Action: The committee unanimously approved **SOP#4-28-16 Husbandry Procedures for Rodents in Level 4 Biocontainment (update)** as written.
Item 12:	**Standard Operating Procedure: SOP#4-28-38 Husbandry Procedures for Ferrets in Level 4 Biocontainment (Update)** ▪ The committee had no additional comments or concerns. Action: The committee unanimously approved **SOP#4-28-38 Husbandry Procedures for Ferrets in Level 4 Biocontainment (update)** as written.
Item 13:	**Standard Operating Procedure: SOP#4-28-39 ABSL-4 Ferret, Rabbit, and Chicken Anesthesia, Sedation, and Immobilization (update)** ▪ Alida Merritt questioned by email if there are any maximum doses for anesthetics in animals and if so, are animals euthanized if they reach the maximal dose? Rachel LaCasse stated that she is not aware of any maximal doses, but will look into it. Typically animals are not on long term studies so their lifetime exposures are not very high. ▪ Rachel LaCasse added that the statement, "Usage will be recorded in the controlled substance log" should be deleted from section 10. Drugs are recorded prior to being taken into the MCL. Action: The committee unanimously approved **SOP#4-28-39 ABSL-4 Ferret, Rabbit, and Chicken Anesthesia, Sedation, and Immobilization (update)** with the following minor modifications: 1. Delete the following statement from section 10. "Usage will be recorded in the controlled substance log".
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ See attached BSO report ▪ Nancy Hoe summarized to the committee the incident report of a HEPA filter falling out of a PAPR while in use in the (b)(6). See attached incident report.

Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ We had a natural gas line hit last week. The line was well marked, there were 3 visual indicators in place. Unfortunately, the contractor was in a hurry and operating equipment that he should not have been running. In response to the incident, remedial training has been given to all RML maintenance employees as well as all the contractors working on site. ▪ Several inspections have occurred, the NIH Fire Marshall was onsite, AAALAC visit occurred the beginning of August, DOHS performed an audit to ensure RML was following the same procedures as Bethesda, and there will be an HHS safety audit coming up in October.
Report	**IRF Biosafety Manager Report/Megan Morgan** ▪ We are busy preparing for the 3 year renewal CDC Inspection.
Report	**Associate Director Report/Marshall Bloom** ▪ Not in attendance.
Around the room	▪ Becky Anderson informed the committee that to be in compliance with the Bloodborne Pathogen Standard, we review safer sharps devices annually. This review was conducted with RML employees that work with sharps and mice frequently. The group assessed three BD devices: Safety Glide, Integra Syringe, and Safety Lok. See attached review of the safer sharps evaluation.

Other issues	▪ None

Next Meeting:

- Date: 9/18/14
- Place: Bldg A Seminar Room
- Time: 1:00 PM

RML Biosafety Committee Meeting
August 21, 2014
Biosafety Officer/Responsible Official Report

1) Requests approved by BSO since last meeting:

a) <u>*Registration of Material Potentially Infectious for Humans*</u>

i) *Feldmann (LV)*

(a) ***HPRD-12-143 AMEND:*** *MERS-CoV*

(a) *Add intranasal route of infection*

3) ***New requests approved by committee via electronic review:***

a) *None*

4) ***New requests***

a) <u>*Registration of Material Potentially Infectious for Humans*</u>

i) ***New***

(a) *Hasenkrug (LPVD)*

(a) ***HPRD-14-161:*** *Diptheria toxin*

ii) ***Amend***

(a) *Feldmann (LV)*

(a) ***HPRD-14-158:*** *Field Samples*

(i) Change from storage-only to active work

(b) ***HPRD-12-81****: Hantavirus*

(i) Add rabbits as an animal model

(b) *Best (LV)*

(a) ***HPRD-12-136****: Kyasenur Forest Disease Virus*

(i) Add mice as an animal model

b) <u>*Registration Documents for Recombinant DNA Experiments*</u>

i) ***New***

(a) *Priola (LPVD)*

(a) ***RD-14-222:*** *Use of lentiviral vectors to understand prion protein disease*

(b) *Bosio (LICP)*

(a) ***RD-127:*** *Use of lentiviral vectors to develop reporter cell lines*

ii) ***Renew***

(a) *Ebihara (LV)*

(a) ***RD-14-432****: Characterization of the pathogenesis of phleboviruses and viral protein functions and identification of virulence determinants of phleboviruses in vitro.*

(b) ***RD-14-438****: To develop reverse genetics systems for generation of recombinant tick-borne phleboviruses*

a) *Annual Review*

i) *Exposure Control Plan*

b) *Standard Operating Procedures*

i) ***Updates***

(a) ***Coxiella ABSL-3 SOP:*** *general updates*

(b) ***SOP-4-28-16:*** *Rodent Husbandry: updates for caging system*

(c) ***SOP 4-28-38****: Husbandry Procedures for Ferrets: updates for caging system*

(d) ***SOP 4-28-39****: Ferret, Rabbit, and Chicken Anesthesia: updates for caging system*

3) ***Animal Study Protocols Review***

PI	***Title***	***Associated HPRD***	***Associated RD***	***Reviewer***
(b)(6)	*The role of B cells in regulatory T cell responses during persistent viral infection*	*N/A (Friend virus)*	*N/A*	*B. Anderson*
	Efficacy of rVSV pre- and post-exposure treatment of filovirus hemorrhagic fever in a Syrian Golden Hamster model	*13-90 (Ebola and Marburg virus) 13-82 (Vesicular Stomatitis virus)*	*13-404 (replication-competent rVSV)*	*B. Anderson*
	Efficacy of rVSV expressed miRNAs as treatment of Ebola virus infection a a mouse model	*13-90 (Ebola and Marburg virus) 13-82 (Vesicular Stomatitis virus)*	*13-404 (replication-competent rVSV)*	*B. Anderson*
	Efficacy of the rVSV ZEBOV-GP vaccine against a ZEBOV Guinea isolate in NHPs	*13-90 (Ebola and Marburg virus) 13-82 (Vesicular Stomatitis virus)*	*13-404 (replication-competent rVSV)*	*B. Anderson*
	Human DPP4 knock in mice as a small animal model for MERS	*12-143 (MERS)*	*N/A*	*M. Morgan*
	Evaluation of countermeasures against Middle East respiratory syndrome coronavirus (MERS-CoV) in nonhuman primates	*12-143 (MERS)*	*N/A*	*N. Hoe*
	Efficiency of "early phase transmission" of Yersinia pestis by Xenopsylla cheopis	*13-04 (Yersinia pestis)*	*N/A*	*N. Hoe*
	Timing and examination of BBB breakdown following Salmonella typhimurium infection	*12-44 (Salmonella typhimurium)*	*12-108*	*B. Anderson*
	Evaluation of cyclosporine A inhibitors as a potential therapy for tick-borne flavivirus (TBFV) infection in mice	*12-135 (Tick-borne encephalitis virus, Far Eastern subtype) 12-136 (Kyasenur Forest disease virus)*	*N/A*	*M. Morgan*

RML Biosafety Committee Meeting
August 21, 2014
Biosafety Officer/Responsible Official Report

PI	Title	Associated HPRD	Associated RD	Reviewer
(b)(6)	*Initial testing of a recombinant attenuated Salmonella vaccine in mice*	*12-44 (Salmonella typhimurium)*	*14-126*	*B. Anderson*
	Antibody production to antigens of Borrelia burgdorferi and Leptospira species	*N/A Purified proteins*	*N/A*	*N. Hoe*
	Efficacy of combined drugs treatment against ZEBOV in NHPs	*13-90 (Ebola virus)*	*N/A*	*M. Morgan*
	The role of regulatory T cells in modulating antibody response during persistent viral infection	*N/A (Friend virus)*	*N/A*	*B. Anderson*
	Collection of normal tissues from mice	*N/A*	*N/A*	*M. Morgan*

4) ***Biosafety Training Performed – Megan Morgan, Becky Anderson***

Type of Training	Number of Sessions	Number of Employees Trained
Select Agent Initial	***2***	***6***
Select Agent Visitor	***1***	***4***
BSL-3 Laboratory Biosafety	***2***	***3***
BSL-4 Laboratory Biosafety	***2***	***2***

5) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
   a) *Biological Incident Report:*
      i) *HEPA filter fell out of PAPR in BSL-3*

6) ***Select Agent Issues***
   a) *Select Agent annual refresher training scheduled for September*
   b) *RML Select Agent Program 3-year CDC DSAT renewal inspection September 23-26*

7) ***Other Issues***
   a) *None*

Safety Incident Investigation Report		
Date	**Location**	**Brief Synopsis**
8-13-14	(b)(6)	HEPA filter cartridge fell out of PAPR
Report by:	Nancy Hoe	

Report Detail: *(Provide a description of the incident. This should include a timeline of the incident, the agent/animal worked with, PPE worn, description of procedures conducted at the time of the incident, notifications made, follow-up procedures for decontamination and program improvement, and results of root cause analysis. Attach additional sheets if necessary.)*

At ~4:30, an employee reported to DOHS that one of the HEPA filters to their PAPR had fallen out while they were working in the laboratory. The employee had been reconstituting lyophilyzed Oropouche virus stocks. Fifty microliters of the reconstituted virus samples had been incubated in AVL buffer for 10 minutes prior to being surface decontaminated and removed from the BSC. After completing the work the BSC was decontaminated with 5% Microchem. On the bench top, ethanol was added to the inactivated virus samples in AVL and then the tubes were placed in 5% Microchem prior to being removed from the laboratory. After the tubes had been sitting in the Microchem for about 8 minutes, the bottom HEPA filter in the employee's PAPR motor housing fell out. The blower motor was still functioning so the HEPA filter and the portion of the motor housing directly adjacent to where the HEPA filter sits were sprayed with 70% ethanol and the HEPA filter was immediately screwed back into the housing. The employee then exited normally. A second employee (employee #2) had been working with employee #1 in the same lab using the other BSC but had also finished work and decontaminated the BSC at the time of the incident. After exiting, the employee #2 checked the HEPA filters on the other 3M PAPRs plus their own and found that none of the other filters were loose. Employee #1 notified the manager of the (b)(6) and the Chief of LV as they could not find their supervisor. They then notified DOHS at ~4:30. DOHS recommended they report to OMS. The employee was seen by RML OMS at ~5:00pm. The employee's supervisor was notified the next day (8/14/14).

On 8/14/14 I performed the following tests:

1) Smoke testing of a PAPR: to determine if a loose HEPA housing would compromise the PAPR function, a 3M Breathe Easy PAPR was challenged with smoke with all 3 HEPA housings securely seated in the blower motor housing, or with the bottom HEPA housing unscrewed half a turn. The results indicated that the PAPR protected against smoke infiltration with all 3 HEPA filters seated securely, but that unscrewing the HEPA housing half a turn resulted in smoke infiltrating the PAPR hood.

2) Smoke testing of a BSC: a 6ft BSC similar to the one in the (b)(6) was tested. To simulate the worst-case scenario, 2 individuals were seated at the BSC and 1 person was given the smoke stick. Each person then moved their arms vigorously within the cabinet and crossed them several times, both individually and with the other person. At no time during the exercise did smoke exit the cabinet, indicating that under normal operating conditions, the BSC protected against aerosol escape.

On 8/15/14 I interviewed employee #2. The PAPR involved was autoclaved out of the lab the next day (8/14/14). Employee #2 stated that there are only two additional employees who access the (b)(6) and wear the older 3M style PAPR with the 3 filter cartridges. For the last week (8-6-14 to 8-13-14) employees #1 and #2 and another employee (employee #3)) had accessed the laboratory, however they had each been using their "own" PAPR indicating no one else but the affected employee had used the potentially compromised PAPR in the last 7 days. A review of lab access events indicated that only employee #3 might have worked with the compromised PAPR prior to this time period, but upon being interviewed they stated that they had worked in the other lab suite by themselves for the past 3 weeks and had either passaged uninfected cell lines or retrieved tubes from the freezer for work in the BSL-4 lab and had not worked with infectious virus.

Marshall Bloom was notified of the incident and it was decided that the BEAP did not need to be activated as no exposure occurred.

Agent present: No. Employees #1 and #2 were the only persons in the laboratory when the incident occurred. All of their work with infectious virus had taken place in the BSC. The BSC and the laboratory air-handling system functioned normally for the duration of their time in the lab. No spills were reported. The one other person who may have worn the potentially compromised PAPR worked alone in the other lab suite and did not work with infectious material.

Person appropriately protected: No. There are 3 HEPA filters used in the blower motor housing of this brand of PAPR (3M Breathe Easy). Removal of 1 HEPA filter results in unfiltered lab air being drawn into the PAPR and blown down onto the user's face. It is not known how long the filter was loose prior to dropping out of the blower housing.
The results of smoke testing indicate that a loose HEPA housing would compromise the ability of the PAPR to protect the user from aerosols. However, smoke testing indicated that even under the worst conditions (2 people using vigorous arm movements and crossing arms extensively), smoke (aerosol simulant) was not released from the cabinet. Therefore, even if the HEPA filter had been loose for an unknown period of time, the BSC and lab air handling systems had functioned properly to contain any aerosols (if they had been generated) and the compromised PAPR would not have resulted in the individual being exposed to infectious material.

This incident does not meet the definition of an occupational exposure or release of infectious material.

Issues Identified and Follow Up Actions: Loose filter housing: it is not known how the filter housing became loose enough to fall out. This brand of PAPR has been used extensively for years at RML and this type of incident has never been reported. During testing, it was observed that hand-tightening the filter housing made it difficult to loosen. It is possible the filter was loosened as the individual put on and tightened the belt, as it was observed that the bottom housing is automatically grasped during this process. It is also possible that the filter worked loose as the individual worked at the BSC.
Follow up: All BSL-3 and BSL-2+ users will be notified of this issue with this brand of PAPR. Signs will be placed in the anterooms to each BSL-3 and BSL-2+ laboratory with the pre-check procedure including checking that the filter housings are seated securely in the blower motor housing. This information will also be included in BSL-3 and general PAPR training for this type of PAPR.

☑ No Exposure to Biological Hazards *(No further action)*

☐ Potential Exposure to Biological Hazards *(See RML Injury & Exposure Risk Assessment Guide)*

☑ Referred to RML OMS _____ *(List Department/Office)*

_____	_____	_____
RML IRF Biosafety Manager/ARO	Signature	Date
Nancy P. Hoe		8-15-14
_____	_____	_____
RML Biosafety Officer/RO	Signature	Date
_____	_____	_____
RML OMS Nurse	Signature	Date
_____	_____	_____
OMS Physician	Signature	Date

Rocky Mountain Laboratories
Injury and Exposure Risk Assessment Guide

Instructions: Complete the following risk assessment guide, in consultation with the IRF Biosafety Manager or designee and OMS Nurse, following any injury or exposure involving biohazardous agents. Occupational exposure is defined as, "Any event which results in a person not being appropriately protected in the presence of an agent or toxin, including reasonably anticipated skin, eye, mucous membrane, parenteral contact with, or respiratory exposure to infectious agents, blood or other potentially infectious materials that may result from the performance of a person's duties." Both of the following conditions must be met to result in an occupational exposure:

1. An agent or toxin must be present
2. The person must not be appropriately protected from the following routes of exposure: respiratory, skin, eyes, mucous membranes, and parenteral contact

Select the applicable categories below and circle the associated exposure risk classifications in the right column. Assign the final exposure risk classification as the highest level of any of the applicable categories. If there are any factors that increase or mitigate the risk and justifies a different risk classification, provide details in the Notes section. For any minimal, moderate, or high exposure risk classifications, activate the BEAP and notify appropriate personnel and agencies according to procedures outlined in the IRF/Select Agent Emergency Response Plan.

Date: August 13, 2014
Time: 4:30 pm
Location: (b)(6)

Reference Number: RML055
Agent(s) Involved: Oropouche virus
Select Agents Involved: ☐ Yes ☑ No

PERCUTANEOUS (☑ N/A)
**Also complete the Sharps Injury Assessment on page 3.*

Needlestick:	Sharp Instruments or Objects:
☐ Hollow-bore needle *(*May contain more blood/fluid)*	☐ Scalpel
☐ Suture-type needle	☐ Broken Glassware/Lab ware
☐ Other	☐ Other

Injury/Exposure Category	Risk Classification
☐ Sharp had prior contact with solution or culture containing the agent, or prior contact with blood secretions, or tissue of an infected animal that is ill and likely to have organisms in the blood or secretions	HIGH/MODERATE
☐ Sharp had prior contact with blood, secretions, or tissue of an animal infected with an agent, but the animal is not likely to be viremic/bacteremic or shedding organisms (animal is not ill) ** If prior exposure to macaque monkey, consider contamination with Herpes B virus from the skin or mucosal surfaces of the animal.*	MINIMAL
☐ Sharp was sterile (no discernible contact with an infectious agent or an infected animal)	NEGLIGIBLE
☐ Cut occurred near centrifuge or from flasks containing infectious agent(s)	HIGH/MODERATE
☐ Cut resulted from sharp object highly unlikely to be contaminated in a BSL-3 or BSL-4 lab, such as a corner of a desk (no discernible contact with an infectious agent or an infected animal)	NEGLIGIBLE
☐ Injury or breach did NOT occur in the presence of an animal or in a lab with an infectious agent, or resulted in exposure to a substance later determined to be non-infectious	NO RISK
MUCOSAL (☑ N/A)	
☐ Contact of infectious agent with eyes or mucous membranes	HIGH/MODERATE
☐ Contact of body fluids or waste materials of macaque monkeys with eyes or mucous membranes (risk of Herpes B virus)	HIGH/MODERATE
☐ Contact of material unlikely to contain infectious agent with eyes or mucous membranes	MINIMAL
DERMAL (☑ N/A)	
☐ Contact of infectious agent with non-intact skin (abrasions)	HIGH/MODERATE

☐ Contact of infectious agent with intact skin but delay in cleaning the area	HIGH/MODERATE
☐ Contact of body fluids or waste materials of, or contaminated surfaces from, macaque monkeys with non-intact skin (abrasions)	HIGH/MODERATE
☐ Contact of material unlikely to contain infectious agent with non-intact skin (abrasions)	MINIMAL
☐ Direct contact of infectious agent with intact skin and area cleaned immediately	MINIMAL
☐ Injury or breach did NOT occur in the presence of an animal or in a lab with an infectious agent, or resulted in exposure to a substance later determined to be non-infectious	NO RISK
ANIMAL BITE OR SCRATCH (☑ N/A)	
☐ Animal infected with an agent and likely to be viremic or bacteremic (animal ill)	HIGH/MODERATE
☐ Animal infected with an agent but not likely to be viremic/bacteremic or shedding organisms (animal not ill)	MINIMAL
☐ Bite/scratch from a macaque (regardless of infection status)	HIGH/MODERATE
☐ Animal not infected with an agent (*Consider antibiotic prophylaxis against indigenous flora of lab animals.)*	NEGLIGIBLE
AEROSOL (☐ N/A)	
☐ Not wearing respiratory protection:	
☐ Direct splash of infectious agent or aerosolization of dried agent outside the BSC	HIGH/MODERATE
☐ Exposure from centrifuge accident with viable organisms	HIGH/MODERATE
☐ Splash or spill outside BSC of agent unlikely to be viable	MINIMAL
☐ Exposure to equipment/waste that was not adequately decontaminated	HIGH/MODERATE
☐ Exposure to equipment/waste that was decontaminated but did not meet set parameters	NEGLIGIBLE
☑ Break in respiratory protection OR ☐ Compromise of positive pressure suit (In environment <u>with</u> infectious agent or infected animal present)	
☐ Agent likely to be aerosolized	HIGH/MODERATE
☐ Agent unlikely to be aerosolized	MINIMAL
☑ Agent contained in BSC or infected animals unlikely to be shedding organisms	MINIMAL *
☐ Positive pressure suit maintained adequate air flow making it unlikely for air to enter (BSL-4 only)	NEGLIGIBLE
☐ Break in respiratory protection OR ☐ Compromise of positive pressure suit (In environment <u>without</u> an infectious agent or infected animal)	NO RISK
☐ Exposure to equipment (outside BSC) that may have been exposed to agent when under BSC	MINIMAL
☐ Aerosolized solution or liquid highly unlikely to be infectious	NEGLIGIBLE
☐ No discernible increased risk than would normally occur from entering a biosafety lab (used appropriate personal protective measures and no breaches in laboratory technique)	NO RISK

NOTES/DETAILS
(Attach additional sheets if necessary)

*This incident does not meet the definition of an occupational exposure or release of infectious material and should be considered a negligible, not minimal risk. While the PAPR was compromised, no agent was present in the laboratory outside of primary containment at the time of the incident. The results of smoke testing indicated that a loose HEPA housing would compromise the ability of the PAPR to protect the user from aerosols. In addition, smoke testing indicated that, even under the worst conditions (2 people using vigorous arm movements and crossing arms extensively), smoke (aerosol simulant) was not released from the cabinet. Therefore, even if the HEPA filter had been loose for an unknown period of time, the BSC and lab air handling system were functioning properly. Taken together, the results indicate that the compromised PAPR would not have resulted in the individual being exposed to infectious aerosols. It was out of an abundance of caution that the employee was referred to RML OMS.

Final Exposure Risk Classification (Highest level of any applicable category above)	☐ High/Moderate	☐ Minimal	☑ Negligible/No Risk
Biological Exposure Assessment Program (BEAP) Activated?	☐ Yes	☑ No	

_____	_____	_____
RML IRF Biosafety Manager	Signature	Date
Nancy P Hoe		8-15-14
_____	_____	_____
RML Biosafety Officer	Signature	Date
_____	_____	_____
RML OMS Nurse	Signature	Date

NIH OMS Review

Notes:

_____	_____	_____
OMS Physician	Signature	Date

SHARPS INJURY LOG *(Complete for percutaneous injuries involving sharp devices.)*	
Type/brand name of the device involved in the injury/exposure:	
1. Did the device have engineered sharps injury protection?	☐ Yes ☐ No
2. Was the protective mechanism activated?	☐ Yes ☐ No
3. Did the injury/exposure occur before, during, or after activation of the protective mechanism?	☐ Before ☐ During ☐ After
4. How did the injury/exposure occur?	☐ While using the sharp?
	☐ Between steps of a multi-step procedure?
	☐ After use and before disposal of the sharp?
	☐ While placing sharp into sharps container?
	☐ Sharp left in inappropriate place?
	☐ Overfilled sharps container?
	☐ Disassembling the sharp?
	☐ Other

References:

1. Rusnick, JM et al. Management guidelines for laboratory exposures to agents of bioterrorism. JOEM 46(8):791-800; Aug 2004
2. Risi, G. Management of Laboratory Exposures to CDC Category A Infectious Diseases with Emphasis on Biosafety Level 4 Agents. Developed for Rocky Mountain Laboratories.
3. University of Texas Medical Branch (UTMB) Biological Exposure Evaluation and Risk Assessment documents. Developed by A. Nelson Avery, MD
4. Centers for Disease Control and Prevention and National Institutes of Health. 2009. Biosafety in Microbiological and Biomedical Laboratories, 5th ed. U.S. Government Printing Office, Washington, D.C.

Summary of safer sharps evaluation

Date: June 23, 2014

Participants: (b)(6)

Devices Evaluated

Device Name	Manufacture
Safety Glide	BD Medical
Integra Syringe	BD Medical
Safety Lok	BD Medical

Purpose of evaluation: to determine if there are devices available that would reduce the risk of sharps injuries. This is an annual evaluation to maintain compliance with the RML Exposure Control Plan.

Method of evaluation: Safer sharps devices, water for testing, and oranges for test injections were handed out. Evaluation sheets were handed out to the participants to complete after they finished their testing. Four participants filled out the evaluation sheets, there was also much discussion among the participants about the utility of each device.

Results

I. General Feature Assessment: A rating of one (1) indicates the lowest level of agreement with the statement, five (5) the highest. Not applicable (N\A) may be used if the question does not apply to this product.

Shaded blocks indicate highest score for the feature.

II.

	Device Average Score		
	BD Safety Glide	BD Integra Syringe	BD Safety Lok
The safety feature can be activated using a one-handed technique	3.3	2.3	4.3
The user's hands remain behind the needle/sharp until activation of the safety mechanism is complete	3.5	3.8	4.0
The safety feature does not interfere with normal use of this product (including disposal)	3.3	3.0	2.7+
Use of this product requires you to use the safety feature	1.5	1.8	2.0+
A clear and unmistakable change (either audible or visible) occurs when the safety feature is activated	3.8	2.8	3.3+
The device is easy to handle while wearing gloves	3.3	2.8	3.5
This device does not require more time to use than a non-safety device	3.8	3.3	3.8
The exposed sharp is blunted or covered after use and prior to disposal	4.5	3.8	4.3
Use of this product does not increase the number of failed attempts at this procedure	3.5	3.3	2.5
Sterilization (if applicable) of this device is as easy as a standard device	4.7+	4.7+	4.7+
The product does not require extensive training to be operated correctly	3.5	3.5	3.3
The product can be used without causing more patient/animal discomfort	4.3	4.3	3.8

** Each + sign indicates the number of N/A marked down out of 4 participants.

III. Would you recommend this device/Additional Comments

Device	Would you recommend this device?	Additional comments
BD Safety Glide	Yes/No	
	Yes	For certain applications it might be useful
	Yes	Easy to push the needle off while trying to activate the safety mechanism. It is kind of bulky. The bulk makes it difficult to draw up sample from smaller tubes.
	Yes	For certain applications. Difficult to see through the glass at a steep angle. May not turn easily with the inner tube, which may prove difficult when performing intracranial injections.

Device	Would you recommend this device?	Additional comments
BD Integra	No	
	Yes	Maybe for certain applications if you can inject the final animal without the needle retracting.
	Yes/No	Concerned about accidental retraction while injecting animals.
	Yes/No	No sure.

Device	Would you recommend this device?	Additional comments
BD Safety Lok	Yes/No	Would be good for circumstances when you pre fill syringes before a procedure.
	Yes	For certain applications only, and would require some user experience.
	Yes	This would be good for multiple injections; it keeps the needle and surface clean. It is easy to unsheathe again and could lead to false security. It is harder to see the increments through the two tubes.
	Yes	For certain procedures.

Recommendations:

1. Overall the group was interested in the BD Safety Glide. The Safety Glide still allowed for pretty good visibility around the safety device. The gradations on the syringe were still clearly visible and not obstructed by the safety device. The shield was very easy to engage, however 2 users popped the entire needle/safety device off when trying to engage the shield. Experience and practice would be necessary to effectively use this device.

Conclusions:

The group was interested in the BD Safety Glide needle and is willing to test it in non-containment conditions first.

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 9/18/14
Meeting Time: 1:05 PM **Adjourned:** 1:45 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Paul Carlson	☐	☒	Kevin Mora	☐	☒
Bob Heinzen, Vice Chair	☐	☒	Bruce Chesebro (EO)	☐	☒	Megan Morgan	☒	☐
Becky Anderson (EO)	☒	☐	Frank DeLeo (EO)	☐	☒	Karin Peterson	☒	☐
Alan Applebury	☐	☒	Hideki Ebihara	☒	☐	George Risi	☐	☒
Chris Bosio	☒	☐	Heinz Feldmann (EO)	☐	☒	Dana Scott	☒	☐
Marshall Bloom (EO)	☐	☒	Nancy Hoe	☐	☒	Alexandra Scranton	☐	☒
Teresa Borino	☒	☐	Clay Jarrett	☐	☒			
Jeff Burrows	☒	☐	Josh Kellar (EO)	☐	☒			
Carol Calderwood	☐	☒	Scott Kobayashi	☒	☐			
Harlan Caldwell (EO)	☐	☒	Rachel LaCasse	☒	☐			
Marcie Caldwell (EO)	☒	☐	Alida Merritt	☐	☒			

(P=present; A=absent)

Guests: (b)(6)

Minutes: Meeting minutes from 8/21/14 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** Action: Meeting minutes were unanimously approved with the following minor modifications: 1. Attach the incident report and BSO report. 2. Sue Priola pointed out some minor typos.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans (Renew) ▪ Hackstadt (LICP) ▪ **HPRD#14-39: *Rickettsia prowazekii***

	▪ Becky Anderson presented the risk assessment. This registration is for storage only of *R. prowazekii*. When Ted Hackstadt decides to resume work with *R. prowazekii*, he will need to submit an amendment for active work as well as provide an updated SOP that includes validated inactivation procedures for *R. prowazekii.* ▪ The committee discussed the containment requirements. BSL-3 is appropriate for storage of *R. prowazekii*. ▪ No animal studies were submitted, reviewed, or proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **HPRD#14-39** as written.
Item 2:	Registration of Material (Potentially) Infectious for Humans (Renew) ▪ Hackstadt (LICP) ▪ **HPRD#14-41: *Coxiella burnetii*** ▪ Becky Anderson presented the risk assessment. This registration is for storage only of *C. burnetii*. When Ted Hackstadt decides to resume work with *C. burnetii*, he will need to submit an amendment for active work as well as provide an updated SOP that includes validated inactivation procedures for *C. burnetii.* ▪ The committee discussed the containment requirements. BSL-3 is appropriate for storage of *C. burnetii*. ▪ No animal studies were submitted, reviewed, or proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **HPRD#14-41** as written.
Item 3:	Registration of Material (Potentially) Infectious for Humans (New) ▪ Peterson (LPVD) ▪ **HPRD#14-162: Herpes Simplex Virus-1 (HSV-1)** ▪ Becky Anderson presented the risk assessment. The proposed studies are to examine how the innate immune response affects HSV-1 infection and pathogenesis of the CNS. HSV-1 is associated mainly with above the waist infections involving the mouth pharynx, face, eye, and CNS. HSV-2 is associated mainly with below the waist infections. Primary infections with HSV-1 are usually acquired in childhood and may be asymptomatic or subclinical. Symptomatic primary infections present mainly as gingivostomatitis with fever, sore throat, fetor oris, anorexia, cervical adenopathy, and mucosal edema and

	vesicular and ulcerative painful lesions involving the buccal mucosa, tongue, gums, and pharynx. Ulcers heal within 2-3 weeks. HSV-1 can be treated with antiviral drugs like acyclovir, foscarnet, Valacyclovir, etc. The natural route of transmission is through close personal contact and direct contact with contaminated secretions or sexual contact. The primary lab hazards include direct contact with viral isolates, aerosolization of material, droplet or inhalation exposure of mucous membranes of the eyes, nose, or mouth. To mitigate these hazards the committee discussed the containment requirements, see below. ▪ The committee discussed the containment requirements. BSL-2/ABSL-2 is appropriate for studies with HSV-1. When working with purified virus or conducting any procedures that might create splashes, goggles should be worn. ▪ Becky Anderson informed the committee that this HPRD includes aerosol generating procedures that include the use of a tissue homogenizer. The recommendations section should include: precautions should be taken to look for broken/open tubes before opening the Precellys Bead Mill Homogenizer. If tubes are broken, open the Homogenizer inside the BSC. ▪ Becky Anderson informed the committee that this registration includes recombinant strains that will be obtained from a collaborator, no recombinant work will be performed at RML. ▪ Sue Priola pointed out that the description section should be updated to specify that cells run on flow cytometry are "fixed". ▪ Sue Priola also informed the committee that the NIH Guidelines should be removed from the Eukaryote Cells section since no recombinant work will be performed at RML. The strains will be obtained from a collaborator. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **HPRD#14-162** with minor modifications: 1. Add to the recommendations section precautions for opening Precellys Bead Mill Homogenizer if tubes are broken or leaking. 2. Clarify in the Description Section that cells for flow cytometry are "fixed". 3. Delete the reference to the NIH Guidelines in the Eukaryote Cell Section.

Item 4:	Registration of Material (Potentially) Infectious for Humans (New) ▪ Ebihara (LV) ▪ **HPRD#14-163: Nairoviruses** ▪ Becky Anderson presented the risk assessment. The proposed studies are to understand the molecular basis of Nairovirus viral life cycle, pathogenesis, and mechanisms of virulence acquisition and evolution. This HPRD contains a list of Nairoviruses, and not all Nairoviruses listed are known to be human pathogens. Infection with the BSL-2 classified Nairoviruses (as listed in the table) is typically self-limiting illness with symptoms such as fever, headache, photophobia, nausea, and back/joint pains. Illness is short lived in duration and lasts 2-8 days. ▪ Issyk-Kul virus is characterized with symptoms of: abrupt onset of high fever for 3-8 days, headache, dizziness, pharyngitis, cough, muscle pain, nausea and vomiting, rash abdominal pain, chills pain in the eyes and photophobia. Acute period of disease lasts about 8 days, convalescent period is 4-6 weeks and is always followed by weakness. No recorded deaths. ▪ Kasokero virus: not much information is available, when first isolated (in 1970's) laboratory acquired infections occurred resulting in mild to severe illness. Lab infections presented with fever, headache, abdominal pain, diarrhea, chest pain, myalgia and arthralgia. Symptoms lasted approximately 7 to 10 days with a complete recovery, however, joint pain lasted for over a month after recovery. No recorded deaths. ▪ For all the listed Nairoviruses, no specific treatment is available, supportive care is provided. Currently there are no vaccines available. The natural route of transmission is through a tick bite, the primary lab hazards include parenteral inoculation, generation of aerosols, tick bites, and accidental needle sticks. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for all listed viruses, except Issyk-Kul and Kasokero virus, these are BSL-3 viruses. The BSL-2 viruses will be handled at BSL-2 with the following additional precautions: all work with infectious material is performed in the BSC, PPE includes a disposable gown, surgical mask, face shield, double gloves, and disposable shoe covers. ▪ No animal studies were submitted, reviewed, or proposed. ▪ Sue Priola commented that blanket approval could not be given for all Nairoviruses. In the attachment describing Nairoviruses, the first sentence of the last paragraph should be updated to state, "all *known* nairoviruses, *listed in this table* . . . " ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **HPRD#14-163** with the following

	minor modifications: 1. Clarify in the attachment material, first page, last paragraph, first sentence that "all known nairoviruses listed in this table . . ."
Item 5:	<u>Registration of Material (Potentially) Infectious for Humans (Amendment)</u> ▪ Hasenkrug (LPVD) ▪ **HPRD#12-155 Amend: HIV-1** ▪ Becky Anderson presented the risk assessment. This amendment is to add FACS sorting of unfixed cells from HIV infected humanized mice. The primary hazard from this procedure is the generation of aerosols while sorting cells. To mitigate these hazards, Kim Hasenkrug has developed an SOP for sorting of HIV infected, unfixed cells. Included in the attached SOP are the following precautions: 1. moving sorter into smaller, isolated room, with negative airflow 2. FACS Aria is equipped with the Aerosol Management System (AMS) that rapidly evacuates aerosolized particles that are produced inside the sort chamber. The AMS creates a negative pressure inside the sort chamber and draws aerosolized particles into a HEPA filter. 3. FACS Aria is also equipped with a Camera Visualization system, a camera is used to monitor the sort stream and alerts the operator to potential increased aerosols. The operator can control and correct the sort stream. If the stream drifts or clogs, the system will automatically shut down. 4. A Pre-Sort check must be conducted prior to each sort which validates the aerosol containment system, this is a pre-check that was developed at NIH by Kevin Holmes of RTB. 5. A sign is posted on the door that infectious material is being sorted, the door is locked to prevent entry of unauthorized personnel and the following PPE is worn: ▪ PAPR ▪ Front cover gown ▪ Gloves-double 6. Post sort, everything is disinfected with bleach and/or ethanol ▪ Sue Priola questioned the order of spraying and removing PPE in section 2.5.4 of the attached SOP. Please have them clarify the order. Sue Priola also stated that spraying disinfectant on all work surfaces before leaving the lab during an emergency should not be required. Megan Morgan stated that section 5.1.2 could be updated to state that if they have time, they can spray the surfaces down. The committee agreed that would be appropriate.

	▪ The committee discussed the containment requirements. BSL-2 enhanced with the listed precautions are sufficient for FACS sorting of HIV infected cells. ▪ No animal studies were submitted, reviewed, or proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **HPRD#12-155 Amend** with the following minor modifications: 1. Clarify the order in the attached SOP that PPE will be doffed, section 2.5.4. 2. Add to the emergency section 5.1.2 that personnel should spray disinfect work surfaces, "if you have time."
Item 6:	**Standard Operating Procedure: ABSL-3 Operations and Safety Procedures (OSP) (Annual Review)** ▪ Sue Priola informed the committee that the ABSL-3 OSP was updated after undergoing annual review by biosafety. ▪ Sue Priola recommended the following changes: a. Add ARO's to the sentence about needing an SRA on page 9 b. On page 25, bullet e., change "verify" to "ensure", this represents what the RMVB staff is doing each time they open the autoclave. c. On page 25, update bullet c. to reference fever and OMS procedures to make it consistent with other SOPs. d. Page 28, determine what is meant by "ignition sources" and change or clarify if necessary. ▪ The committee agreed with Sue Priola's suggestions and had no additional comments or concerns. Action: The committee unanimously approved **ABSL-3 Operations and Safety Procedures (Annual Review)** with the following minor modifications: 1. Add ARO's to the sentence about needing an SRA on page 9 2. On page 25, bullet e., change "verify" to "ensure". 3. On page 25, update bullet c. to reference fever and OMS procedures to make it consistent with other SOPs. 4. Page 28, determine what is meant by "ignition sources" and change or clarify if necessary.

Item 7:	**Standard Operating Procedure: BSL-3 Operations and Safety Procedures (Annual Review)** ▪ Sue Priola informed the committee that the BSL-3 OSP was updated after undergoing annual review by biosafety. There were very few minor changes which included updating visitor access requirements and added a statement that the PI is responsible for ensuring the shipper complies with all permits and conditions. ▪ Sue Priola recommended the following changes: a. On page 11, add ARO's to the sentence describing the need for an SRA. b. Page 34, bullet e, change "verify" to "ensure". ▪ The committee agreed with Sue Priola's suggestions and had no additional comments or concerns. Action: The committee unanimously approved **BSL-3 Operations and Safety Procedures (Annual Review)** with the following minor modifications: 1. On page 11, add ARO's to the sentence describing the need for an SRA. 2. Page 34, bullet e, change "verify" to "ensure".
Item 8:	**Standard Operating Procedure: BSL-3 Powassan Virus (b)(6) SOP (Update)** ▪ Becky Anderson informed the committee that the Powassan virus SOP was updated to make the inactivation and removal SOP consistent with the Powassan virus SOP that is in place in the (b)(6) The only changes are to BSL3-POW-D-7 Extraction of POWV RNA, cDNA synthesis. ▪ The committee had no comments or concerns. Action: The committee unanimously approved **BSL-3 Powassan Virus (b)(6) SOP (Update)** as written.
Item 9:	**Standard Operating Procedure: (b)(6), *Coxiella burnetii* inactivation procedures (Update)** ▪ Sue Priola informed the committee that all Select Agent PI's were asked to review their inactivation procedures and conduct validation studies of inactivation procedures. Bob Heinzen updated his (b)(6) SOP to add BSL-3-Cb-5, Inactivation of *Coxiella burnetii* and subcomponents for removal from the BSL-3 laboratory. ▪ Sue Priola commented that the following statement in the (b)(6) SOP that will be reviewed next should be added, "Any protocol used to fix or sterilize samples must be validated, and the validation documented, prior to removing samples from the laboratory. A record shall be maintained in the suite of all sterilizing treatments used, and the date the validations are made."

	▪ The committee had no additional comments or concerns. Action: The committee unanimously approved (b)(6) ***Coxiella burnetii* inactivation procedures (Update)** with the following minor modifications: 1. Add the following statement from the (b)(6) SOP, "Any protocol used to fix or sterilize samples must be validated, and the validation documented, prior to removing samples from the laboratory. A record shall be maintained in the suite of all sterilizing treatments used, and the date the validations are made."
Item 10:	**Standard Operating Procedure:** (b)(6) ***Yersinia pestis* inactivation procedures (Update)** ▪ Sue Priola informed the committee that th(b)(6) SOP was also updated to clarify the inactivation procedures. ▪ Sue Priola pointed out that the document does not specify 1% Roccal throughout and the SOP should be updated so that all references to Roccal include 1%. ▪ The committee had no additional comments or concerns. Action: The committee unanimously approved (b)(6) ***Yersinia pestis* inactivation procedures (Update)** with the following minor modifications: 1. Specify 1% Roccal throughout the SOP.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ BSO report will be provided at the next IBC meeting.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ Not in attendance.
Report	**IRF Biosafety Manager Report/Megan Morgan** ▪ We are preparing for the CDC DSAT inspection next week. ▪ There have been no incidents to report since the last IBC meeting.
Report	**Associate Director Report/Marshall Bloom** ▪ Nothing to report.
Around the room	▪ Sue Priola reminded the committee that the minutes are available to the public upon request. Our IBC received a request from (b) (6) for the last 4 months of IBC meeting minutes and these minutes were sent to him.

Other issues	▪ None

Next Meeting:

- Date: 10/16/14
- Place: Bldg A Seminar Room
- Time: 1:00 PM

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 10/16/14
Meeting Time: 1:03 PM **Adjourned:** 2:30 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Paul Carlson	☒	☐	Kevin Mora	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Megan Morgan	☒	☐
Becky Anderson (EO)	☒	☐	Frank DeLeo (EO)	☐	☒	Karin Peterson	☒	☐
Alan Applebury	☒	☐	Hideki Ebihara	☒	☐	George Risi	☒	☐
Chris Bosio	☒	☐	Heinz Feldmann (EO)	☐	☒	Dana Scott	☐	☒
Marshall Bloom (EO)	☒	☐	Nancy Hoe	☒	☐	Alexandra Scranton	☐	☒
Teresa Borino	☒	☐	Clay Jarrett	☒	☐			
Jeff Burrows	☐	☒	Josh Kellar (EO)	☐	☒			
Carol Calderwood	☐	☒	Scott Kobayashi	☒	☐			
Harlan Caldwell (EO)	☐	☒	Rachel LaCasse	☐	☒			
Marcie Caldwell (EO)	☐	☒	Alida Merritt	☒	☐			

(P=present; A=absent)

Guests: (b)(6)

Minutes: Meeting minutes from 9/18/14 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** Action: Meeting minutes were unanimously approved with the following minor modifications: 1. On page 8, delete "should be added" in bullet 1, first sentence. 2. On page 8, specify that IBC meeting minutes are available to the public, "upon request".

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans (New) ▪ Hinnebusch (LZP)

	▪ **HPRD#14-164: *Staphylococcus aureus*** ▪ Becky Anderson presented the risk assessment. The goal of the studies is to compare and contrast the fates of *S. aureus* and *Y. pestis* during interactions with neutrophils. *S. aureus* will serve as a control in experiments aimed at characterizing the interactions of *Y. pestis* with neutrophils. *S. aureus* is an opportunistic pathogen that can cause a variety of self-limiting to life-threatening diseases in humans. *S. aureus* is one of the most common causes of skin, soft-tissue, and nosocomial infection. The bacteria are a leading cause of food poisoning, resulting from the consumption of food contaminated with enterotoxins. Staphylococcal food intoxication involves rapid onset of nausea, vomiting, abdominal pain, cramps, and diarrhea. Symptoms usually resolve after 24 hours. If treatment is necessary *S. aureus* infections can be treated with cloxacillin and cephalexin. The natural route of transmission is ingestion of contaminated food, vertical transmission, and human to human transmission if in contact with purulent lesions. The primary lab hazards include, ingestion of infected material, generation of aerosols, and accidental sharps injury. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for studies with *S. aureus*. ▪ No animal studies were submitted, reviewed, or proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved (Clay Jarrett and Chris Bosio abstained) **HPRD#14-164** as written.
Item 2:	<u>Registration of Material (Potentially) Infectious for Humans (Renew)</u> ▪ Ebihara (LV) ▪ **HPRD#14-110: Bunyamwera virus** ▪ Becky Anderson presented the risk assessment. She informed the committee that this is a renewal of two separate HPRDs that are being combined, HPRD 12-110 and HPRD 12-111. They were originally separated because one HRPD contained BSL-2 orthobunyaviruses and one contained BSL-3 orthobunyaviruses. The proposed studies include understanding the molecular basis of the orthobunyavirus viral life cycle, pathogenesis, mechanisms of virulence acquisition and evolution. Some of the orthobunyaviruses cause disease in humans. Most commonly, the orthobunyaviruses that are worked with at BSL-2 cause a self-limiting illness that presents with fever, headache, photophobia, stiff neck, arthralgia, rash and back or joint pain. Typically illness lasts approximately 2-7 days and is followed by a period of weakness. Some of the bunyaviruses are asymptomatic or present with minimal symptoms and the infection is unrecognized unless seroconversion is detected. The BSL-2 classified viruses that can cause a more severe illness in humans include: Cache

	Valley virus, La Crosse virus, and Ilesha virus. Cache Valley virus has 1 reported case where a severe systemic infection was reported. La Crosse virus can cause severe illness with encephalitis, especially in children under 16 years old. Ilesha virus causes a febrile illness with exanthema and erythema, and in some cases meningoencephalitis or hemorrhagic fever has developed. ▪ For the BSL-3 classified viruses: Ngari, Germiston, Oropouche, Iquitos, Madre de Dios, and Enseada viruses: disease can range from febrile illness to severe headache, myalgia, arthralgia, anorexia, nausea, vomiting, weakness, dizziness, and photophobia, some patients can even exhibit meningitis symptoms. There are no specific treatments, typically supportive care is given, and treatment with IV ribavirin has been tried in some cases. The natural route of transmission is through arthropods such as mosquitos, ticks and sand flies. The primary lab hazards include accidental sharps injuries, parenteral inoculation, and generation of aerosols. ▪ The committee discussed the containment requirements. BSL-3 Bunyamwera viruses include Ngari, Germiston, Oropouche, Iquitos, Madre de Dios, and Enseaeda virus and will be handled at BSL-3. All other Bunyamwera viruses listed on this HPRD are to be handled at BSL-2. ▪ Becky Anderson informed the committee that dual use question A1 was answered yes due to the proposed generation of genetic reassortants by co-infection. The Eukaryotic Cell section contained a detailed description of the proposed combinations and the HPRD contained a description of why the PI believes the proposed studies are not of dual use concern. The committee extensively discussed the dual use potential, and agreed that the reassortants likely will result in attenuation of the viruses. Hideki Ebihara explained that most will result in attenuation, but one particular combination comparable to Ngari virus should result in a virus of similar virulence. The committee requested a more detailed description of the expected outcomes and what "as virulent" means for which reassortants. Sue Priola pointed out to the committee that the attachment states that they will not do further combinations between strains until they have more data to predict the results of additional reassortant combinations. They are not planning to do random combinations. The committee agreed that there are no overall dual use concerns with the proposed studies. ▪ Sue Priola pointed out that flow cytometry is listed in the registration. She clarified with Hideki Ebihara that this will be on fixed cells only. The registration should be updated to state fixed cells. ▪ Sue Priola noted that in the Eukaryotic Cell section, Experiment 6, Ilesha is spelled incorrectly. She also noted in the recommendations section that it clearly indicates that BSL-2 viruses will be handled at BSL-2. The same statement should be made for the BSL-3 viruses, that they will be handled at BSL-3.

	▪ No animal studies were submitted, reviewed, or proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Hideki Ebihara abstained) **HPRD#14-110** with the following minor modifications: 1. On the attached dual use assessment, clarify what "as virulent" means and that it is not expected to be more virulent than parental strains. 2. Specify throughout that flow cytometry will be on fixed cells 3. Correct the spelling of "Ilesha" on Experiment 6 of the Eukaryote Cell section. 4. Specify in the recommendations section that BSL-3 viruses will be handled at BSL-3.
Item 3:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Ebihara (LV) ▪ **RD#14-419**: Characterization of viral protein functions in of human pathogenic orthobunyaviruses ▪ Reviewers: Karin Peterson, Bob Heinzen ▪ **Summary:** Characterization of viral protein functions in viral life cycle and identification of virulence determinants of human pathogenic orthobunyaviruses by reverse genetics systems ▪ Karin Peterson summarized the registration. This is a renewal of the Bunyamwera virus RD. This RD is for the development of reverse genetics systems for Bunyamwera viruses, minigenomes/replicon systems, and transcription/replication competent virus like particles (VLPs). Karin Peterson stated that the description was confusing about the replication incompetent VLPs in the synopsis section. Karin Peterson clarified that these VLPs can infect a cell, but cannot replicate within the cell. The committee discussed that the wording might be clearer if the wording in the parenthesis is deleted. Nancy Hoe stated that technically, they are genome replication competent, which is why the wording is confusing. ▪ Karin Peterson went on to inform the committee that most of the RD is a renewal of the same research, but there is a new section proposed that includes generating and characterizing hypothetical viruses possessing the ancestral genome reconstructed using genome sequences from human pathogenic, non-pathogenic, and less-pathogenic viruses. The dual use questions A1 and B are answered yes in regard to these experiments because they generate new recombinant viruses. The other studies that were previously reviewed by the IBC, but are described in the dual use section, include generating reassortants and chimeric viruses with either the current circulating viruses or the ancestral viruses. Hideki Ebihara attached to the RD descriptions

	of why these strains will not likely be more virulent than the currently circulating strains. ▪ The committee extensively discussed the potential dual use concerns of generating the ancestral viruses and potential for increased virulence. Sue Priola questioned if it was possible that the current strains were attenuated compared to the previous strains. She asked what data is available to support the hypothesis that the current strains are more virulent than the ancestral strains. Hideki stated that the ancestral strains are only about 150 years old, so it is not that long in evolution. He also informed the committee that he has studied the ancestral viral proteins (not live virus) and the main virulence factor is missing in many of the ancestral viruses, suggesting that the current strains are more virulent. Hideki Ebihara also stated that they evaluate these hypothetical ancestral strains by characterizing proteins first, and then would move on to the next step of generating the viruses. This approach gives them more information on the ancestral viruses before they generate them. He further stated that the phylogenic studies show the viruses are all close, so they do not expect big changes between the current and ancestral strains. ▪ Bob Heinzen questioned how virulence and pathogenicity testing would be determined for reassortants and for the ancestral viruses. Hideki Ebihara stated that they would perform *in vitro* studies in human macrophages to assess growth kinetics. Bob Heinzen stated that he didn't expect them to put all the new viruses through animal studies, but that is the only way to determine pathogenicity. Karin Peterson agreed with Hideki Ebihara that the *in vitro* studies would help to predict virulence. The committee discussed and agreed that there were no overall dual use concerns, but it would be helpful if Hideki Ebihara updated the attached dual use description to describe that the phylogenic study shows the ancestral viruses are not that different from current strains, add information on the initial biochemical data from protein analysis of ancestral proteins, and also discuss in better detail reasons why it is not expected to generate a more virulent virus. ▪ Sue Priola pointed out that the sections that describe flow cytometry should be clarified to state "fixed" cells. She also noted on the attached dual use sheets that the first page, description section 1, first sentence, HPRD should be changed to RD. ▪ Sue Priola also informed the committee that sections III-D-1-a and III-D-1-b of the NIH Guidelines should be added to the Research Product section and III-D-1-b should be added to the Eukaryotic Cell section. ▪ The committee discussed the containment requirements. Generation of replicons/minigenomes, transcription/replication-competent virus like particles, and replication incompetent recombinant viruses can be worked with under BSL-2 conditions. Generation of recombinant infectious bunyaviruses must be carried out at BSL-2 or BSL-3 depending on the highest level of the parental

	virus. ▪ No animal studies were submitted, reviewed, or proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Hideki Ebihara abstained) **RD#14-419** with the following minor modifications: 1. On the attached dual use assessment, describe that the phylogenic study shows the ancestral viruses are not that different and add information on the initial biochemical data on ancestral proteins. Also describe in further detail that the genetic divergence of the ancestral genes is small and it is not expected to generate a more virulent virus, etc. 2. Specify throughout that flow cytometry will be on fixed cells 3. Delete in the Description section, "non-infectious/non-viral replication-incompetent" 4. In the Eukaryotic cells section, Experiment 2, change "replication-competent" to "genome replication competent" 5. For the research product section, add III-D-1-a and III-D-1-b to the NIH Guidelines section. 6. For the Eukaryotic cells section, add III-D-1-b to the NIH Guidelines section. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-2-a of the NIH Guidelines. Research using eukaryotic cells will be performed at BSL-2 or BSL-3 and is approved under sections III-D-1-a, III-D-3-a, and III-D-1-b of the NIH Guidelines.
Item 4:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Ebihara (LV) ▪ **RD#14-431 Amend**: The amendment is to add rabbits ▪ Reviewers: Rachel LaCasse, Dana Scott ▪ **Summary:** The amendment is to add animal work with rabbits. ▪ Both Rachel LaCasse and Dana Scott were not in attendance. Rachel LaCasse informed Megan Morgan by email that she had no concerns with the amendment. Sue Priola summarized the registration. The amendment is to add animal work with rabbits. Hideki Ebihara would like to generate antibodies in rabbits against 15 different proteins from Phleboviruses. ▪ The committee discussed the containment requirements. BSL-2/ABSL-2 is appropriate for studies generating antibodies with Phlebovirus protein in rabbits.

	▪ Animal studies with rabbits were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Hideki Ebihara abstained) **RD#14-431 Amend** as written. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-2-a of the NIH Guidelines. Research using eukaryotic cells will be performed at BSL-2 and is approved under III-D-2-a and III-E-1 of the NIH Guidelines. Animal experiments with recombinant protein are approved at ABSL-2.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Nancy Hoe reviewed the BSO report. ▪ Nancy Hoe informed the committee that DOHS will soon begin performing compliance checks for NIH's Clean Sweep. ▪ Nancy Hoe updated the committee on the CDC DSAT inspection that occurred September 23-26 for the 3 year program renewal. Overall, the inspection went well and there were only a few minor comments that were brought up at the exit briefing.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ We have completed the 2014 lab inspections. The top labs were Bob Heinzen's and Olivia Steele-Mortimer's. ▪ Since the last meeting, there have been 2 on the job injuries. The first was a lifting injury and the second was a motorcycle rider that was hit by the front gate at the guard station. Paul Carlson is working with ORF to modify the front gate to be user friendly to bicyclists and motorcyclists.
Report	**IRF Biosafety Manager Report/Megan Morgan** ▪ We are starting our annual shutdowns of the BSL-4 labs for maintenance activities.
Report	**Associate Director Report/Marshall Bloom** ▪ Today at 3:30 in (b)(6) there will be a presentation by George Risi and Andrea Marzi describing their experiences in Africa and the Ebola outbreak.
Around the room	▪ None

Other issues	▪ None

Next Meeting:

- Date: 11/20/14
- Place: Bldg A Seminar Room
- Time: 1:00 PM

1) Requests approved by BSO since last meeting:

a) *Student Projects*

i) *Rosa (Stewart)*

(a) *isolate genomic DNA from cultures of Borrelia burgdorferi and Leptospira biflexa (non-infectious saprophyte); perform restriction digests and PCR and analyze results using agarose gel electrophoresis.*

3) ***New requests approved by committee via electronic review:***

a) *None*

4) ***New requests***

a) *Registration of Material Potentially Infectious for Humans*

i) ***New***

(a) *Hinnebusch (LZP)*

(a) ***HPRD-14-164:*** *Staphylococcus aureus*

ii) ***Renew***

(a) *Ebihara (LV)*

(a) ***HPRD-14-110:*** *Bunyamwera virus*

b) *Registration Documents for Recombinant DNA Experiments*

i) ***Renew***

(a) *Ebihara (LV)*

(a) ***RD-14-419****: Characterization of viral protein functions in viral life cycle and identification of virulence determinants of human pathogenic orthobunyaviruses by reverse genetics*

ii) ***Amend***

(a) *Ebihara (LV)*

(a) ***RD-14-431****: Molecular characterization of viral proteins of pathogenic RNA viruses*

(i) Add rabbit model of infection

a) ***Animal Study Protocols Review***

Title	*Associated HPRD*	*Associated RD*	*Reviewer*
Regulation of innate immune responses in mouse model of HSV-1 infection	*12-183 (La Crosse virus) 14-162 (HSV-1)*	*N/A*	*B. Anderson*

Title	*Associated HPRD*	*Associated RD*	*Reviewer*
Antiretroviral efficacy of RetroMad1 in HIV-infected humanized mice	*12-55 (HIV) 12-104 (HBBF)*	*N/A*	*M. Morgan*
Virulence determinants of rOmpA mutants of spotted fever group rickettsia in Guinea pigs	*14-38 (Rickettsia spp (select-agent exempt)*	*14-110*	*N. Hoe*
Evaluation of Fx06 for the treatment of Ebola hemorrhagic fever in Syrian hamsters	*13-90 (Ebola)*	*N/A*	*M. Morgan*
Role of Gm-CSF in pneumonic tularemia in the mouse	*13-71 (F. tularensis)*	*N/A*	*B. Anderson*
Antibody production against phlebovirus NSs Protein	*N/A*	*14-431*	*B. Anderson*
Modulating effects of the Ebola virus L gene upstream open reading frame on virulence in mice	*13-90 (Ebola)*	*12-407*	*B. Anderson*
Systems biology approach to examine the host response to Ebola virus infection; the role of sGP/ssGP and the GP mucin-like domain in viral pathogenicity	*13-90 (Ebola)*	*12-407*	*B. Anderson*
Defining early target cells of Nipah virus infection	*13-91 (Nipah virus)*	*N/A*	*B. Anderson*
The mechanism of Treg suppression during persistent viral infection	*N/A (Friend virus)*	*N/A*	*B. Anderson*
Evaluation of ocular attenuation of a plasmid deficient STD Chlamydia trachomatis strain in cynomologus monkeys	*13-32 (C. trachomatis)*	*N/A*	*B. Anderson*

2) ***Biosafety Training Performed – Megan Morgan, Becky Anderson***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
Select Agent Annual Refresher	***8***	***142***
Hazard Training (for construction contractors)	***2***	***20***
BSL-3 Laboratory Biosafety	***1***	***3***
BSL-4 Annual Refresher	***3***	***15***

3) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
   a) *Biological Incident Report:*
      i) *None*

4) ***Select Agent Issues***
   a) *RML Select Agent Program 3-year CDC DSAT renewal inspection September 23-26*

5) ***Other Issues***
   a) *Clean Sweep compliance checks*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 10/29/14
Meeting Time: 1:33 PM **Adjourned:** 1:50 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Paul Carlson	☐	☒	Kevin Mora	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Megan Morgan	☒	☐
Becky Anderson (EO)	☒	☐	Frank DeLeo (EO)	☐	☒	Karin Peterson	☒	☐
Alan Applebury	☐	☒	Hideki Ebihara	☒	☐	George Risi	☐	☒
Chris Bosio	☒	☐	Heinz Feldmann (EO)	☐	☒	Dana Scott	☐	☒
Marshall Bloom (EO)	☐	☒	Nancy Hoe	☒	☐	Alexandra Scranton	☐	☒
Teresa Borino	☒	☐	Clay Jarrett	☒	☐			
Jeff Burrows	☒	☐	Josh Kellar (EO)	☐	☒			
Carol Calderwood	☒	☐	Scott Kobayashi	☒	☐			
Harlan Caldwell (EO)	☐	☒	Rachel LaCasse	☒	☐			
Marcie Caldwell (EO)	☒	☐	Alida Merritt	☐	☒			

(P=present; A=absent)

Guests: (b)(6)

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** ▪ Since this was not a regularly scheduled committee meeting, the minutes from the previous meeting were not reviewed. The minutes from the October 26th meeting will be reviewed at the November meeting.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	<u>Purpose of Special Committee Meeting</u> ▪ This meeting was called to select a working group to review the inactivation procedures used at RML for Ebola virus and other enveloped, negative stranded RNA viruses at BSL-4. ▪ No human pathogen or recombinant DNA registration documents were reviewed at this meeting.
Item 2:	<u>Meeting Discussion</u> ▪ Sue Priola informed the committee that the data for the inactivation of Ebola

virus is unpublished. In order to keep the data confidential while allowing for a thorough scientific review by the IBC, it was suggested that a working group could be established to meet separately, review the scientific data, and make a recommendation to the full committee on their findings. Sue Priola stated that the charter for the IBC allows working groups to meet and review material, with the IBC establishing the working group and reviewing the summary of their meeting.

- The recommended working group members are Nancy Hoe, Sue Priola, Bob Heinzen, Karin Peterson, and Chris Bosio. Each of these members were selected based on their knowledge and expertise. The committee had no comments or concerns on the selection of the working group members.
- Sue Priola reviewed for the committee the points that the working group would consider as the reviewed the data for the inactivation procedures of Ebola virus. They would review on two major points:
    - The scientific approach: use of appropriate controls, sample types, infectivity of sample, sensitivity of the assay used, in vitro or in vivo based assay, numbers of samples tested, etc.
    - The results: what level of inactivation do the methods achieve, are the results relevant, etc.
- There were no additional comments to add to the list of points to review.
- Sue Priola asked the group if they would be ok with potentially minor updates or changes that may be necessary to add to the SOPs once the working group has reviewed the inactivation data. The committee agreed that the working group could make a recommendation to the full committee at the next regularly scheduled IBC meeting. The SOPs that include inactivation procedures are:
    - SOP#4-28-27 Removal of Specimens for Irradiator
    - SOP#4-28-31 Removal of Specimens for Protein Analysis
    - SOP#4-28-32 Removal of Specimens for Nucleic Acid Extraction
    - SOP#4-28-33 Removal of Specimens for Fluorescence, Immunofluorescence, Histopathology, Immunohistopathology, and flow cytometry
- Theresa Borino asked if these SOPs are only for work conducted here at RML or do they include procedures for work in West Africa. (b)(6) stated that the SOPs are for RML, but the same procedures that are validated at RML are used by the RML group in West Africa.
- There were no additional questions or comments from the committee. The committee will receive an electronic recommendation from the working group about the inactivation procedures and the committee will be asked to vote to

	accept the recommendations of the working group.
Around the room	▪ None

Other issues	▪ None

Next Meeting:

- Date: 11/20/14
- Place: Bldg A Seminar Room
- Time: 1:00 PM

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 11/20/14
Meeting Time: 1:04 PM **Adjourned:** 1:53 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Paul Carlson	☒	☐	Kevin Mora	☐	☒
Bob Heinzen, Vice Chair	☐	☒	Bruce Chesebro (EO)	☐	☒	Megan Morgan	☒	☐
Becky Anderson (EO)	☒	☐	Frank DeLeo (EO)	☐	☒	Karin Peterson	☒	☐
Alan Applebury	☐	☒	Hideki Ebihara	☒	☐	George Risi	☐	☒
Chris Bosio	☒	☐	Heinz Feldmann (EO)	☐	☒	Dana Scott	☐	☒
Marshall Bloom (EO)	☒	☐	Nancy Hoe	☒	☐	Alexandra Scranton	☐	☒
Teresa Borino	☒	☐	Clay Jarrett	☒	☐			
Jeff Burrows	☐	☒	Josh Kellar (EO)	☐	☒			
Carol Calderwood	☐	☒	Scott Kobayashi	☒	☐			
Harlan Caldwell (EO)	☐	☒	Rachel LaCasse	☐	☐			
Marcie Caldwell (EO)	☒	☐	Alida Merritt	☐	☒			

(P=present; A=absent)

Guests: (b)(6)

Minutes: Meeting minutes from 10/16/14 and 10/29/14 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** Action: Meeting minutes for 10/16/14 and 10/29/14 were unanimously approved as written.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans (Amendment) ▪ Feldmann (LV) ▪ **HPRD#13-90 Amend: Filoviridae** ▪ Becky Anderson presented the risk assessment. The amendment is to add the aerosol route of infection to the Filoviridae HPRD. This route of infection is

	pending DSAT approval. The ASP is attached and describes aerosol infection of NHPs by the Biaera MP aerosol exposure system. The primary lab hazards include generation of aerosols by the aerosol exposure system. To mitigate these hazards, the IBC previously reviewed and approved the SOP for the aerosol system: SOP#4-28-43 Aerosol Exposure System Operation. The SOP outlines that the aerosol generation system is placed inside a Class II BSC within the ABSL-4 suite. The NHP's will use a head only system, so the heads are the only part of the body that will be exposed. Once the procedure is complete, the head of the NHP will be wiped down with 70% EtOH, a clean diaper will be placed in the transport container for each NHP, and caution will be taken to not touch the head during transport ▪ The committee discussed the containment requirements. BSL-4/ABSL-4 is appropriate for aerosol exposure studies on non-human primates with Ebola virus. ▪ Animal studies with non-human primates were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **HPRD#13-90 Amend** as written. **PENDING DSAT AUTHORIZATION**.
Item 2:	<u>Registration of Material (Potentially) Infectious for Humans (Renew)</u> ▪ Feldmann (LV) ▪ **HPRD#13-92 Amend: Bunyaviridae (Crimean-Congo Hemorrhagic Fever virus, CCHFV)** ▪ Becky Anderson presented the risk assessment. The amendment is to add another animal specials, they are adding animal work with hamsters. The ASP is attached and describes testing hamsters as a new model of CCHFV. These hamsters are STAT2 knock outs and are proposed to be a more suitable hamster model as the wild type hamsters are resistant to infection. The primary hazards include rodent bites or scratches. There are several IBC approved rodent SOPs already in place to mitigate the hazards of working with rodents. Hamsters are not a new animal species to BSL-4, only for the CCHFV HPRD. The IBC approved rodent SOPs include: 1. 4-28-16 Husbandry Procedures for Rodents in Level 4 Biocontainment 2. 4-28-21 ABSL4 Rodent Inhalant Anesthesia 3. 4-28-41 Recapture of Escaped Rodents in Level 4 Containment 4. 4-28-48 Inoculation/Infection and Blood Collection Procedures for Rodents in Level 4 Biocontainment ▪ The committee discussed the containment requirements. BSL-4/ABSL-4 is appropriate for studies with CCHFV in hamsters.

	▪ Animal studies with hamsters were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **HPRD#13-92 Amend** as written.
Item 3:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Feldmann (LV) ▪ **RD#14-407**: Generation and characterization of recombinant Ebola viruses ▪ Reviewers: Sue Priola, Chris Bosio ▪ **Summary:** Generation of mutant Ebola virus for *in vitro* and *in vivo* studies. ▪ Sue Priola summarized the registration. She informed the committee that this RD is a renewal for work generating recombinant Ebola viruses. This RD combines work described in RD#08-411, RD#11-428, and RD#12-407 into a new RD-14-407. The other two RDs will be inactivated now that this work is covered in one registration. The work describes using full length clones and recombinant clones for use *in vitro* and *in vivo* for pathogenesis studies. They will also generate mutant Ebola viruses and take genes from less virulent strains and introduce them into more virulent strains and vice versa. They have marked the dual use question 1A yes, but state that it is unlikely to generate a more virulent strain than that of the parent strains. Sue Priola agreed with that statement. She stated the dual use question B should be marked yes, because they are using synthetic biology techniques to generate the recombinant viruses. The committee discussed and agreed that B should be check yes. Sue Priola noted that work with full length clones can be performed in the restricted access BSL-2 lab, the full length clone lab. Please note that attached to the registration is the waiver letter from OBA. ▪ For the NIH Guidelines, Sue Priola stated that III-D-2-a is appropriate. Nancy Hoe stated that III-E-1 should be removed because it applies to cultivating constructs in tissue culture. ▪ Sue Priola stated that Section B addresses generating recombinant Ebola viruses, but does not include the types of cell lines that will be used, this should be added. Also, in section B on the attached sheets, there is a reference number listed, (1). This should be deleted, there are no references included. ▪ Chris Bosio had no additional comments or concerns. ▪ The committee discussed the containment requirements. BSL-4/ABSL-4 is appropriate for studies with recombinant Ebola viruses. ▪ Animal studies with mice and guinea pigs were proposed. ▪ The committee discussed the dual-use potential of these experiments as

	described above. The committee agreed that there were no overall dual-use concerns with the proposal. Action: The committee unanimously approved **RD#14-407** with the following minor modifications: 1. In Section A, Section III-E-1 of the NIH Guidelines should be deleted. 2. On the dual use form, question B should be checked yes. 3. In the attached description for Section B, a list of cell lines should be added. 4. In the attached description for Section B, delete the reference number (1) in the text. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-2-a of the NIH Guidelines. Research using eukaryotic cells will be performed at BSL-4 and is approved under sections III-D-1-a, III-D-3-c, and III-D-1-c of the NIH Guidelines.
Item 4:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Feldmann (LV) ▪ **RD#14-427**: Ebola and Marburg virus minigenome and transcription/replication competent virus-like particle (VLPs) systems ▪ Reviewers: Scott Kobayashi, Clay Jarrett ▪ **Summary:** Generation of Ebola and Marburg minigenomes and transcription/replication competent VLP systems to establish life cycle modeling systems ▪ Scott Kobayashi summarized the registration. Similar to the previous RD, the Feldmann lab is combining two RDs, one of which will now be inactivated (RD 12-403). This RD will either use Ebola or Marburg in regards to making VLPs and minigenomes. They will generate these systems to monitor expression of small portions of the genome. They will conduct experiments with or without helper virus. The studies without helper virus will be conducted at BSL-2, the studies with helper virus will be conducted at BSL-4. ▪ Sue Priola questioned if they are actually using helper virus or helper plasmid in section B. This should be clarified. ▪ The committee discussed the containment requirements. The studies without helper virus will be conducted at BSL-2, the studies with helper virus will be conducted at BSL-4. Animal studies will be conducted at ABSL-4. ▪ Animal studies with mice and non-human primates were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#14-427** with the following minor modifications:

	1. Clarify if helper plasmid or helper virus is being used in Section B. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-2-a of the NIH Guidelines. Research using eukaryotic cells will be performed at BSL-2 or BSL-4 and is approved under sections III-D-1-a, III-D-3-c, and III-E-1 of the NIH Guidelines.
Item 5:	**Standard Operating Procedure: MCL Operations and Safety Procedures (OSP) (Annual Review)** ▪ Sue Priola informed the committee that the MCL OSP was updated after undergoing annual review by biosafety. ▪ Becky Anderson informed the committee that the two larger updates to the document were to page 33 to add a paragraph describing safety procedures for personnel and samples during inventory audits. The second update was on page 65 to describe that two people should be present while handling sharps with animals. ▪ Nancy Hoe stated that the 2 person rule should be clarified as to what the second person's role is and where they need to be. Becky Anderson stated that she would discuss wording with (b)(6) to make sure the description matched the way they currently operate when handling sharps in the lab. Action: The committee unanimously approved **MCL Operations and Safety Procedures (OSP) (Annual Review)** with the following minor modifications: 1. Clarify the statement describing the two-person rule for handling sharps with animals.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Nancy Hoe reviewed the BSO report.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ There has been one injury since the last IBC meeting. It was an injury caused by lifting and twisting at the same time, the employee was absent from work for a day and a half. ▪ Employees are reminded to be careful while crossing campus during the winter conditions.
Report	**IRF Biosafety Manager Report/Megan Morgan** ▪ We are working on the annual shutdown of BSL-4 suites. Currently one suite is down, the next suite is scheduled for December.

Report	**Associate Director Report/Marshall Bloom** ▪ Nothing to report.
Around the room	▪ None

Other issues	▪ None

Next Meeting:

- Date: 12/18/14
- Place: Bldg A Seminar Room
- Time: 1:00 PM

RML Biosafety Committee Meeting
November 20, 2014
Biosafety Officer/Responsible Official Report

1) Requests approved by BSO since last meeting:

a) Registration Documents for Recombinant DNA Experiments

i) Amend

(1) Hinnebusch (LZP)

***(a)* RD-12-320:** Site-specific mutagenesis of *CDC-exempt Yersinia pestis strains*

(i) *Add subcutaneous, intravenous, and intraperitoneal routes of infection for mouse studies*

2) ***New requests approved by committee via electronic review:***

a) *None*

3) ***New requests***

a) *Registration of Material Potentially Infectious for Humans*

i) ***Amend***

(a) *Feldmann (LV)*

(a) ***HPRD-13-90:*** *Filoviridae, Ebolavirus and Marburgvirus*

(i) Add aerosol route of inoculation

(b) ***HPRD-13-92****: Bunyaviridae*

(i) Add hamsters

b) *Registration Documents for Recombinant DNA Experiments*

i) ***Renew***

(a) *Feldmann (LV)*

(a) ***RD-14-407:*** *generation of mutant Ebola virus*

(b) ***RD-14-427****: generation of Ebola/Marburg virus VLPs, minigenomes, and transcription/replication competent VLPs*

4) ***Animal Study Protocols Review***

Title	***Associated HPRD***	***Associated RD***	***Reviewer***
Evaluation of eye drop vaccination for effective delivery of plasmid-minus strain in a murine model of C. trachomatis genital tract infection	*13-32 (C. trachomatis)*	*N/A*	*B. Anderson*
The role of mitochondria in neuronal degeneration of scrapie infected mice	*N/A*	*N/A*	*M. Morgan*
Evaluation of STAT2 KO hamsters as disease models for multiple agents of viral hemorrhagic fever	*12-81 (Hantavirus) 13-92 (CCHF) 13-94 (Arenaviridae) 13-90 (Filovridae)*	*N/A*	*M. Morgan*

RML Biosafety Committee Meeting
November 20, 2014
Biosafety Officer/Responsible Official Report

Title	*Associated HPRD*	*Associated RD*	*Reviewer*
Injection of human CJD isolates of the of the genotype Met/Val into transgenic mice expressing the human prion protein	*12-51 (CJD)*	*N/A*	*B. Anderson*
Immunotherapeutic blockade of PD-1, TIM-3, and SIRPα to treat murine retrovirus infection in mice	*N/A*	*N/A*	*B. Anderson*
The role of transcription factors Foxo1 and Foxo3 on infection levels and effector and regulatory T cell responses to a murine retrovirus	*N/A*	*N/A*	*B. Anderson*
Aerosol challenge and the generation of aerosols by Ebola virus in cynomolgous macaques	*13-90 (Ebola)*	*N/A*	*N. Hoe*
Analysis of CD4+ T cells in a murine model of C. trachomatis genital tract infection in mice	*13-32 (C. trachomatis)*	*N/A*	*B. Anderson*
Immunization of mice with live-attenuated Y. pestis	*11-66 (Y. pestis (exempt)*	*12-320*	*M. Morgan*
Post-exposure of rVSV/ZEBOV in Rhesus Macaques against challenge with a West African Zaire Ebolavirus strain	*13-90 (Filoviridae) 13-82 (VSV)*	*13-404*	*M. Morgan*
Efficacy of sodium stibogluconate against tularemia in mice	*13-71 (F. tularensis)*	*N/A*	*N. Hoe*

5) ***Biosafety Training Performed – Megan Morgan, Becky Anderson***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
Select Agent Initial Training	***1***	***3***
Select Agent Visitor Training	***1***	***12***
Full-length Clone Lab Annual Refresher	***1***	***1***
BSL-4 Annual Refresher	***2***	***2***

6) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
a) *Biological Incident Report:*
i) *None*

7) ***Select Agent Issues***
a) *None*

8) ***Other Issues***
a) *Clean Sweep compliance checks*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 12/18/14
Meeting Time: 1:02 PM **Adjourned:** 2:04 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☐	☒	Paul Carlson	☒	☐	Kevin Mora	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Megan Morgan	☒	☐
Becky Anderson (EO)	☒	☐	Frank DeLeo (EO)	☐	☒	Karin Peterson	☒	☐
Alan Applebury	☐	☒	Hideki Ebihara	☐	☒	George Risi	☒	☐
Chris Bosio	☒	☐	Heinz Feldmann (EO)	☐	☒	Dana Scott	☒	☐
Marshall Bloom (EO)	☐	☒	Nancy Hoe	☐	☒	Alexandra Scranton	☐	☒
Teresa Borino	☐	☒	Clay Jarrett	☒	☐			
Jeff Burrows	☐	☒	Josh Kellar (EO)	☐	☒			
Carol Calderwood	☐	☒	Scott Kobayashi	☒	☐			
Harlan Caldwell (EO)	☐	☒	Rachel LaCasse	☒	☐			
Marcie Caldwell (EO)	☒	☐	Alida Merritt	☐	☒			

(P=present; A=absent)

Guests: (b)(6)

Minutes: Meeting minutes from 11/20/14 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** Action: Meeting minutes for 11/20/14 were unanimously approved as written.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans (New) ▪ Hackstadt (LICP) ▪ **HPRD#14-165: *Yersinia pseudotuberculosis*** ▪ Becky Anderson presented the risk assessment. The proposed studies describe using *Y. psuedotuberculosis* to express Chlamydial genes to see if the products are secreted by the type III secretion system. The recombinant work will be

	described in the RD later this meeting. *Yersinia pseudotuberculosis* is a rare cause of acute enteric disease with symptoms such as acute mesenteric lymphadenitis and gastroenteritis associated with abdominal pain and fever (diarrhea is unusual). One to 3 weeks after the acute phase of the disease, post-infectious complications can occur, such as reactive arthritis and erythema nodosum. The arthritic phase of the disease can last up to 6 months. Other complications include lesions to lymph nodes, spleen and liver, as well as septicemia in immunocompromised patients. The disease is most common in children and young adults and immunocompromised individuals are at greater risk of severe disease or death. Infections are usually self-limiting, but *Y. psuedotuberculosis* is susceptible to ampicillin, third generation cephalosporins, aminoglycosides, tetracyclines, and chloramphenicol. The natural route of transmission is through the fecal-oral route, consumption of contaminated food and/or water, and contact with infectious soil. The primary lab hazards include: accidental sharps injuries, ingestion, or generation of aerosols. ▪ To mitigate these hazards, the committee discussed the containment requirements. BSL-2 is appropriate for work with *Y. pseudotuberculosis*. ▪ Alex Scranton was not present, but submitted questions to Bob Heinzen by email. She asked why the antibiotic resistance question was answered yes, but they do not expand upon that comment. Becky Anderson informed the committee that the antibiotic resistance profiles are fully described in the RD that is referenced in that section. The committee agreed that the reference to the appropriate RD was sufficient information in the HPRD. Alex Scranton also pointed out that the RD number should be corrected from RD 14-126 to RD 14-128. ▪ No animal studies were submitted, proposed or reviewed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **HPRD#14-165** with minor modifications: 1. In the antibiotic resistance line under Pathogen and/or Toxin, change RD 14-126 to RD 14-128.
Item 2:	<u>Registration of Material (Potentially) Infectious for Humans (New)</u> ▪ Chesebro (LPVD) ▪ **HPRD#14-166: Human blood and body fluids containing human transmissible spongiform encephalopathy agents** ▪ Becky Anderson presented the risk assessment. The purpose of the study is to test the transmissibility of humans TSEs in a transgenic mouse model. 1. The disease course for persons with CJD see a gradual onset of confusion, progressive dementia, myoclonic jerks with spasticity,

wasting and coma; slight elevation of CSF proteins; death usually occurs in less than 1 year; 10% cases have family history of dementia; amorphous amyloid plaques in cerebellum of 15% of cases.

2. Gerstmann-Straussler-Scheinker disease (GSS) is an extremely rare, neurodegenerative brain disorder. It is almost always inherited and is found in only a few families around the world. Onset of the disease usually occurs between the ages of 35 and 55. In the early stages, patients may experience varying levels of a lack of muscle coordination, including clumsiness, unsteadiness, and difficulty walking. As the disease progresses, the ataxia becomes more pronounced and most patients develop dementia. Other symptoms may include slurring of speech, involuntary movements of the eyes, rigid muscle tone, and visual disturbances, sometimes leading to blindness. Deafness also can occur. In some families, parkinsonian features are present.

- The incubation period is 15 months to 2 years. There are no specific treatments available, just treatment for the symptoms. CJD is not known to be transmitted through the air or other forms of casual contact. Exposure to brain tissue and spinal cord fluid from infected individuals should be avoided to prevent transmission of the disease through these materials. In some cases, CJD has spread to other people from grafts of dura mater (a tissue that covers the brain), transplanted corneas, implantation of inadequately sterilized electrodes in the brain, and injections of contaminated pituitary growth hormone derived from human pituitary glands taken from cadavers. There are no reported cases of someone contracting CJD from a blood transfusion. The primary lab hazards include: accidental parenteral inoculation or ingestion. The risk of infection from aerosols, droplets, and exposure of intact skin, gastric, and mucous membranes is unknown; however there is experimental evidence in hamsters that nasal mucosa is an effective route of infection.
- To mitigate these hazards, the committee discussed the containment requirements. BSL-2/ABSL-2 is appropriate for studies with human TSE agents. These studies will be conducted in a restricted access BSL-2 lab with the following PPE: gown, respirator, and gloves. Typical disinfectants are not effective on these agents. NaOH, Environ LpH, and incineration, or moist heat with autoclaving for longer than average periods of time are effective and therefore required.
- Animal studies with mice were proposed.
- Alex Scranton asked by email, the HPRD describes using NHP models at a later date. Will the committee get to review that before the work is started? Becky Anderson informed the committee that yes, any new animal species to an HPRD or RD is reviewed by the IBC in order for the PI to obtain approval to perform those studies.
- The committee discussed the dual-use potential of these experiments. Dual

	use question 4 was checked yes. The committee discussed the included description by the PI that described why it was not a dual use concern. The committee agreed that there were no overall dual-use concerns with the proposal. Action: The committee unanimously approved **HPRD#14-166** as written.
Item 3:	Registration of Material (Potentially) Infectious for Humans (New) ▪ Chesebro (LPVD) ▪ **HPRD#14-167: Human Immunodeficiency virus (HIV)** ▪ Becky Anderson presented the risk assessment. This HPRD is for storage only of HIV samples. When they wish to resume work with these samples they will update the HPRD and procedures will be reviewed by the IBC. ▪ The committee discussed the containment requirements. These samples for storage only and can be stored in the BSL-2 lab freezers. ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **HPRD#14-167** as written.
Item 4:	Registration of Material (Potentially) Infectious for Humans (Renew) ▪ Hinnebusch (LZP) ▪ **HPRD#14-66: *Yersinia pestis* (exempt)** ▪ Becky Anderson presented the risk assessment. The purpose of the study is to identify the mechanisms of plague transmission, infection, and immunity and to develop medical countermeasures against plague. The strains are all attenuated strains of *Y. pestis*. Lcr- strains of *Y. pestis* lack the 75 kb low-calcium response (Lcr) virulence plasmid. Strains lacking the Lcr plasmid (Lcr^-) are irreversibly attenuated due to the loss of a virulence plasmid. An Lcr^- strain of *Y. pestis* (Tjiwidej S) has been extensively used as a live vaccine in humans in Java. Pgm^- mutants of *Y. pestis* occur at a high frequency (ca 10^{-5}) and result in attenuation. These strains have been used for years as live human vaccines with no significant plague-associated problems. The mutation in question is due to the excision of about 102-kb of chromosomal DNA via reciprocal recombination between adjacent IS 100 elements. The lost DNA sequence encodes the ability to synthesize and utilize the siderophore yersiniabactin, which is necessary for growth in mammalian peripheral tissue, as well as the Hms^+ locus, which is necessary for biofilm production in the flea vector. ▪ The committee discussed the containment requirements. BSL-2/ABSL-2 is appropriate for work with attenuated strains of *Yersinia pestis*.

	▪ Animal studies with mice were proposed. ▪ Dual use question 3 was checked yes. The description by the PI states that certain strains contain IBC approved antibiotic resistance. The committee discussed that this response relates to work that is outlined in the RD and is not a dual use concern because none of the antibiotics are used clinically for treatment. The committee agreed that the dual use answer should be changed from "Yes" to "No", but leave the comment from the PI in place for clarity. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no overall dual-use concerns with the proposal. Action: The committee unanimously approved **HPRD#14-166** with minor modifications: 1. Change dual use question 3 from "Yes" to "No".
Item 5:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Gherardini (LZP) ▪ **RD#14-319 Amend**: The infectious cycle of *Borrelia burgdorferi* ▪ Reviewers: Dana Scott, Clay Jarrett ▪ **Summary:** The amendment is to add animal work with rabbits. ▪ Dana Scott summarized the registration. The amendment is to add work with rabbits. The ASP is attached to the registration. Dana Scott had no comments or concerns with the additional animal species. ▪ Clay Jarrett had no addition comments or concerns. ▪ The committee discussed the containment requirements. ABSL-2 is appropriate for animal studies with *B. burgdorferi* proteins in rabbits. ▪ Animal studies with rabbits were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#14-319 Amend** as written. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-1-a and III-D-2-a of the NIH Guidelines. Animal work with rabbits is approved at ABSL-2.
Item 6:	Registration Documents for Recombinant DNA Experiments (New) ▪ Bloom (LV) ▪ **RD#14-445**: Analysis of molecular signaling pathways in tick-borne flavivirus persistence

	▪ Reviewers: Karin Peterson, Bob Heinzen ▪ **Summary:** The proposed studies describe the use of lentiviral vectors to deliver short hairpin RNAs to elucidate the role of certain signaling pathways in the initiation and maintenance of tick-borne flavivirus persistence. ▪ Karin Peterson summarized the registration. She informed the committee that the proposed studies include using commercially available lentiviral particles to knock down specific host proteins in cells infected with Langat virus or Powassan virus. The registration also describes over expressing the same host proteins that will be knocked down, however the description makes it sound like the same lentiviral system would be used. Bob Heinzen clarified that they will be using overexpression plasmids to overexpress specific proteins. The registration needs to be clarified in several places to describe the Lentiviral particles vs. the overexpression plasmids. ▪ Karin Peterson also stated that they need to specify throughout the registration when and where Powassan and Langat are being used. She questioned if the biosafety level should be changed in the document for when Powassan is being used to BSL-3. Becky Anderson clarified that the information for the infections with Langat and Powassan will be added to the recommendations section and the appropriate biosafety level for those experiments will be included. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for studies with Lentiviral particles. If cells are also infected with Powassan virus, the biosafety level is then raised to that of Powasasn virus, BSL-3. Studies with Langat virus and Lentiviral particles can be conducted at BSL-2. ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **RD#14-445** with the following minor modifications: 1. Please update registration through out to clarify work with Lentiviruses vs. work with overexpression plasmids. 2. Add Powassan or Langat virus to all sections where they will be used. 3. Add the biosafety level to the recommendations section for studies that will be conducted with Langat (BSL-2) and Powassan (BSL-3) viruses. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-2-a of the NIH Guidelines. Research using Eukaryote Cells is approved at BSL-2 under sections III-D-2-a of the NIH Guidelines.
Item 7:	<u>Registration Documents for Recombinant DNA Experiments (New)</u>

	▪ Hackstadt (LICP) ▪ **RD#14-128**: Chlamydial type III secretion from *Yersinia pseudotuberculosis* ▪ Reviewers: Scott Kobayashi, Rachel LaCasse ▪ **Summary:** Demonstration of chlamydial type III secreted effector proteins from a heterologous host ▪ Scott Kobayashi summarized the registration. This is an RD to test if chlamydial proteins are secreted in the *Y. pseudotuberculosis* type III secretion system. Specific chlamydial genes will be expressed in type III secretion competent and mutant strains to determine if they are recognized and secreted by this mechanism. The genes are unknown chlamydial genes, but are essentially effector molecules. They will use ampicillin resistance as a selection marker. Scott Kobayashi states that ampicillin can be used clinically, but it is also widely used in the field as a selection marker. The committee discussed that there are several options for treatment of *Y. pseudotuberculosis* and ampicillin is not the only first line treatment. The committee discussed that dual use question 3 should be changed from "No" to "Yes", and there should be a short description added as to why this is not a concern. ▪ Scott Kobayashi also stated that they are inserting genes from *Chlamydia trachomatis* into *Y. pseudotuberculosis,* the question should be asked if they are going to increase host range or susceptibility. Scott Kobayashi did not think that this research would result in a change unless it included a known toxin or virulence factor, which it does not. Bob Heinzen added that this is a common method and he cannot envision that this would result in a host range change, increase in virulence, etc. The committee agreed that dual use question 3 should be changed from "No" to "Yes" with a brief description of why inserting chlamydial genes into *Y. pseudotuberculosis* is not a dual use concern. ▪ Rachel LaCasse had no comments or concerns. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for studies with *Y. pseudotuberculosis.* ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no overall dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **RD#14-128** with the following minor modifications: 1. Change dual use question 3 from "No" to "Yes". Include a description in the comments section that ampicillin will be used for selection and can be used clinically but there are alternative treatments. Also include in the comment section why inserting Chlamydial genes into *Y. pseudotuberculosis* is unlikely to

	increase virulence, host range, host tropism, etc. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-1-a of the NIH Guidelines.
Item 8:	<u>Registration Documents for Recombinant DNA Experiments (Renewal)</u> ▪ Hackstadt (LICP) ▪ **RD#14-119**: Plasmid transformation of Chlamydia ▪ Reviewers: Chris Bosio, Dana Scott ▪ **Summary:** The proposed experiments describe genetically modifying chlamydia to determine any effects on virulence as determined by cellular interactions in cell culture. ▪ Chris Bosio summarized the registration. The renewal of this RD describes using a published method of plasmid transformation on *Chlamydia trachomatis* and *C. caviae*. They will modify the plasmids by introducing a multiple cloning site for the purpose of re-introducing chlamydial genes to complement defects in specific strains. The listed antibiotics for selection are not used clinically and the NIH Guidelines are appropriate. Chris Bosio had no concerns with the proposed registration. ▪ Dana Scott had no comments or concerns. ▪ The committee discussed the containment requirements. BSL-2 with 3 practices is appropriate for plasmid transformation of the listed Chlamydia spp. ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **RD#14-119** as written. Research using prokaryotic hosts is approved at BSL-2 with 3 practices under sections III-D-1-a and III-D-2-a of the NIH Guidelines. Research using Eukaryote Cells is approved at BSL-2 with 3 practices under sections III-D-1-a of the NIH Guidelines.
Item 9:	<u>Registration Documents for Recombinant DNA Experiments (Renewal)</u> ▪ Hackstadt (LICP) ▪ **RD#14-120**: Introduction of Mariner-based Himar1 transposon system into Chlamydial spp. ▪ Reviewers: Clay Jarrett, Karin Peterson ▪ **Summary:** The proposed experiments describe experiments to genetically

	modify chlamydia to determine any effects on virulence as determined by cellular interactions in cell culture. ▪ Clay Jarrett summarized the registration. This is a renewal for an RD that describes a system for mutating chlamydia. This work is carried out by the use of a Mariner-based Himar1 transposon system. By generating these mutants, they will determine any effects on virulence as determined by cellular interactions in cell culture. The proposed antibiotics for selection are not used clinically and are appropriate. ▪ Clay Jarrett did point out that the NIH Guidelines for the Research Product needed to be filled in. Becky Anderson stated that they should be III-D-1-a. ▪ Karin Peterson noted that dual use question A1 was indicated as "N/A". This is not appropriate because the question is applicable to the proposed research. The "N/A" should be changed to "No". The committee agreed that the answer should be changed. ▪ The committee discussed the containment requirements. BSL-2 with 3 practices is appropriate for recombinant work with the listed Chlamydia spp. ▪ Animal studies with rabbits were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **RD#14-120** with the following minor modifications: 1. Add III-D-1-a to the NIH Guidelines section in the Research Product Section. 2. In the dual use questionnaire, change A1 from "N/A" to "No". Research using prokaryotic hosts is approved at BSL-2 with 3 practices under sections III-D-1-a and III-D-2-a of the NIH Guidelines. Research using Eukaryote Cells is approved at BSL-2 with 3 practices under sections III-D-2-a of the NIH Guidelines.
Item 10:	<u>Registration Documents for Recombinant DNA Experiments (Renewal)</u> ▪ Feldmann (LV) ▪ **RD#14-426**: ▪ Reviewers: Rachel LaCasse, Chris Bosio ▪ **Summary:** Identification of mechanisms and viral/host factors determine Zaire Ebola virus cellular tropisms ▪ Rachel LaCasse summarized the registration. This registration is very similar to the Ebola RD that was submitted for renewal from the Feldmann group last

	month at the November meeting. The proposed methods are all the same as before. Rachel LaCasse had no concerns with the proposed studies. She did state that the personnel list needs to be updated, mostly for personnel that have left RML. ▪ Alex Scranton submitted questions by email. She stated that it was difficult to tell new experiments in the renewal versus previously IBC reviewed experiments. Perhaps it would be helpful if new experiments to renewals could be put in red, similar to what we do for amendments. The committee agreed that should be done for all future renewals. ▪ Bob Heinzen also added that some of the sequences in the table do not encode proteins, so change the reference on page 1, section A, from "additional proteins" to "additional nucleic acid sequences". ▪ Chris Bosio had no comments or concerns. ▪ The committee discussed the containment requirements. The studies without helper virus, described in Section A will be conducted at BSL-2, studies that generate infectious Ebola virus will be conducted at BSL-4. Animal studies will be conducted at ABSL-4. ▪ Animal studies mice, hamsters, and guinea pigs were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. Dual use questions A1, A5, and B were checked yes. The committee reviewed and discussed the attached description provided by the PI as to why there is no dual use concern with the proposed studies. The committee agreed that there were no overall dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **RD#14-120** with the following minor modifications: 1. Update personnel list, mostly removal of personnel that have left RML. 2. The new experiments to the renewal should be in red. 3. Change the reference on page 1, section A, from "additional proteins" to "additional nucleic acid sequences". Research using prokaryotic hosts is approved at BSL-2 under sections III-D-2-a and III-D-2-b of the NIH Guidelines. Research using Eukaryote Cells is approved at BSL-4 under sections III-D-1-c, III-D-3-c, and III-D-1-a of the NIH Guidelines.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Nancy Hoe was not in attendance. A BSO report will be provided at the January meeting.

Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ St. Patrick hospital in Missoula hosted a drill with simulated Ebola infected patients. They practiced transport of patients by ambulance crews from the fire station to Community Medical Center and St. Patrick Hospital. It was beneficial for all parties involved.
Report	**IRF Biosafety Manager Report/Megan Morgan** ▪ (b)(6); (b)(3):42 U.S.C. 262a(b) animal side annual shutdown is scheduled to start next week and will go into the middle of January. We will then move on to (b)(6); (b)(3):42 U.S.C. 262a(b) /Public Health ▪ BSL-3 annual shutdown will be planned for the third week of March. We will hold a user's meeting soon to plan and discuss.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ None

Other issues	▪ None

Next Meeting:

- Date: 1/15/15
- Place: Bldg A Seminar Room
- Time: 1:00 PM

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 1/15/15
Meeting Time: 1:02 PM **Adjourned:** 1:30 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Paul Carlson	☒	☐	Kevin Mora	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Megan Morgan	☒	☐
Becky Anderson (EO)	☒	☐	Frank DeLeo (EO)	☐	☒	Karin Peterson	☒	☐
Alan Applebury	☐	☒	Hideki Ebihara	☐	☒	George Risi	☒	☐
Chris Bosio	☒	☐	Heinz Feldmann (EO)	☐	☒	Dana Scott	☐	☒
Marshall Bloom (EO)	☒	☐	Nancy Hoe	☒	☐	Alexandra Scranton	☐	☒
Teresa Borino	☐	☒	Clay Jarrett	☒	☐			
Jeff Burrows	☐	☒	Josh Kellar (EO)	☐	☒			
Carol Calderwood	☐	☒	Scott Kobayashi	☒	☐			
Harlan Caldwell (EO)	☐	☒	Rachel LaCasse	☐	☒			
Marcie Caldwell (EO)	☒	☐	Alida Merritt	☐	☒			

(P=present; A=absent)

Guests: (b)(6) **Alex Scranton participated via teleconference**

Minutes: Meeting minutes from 12/18/14 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** Action: Meeting minutes for 12/15/14 were approved with minor modifications: 1. For item 2, change "encephalitis" to "encephalopathy" after the HPRD#. 2. In item 4, in the risk assessment Becky Anderson provided, change "avirulence" to "attenuation". 3. Add to Item 7, "Rachel LaCasse had no comments or concerns". 4. Add to Item 10, "Chris Bosio had no comments or concerns". 5. Clarify in Item 10 that Alex Scranton did not state that some of the sequences in the table do not encode proteins. Bob Heinzen made that statement.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans (New) ▪ Hasenkrug (LPVD) ▪ **HPRD#15-168: Vaccinia virus** ▪ Becky Anderson presented the risk assessment. This is a new registration for storage only of Vaccinia virus, WR strain. They will store it in their BSL-2 lab until they wish to actively work with the material. At that time they will need to submit an updated HPRD to the committee describing their proposed research. ▪ Nancy Hoe stated that the recommendations section should be updated to include the following statement, "Before beginning any active work or removing from the freezer, submit an updated HPRD to the IBC." ▪ BSL-2 is appropriate for storage of Vaccinia virus. ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **HPRD#15-168** with minor modifications: 1. Add to the recommendations section, "Before beginning any active work or removing from the freezer, submit an updated HPRD to the IBC."
Item 2:	Registration of Material (Potentially) Infectious for Humans (New) ▪ Hasenkrug (LPVD) ▪ **HPRD#15-169: Staphylococcal Enterotoxin B (SEB)** ▪ Becky Anderson presented the risk assessment. SEB is used in the Hasenkrug lab as a potent activator of T cells. These T cells are then used as a positive control in their *in vitro* assays. SEB is a toxin produced by the *Staphylococcus aureus* bacterium. SEB is most commonly associated with food poisoning and presents with symptoms including a sudden onset of fever, chills, headache, myalgia, and a non-productive cough. Some patients can develop a shortness of breath and chest pain. The fever can last 2-5 days and a cough may continue for up to a month. Patients may also present with nausea, vomiting, and diarrhea when the toxin is swallowed. High levels of aerosol exposure can lead to septic shock and death. Because SEB can easily be aerosolized, it is considered a potential biological warfare agent and regulated by the CDC Division of Select Agents and Toxins. Typically, the illness is self-limiting, but treatment of symptoms may be warranted if the toxin is absorbed into the blood stream. The natural route of transmission is through consumption of contaminated food. It is not contagious and cannot be transmitted from person to person. The primary lab hazards include: accidental sharps injuries,

	ingestion, or generation of aerosols. ▪ To mitigate the hazards, the committee discussed the containment requirements: BSL-2 with lab coat, gloves, and eye protection when necessary. Preparative work with the toxin should be done in a Class II B2 BSC or CFH with proper PPE being worn. Please see BMBL Appendix I for working with toxins. Staphylococcal enterotoxin B can be possessed and used if kept under Select Agent exempt quantities which is 5 mg. A logbook must be kept and document all purchases and acquisitions, including all usage and disposal of the registered toxin as they occur in mg quantities. This inventory will be inspected by the RML Select Agent Program (SAP) on a regular basis. The SEB should be secured in a locked freezer or locked box within a freezer. Attached to the registration will be the signed Toxin Exclusion Certification from the PI and all personnel on the HPRD documenting that they will not possess more than 5 mg at any time. ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no overall dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **HPRD#15-169** as written. The signed toxin exclusion form should be signed and attached to the HPRD.
Item 3:	<u>Registration Documents for Recombinant DNA Experiments (Renew)</u> ▪ Heinzen (LICP) ▪ **RD#15-107**: Understanding the function of *C. burnetii* genes ▪ Reviewers: Chris Bosio, Sue Priola ▪ **Summary:** To better understand the function of *C. burnetii* genes with an emphasis on those encoding proteins predicted to modulate host cell function. ▪ Chris Bosio summarized the registration. This was a straight forward registration that describes studies testing the function of individual genes from Coxiella in *Legionella pneumophila*. *L. pneumophila* is routinely used to study Coxiella gene function and to identify proteins secreted into the host cell cytosol. Candidate Coxiella genes will also be ectopically expressed by transfection of eukaryotic cell lines using expression vectors described in the RD. The listed antibiotics for selection are appropriate. Chris Bosio had no concerns with the RD. ▪ Sue Priola questioned on page 4 in the percent source genome section, why was zero listed? Bob Heinzen informed the committee that it is such a small percentage, it is less than 1 percent. Sue Priola stated that it would be better to state, "less than 1 percent" in that section. ▪ Nancy Hoe added that in the Associated Registrations section, HPRD 13-70 should be included. She also stated in the Eukaryotic Cell section that III-D-2-a

	should be changed to III-D-1-a for the NIH Guidelines. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for studies with *C. burnetii*. ▪ No animal studies were submitted proposed or reviewed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **RD#15-107** with minor modifications: 1. In the percent source genome, change "0" to "less than 1 percent". 2. Add to the Associated Registrations, HPRD 13-70 3. In the Eukaryotic cell section, change the NIH Guidelines from III-D-2-a to III-D-1-a. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-1-a and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under section III-D-1-a of the NIH Guidelines.
Item 4:	<u>Registration Documents for Recombinant DNA Experiments (Renew)</u> ▪ Heinzen (LICP) ▪ **RD#15-123**: Understanding vacuole biogenesis ▪ Reviewers: Scott Kobayashi, Hideki Ebihara ▪ **Summary:** To better understand mechanisms of pathogen vacuole biogenesis. To identify proteins secreted by type IV secretion machinery. ▪ Scott Kobayashi summarized the registration. This RD describes using *C. burnetii* as a surrogate for the type 4 secretion system (T4SS) apparatus for proteins from *Anaplasma phagocytophilum* and *Orientia tsutsugamushi*. Both bacteria lack methods for genetic manipulation, so *C. burnetii* is used because it has an established T4SS assay for screening secretion of proteins. They will test proteins that have been revealed by bioinformatics analysis to be T4SS substrates from *A. phagocytophilum* and *O. tsutsugamushi*. The antibiotics used for selection are all appropriate and have been previously approved by the IBC committee. Scott Kobayashi has no concerns with the registration. ▪ Hideki Ebihara had no addition comments or concerns. ▪ Sue Priola pointed out that the percent source genome needs to be changed to "less than 1 percent" on this RD as well. ▪ Alex Scranton added that in the first sentence in the Purpose Section, "vacuole" was spelled incorrectly.

	▪ The committee discussed the containment requirements. BSL-2 is appropriate for studies with *C. burnetti* Nine Mile II. ▪ No animal studies were submitted proposed or reviewed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#15-123** with minor modifications: 1. In the percent source genome, change "0" to "less than 1 percent". 2. Fix the spelling of "vacuole" in the first sentence of the Purpose Section. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-1-a and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under section III-D-1-a and Appendix G-II-B of the NIH Guidelines.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Reviewed the BSO report.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ There have been a few more slips and falls due to the winter weather. Employees are reminded to use caution on the sidewalks. ▪ One employee cut their fingertip while cutting an Eppendorf tube open. Employee has been retrained and advised on how to do the procedure safely. ▪ Paul Carlson informed the committee that there were 7 OSHA recordable events on campus in 2014.
Report	**IRF Biosafety Manager Report/Megan Morgan** ▪ Currently completing the (b)(6); (b)(3):42 U.S.C. 262a(b)(Public Health side annual shutdown activities. ▪ (b)(6); (b)(3):42 annual shutdown will be carried out during the month of February. ▪ The buffer corridor construction project is due to be completed in February. At the February IBC meeting, we will review documentation regarding new procedures for the buffer corridor and Kevin Mora will describe the construction project to the group.
Report	**Associate Director Report/Marshall Bloom** ▪ Thank you to all of the IBC members for their hard work, especially the community members.

Around the room	▪ None

Other issues	▪ None

Next Meeting:

- Date: 2/19/15
- Place: Bldg A Seminar Room
- Time: 1:00 PM

RML Biosafety Committee Meeting
January 15, 2015
Biosafety Officer/Responsible Official Report

1) Requests approved by BSO since last meeting:

a) *Registration of Material Potentially Infectious for Humans*

i) Amend

(1) Ebihara (LV)

(a) **HPRD-14-110:** Orthobunyaviruses

(i) *Add intra-dermal and intra-muscular routes of infection for mouse studies*

(2) *Feldmann (LV)*

(a) ***HPRD-12-83****: Human and non-human primate tissues, blood and body fluids*

(i) *Added description of human samples*

(b) ***HPRD-13-82****: Vesicular Stomatitis virus*

(i) *Add intranasal route of infection for hamster studies*

b) *Registration Documents for Recombinant DNA Experiments*

i) Amend

(1) *Feldmann (LV)*

(a) *RD-13-404: Replication-competent Vesicular Stomatitis virus*

(i) *Add intranasal route of infection for hamster studies*

c) *Standard Operating Procedures*

i) SOP-4-28-43 "Aerosol Exposure System Operation"

(1) Section 6.3.D.7.(d) addressing maintenance of sedation during aerosol delivery was expanded and clarified.

2) ***New requests approved by committee via electronic review:***

a) *None*

3) ***New requests***

a) *Registration of Material Potentially Infectious for Humans*

i) ***New***

(a) *Hasenkrug (LPVD)*

(a) ***HPRD-15-168:*** *Vaccinia virus, storage only*

(b) ***HPRD-15-169****: Staphylococcal enterotoxin B (select agent exempt quantity)*

b) *Registration Documents for Recombinant DNA Experiments*

i) ***Renew***

(a) *Heinzen (LICP)*

(a) ***RD-15-107:*** *Understanding function of C. burnetii gene products*

(b) ***RD-15-123****: Understanding mechanisms of pathogen vacuole biogenesis*

RML Biosafety Committee Meeting
January 15, 2015
Biosafety Officer/Responsible Official Report

4) ***Animal Study Protocols Review (December 2014 and January 2015***

Title	*Associated HPRD*	*Associated RD*	*Reviewer*
Understanding the role of MAVS in protection from TBEV infection in the mouse model	*12-135 (TBEV Far Eastern Subtype)*	*N/A*	*N. Hoe*
The transmissibility of Human Prion Diseases PrP226 and G131V to transgenic mice	*14-166 (HBBF containing human TSE agents)*	*N/A*	*N.Hoe*
Antibody production to antigens of Borrelia species in rabbits	*N/A*	*14-139*	*N. Hoe*
Murine infectivity of C. trachomatis chxR null mutant strains in mice	*13-32 (C. trachomatis)*	*N/A*	*B. Anderson*
Efficacy testing of MERS-CoV S1 vaccination in human DPP4 knock-in mice	*12-143 (MERS-CoV)*	*N/A*	*B. Anderson*
Defining post-exposure immune response of VSV vector vaccines in hamsters	*13-82 (VSV)*	*13-404*	*M. Morgan*
Efficacy of computationally predicted Ebola antiviral compounds in mice	*13-90 (Ebola)*	*N/A*	*M. Morgan*
Contribution of capsule in Francisella tularensis mediated suppression of pulmonary inflammation in mice	*13-71 (F. tularensis)*	*N/A*	*M. Morgan*
Assessing therapeutic potential of human anti-Sin Nombre virus IgG antibodies against development of HPS in NHPs	*12-81 (Hantavirus)*	*N/A*	*M. Morgan*
Production of prion infected mouse tissues for in vitro experimentation	*N/A (rodent tissues)*	*N/A*	*B. Anderson*
Evolution of FX06 for the treatment and prevention of hantavirus pulmonary syndrome in Syrian hamsters	*12-81 (Hantavirus)*	*N/A*	*B. Anderson*
Surveillance of natural foci of African HFVs	*14-158 (Field Samples)*	*N/A*	*N. Hoe*
Global Surveillance of Known and Potential Zoonotic Foci for Pathogens to Assess Human Risk	*14-158 (Field Samples)*	*N/A*	*N. Hoe*
Assessing bioavailability and half-life of human anti-Ebola virus polyclonal IgG antibodies in Rhesus macaques	*N/A*	*N/A*	*M. Morgan*

5) ***Biosafety Training Performed – Megan Morgan, Becky Anderson***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
Select Agent Initial Training	***1***	***1***
MCL Visitor Training (Contractors for construction project)	***2***	***14***
BSL-3 Laboratory Biosafety Training	***2***	***6***
BSL-3 Refresher Training	***1***	***1***

BSL-4 Annual Refresher	***1***	***1***

6) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
   a) *Biological Incident Report:*
      i) *None*

7) ***Select Agent Issues***
   a) *Annual BSL-4 Inspection*

8) ***Other Issues***
   a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 2/19/15
Meeting Time: 1:02 PM **Adjourned:** 2:38 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Paul Carlson	☒	☐	Kevin Mora	☒	☐
Bob Heinzen, Vice Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Megan Morgan	☒	☐
Becky Anderson (EO)	☐	☒	Frank DeLeo (EO)	☐	☒	Karin Peterson	☒	☐
Alan Applebury	☐	☒	Hideki Ebihara	☒	☐	George Risi	☐	☒
Chris Bosio	☒	☐	Heinz Feldmann (EO)	☐	☒	Dana Scott	☐	☒
Marshall Bloom (EO)	☒	☐	Nancy Hoe	☒	☐	Alexandra Scranton	☐	☒
Teresa Borino	☐	☒	Clay Jarrett	☒	☐			
Jeff Burrows	☐	☒	Josh Kellar (EO)	☐	☒			
Carol Calderwood	☐	☒	Scott Kobayashi	☒	☐			
Harlan Caldwell (EO)	☐	☒	Rachel LaCasse	☒	☐			
Marcie Caldwell (EO)	☐	☒	Alida Merritt	☒	☐			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 1/15/15 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** Action: Unanimously approved as written.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Addition of (b)(6); (b)(3):42 U.S.C. 262a(h) to BSL-4 (b)(6); (b)(3):42 U.S.C. ▪ Megan Morgan and Kevin Mora summarized the construction project that added a (b)(6); (b)(3):42 U.S.C. 262a(h) (Public Heatlh Security and Bioterrorism Preparedness and Response Act) Megan Morgan also presented RML's responses as to how RML meets OBA's Options for Achieving BL4 Containment for Research Involving Non-Human Primates. ▪ **OBA Options for Achieving BL4 Containment for Research Involving Non-**

	Human Primates: ▪ Alex Scranton submitted by email a comment that page 3 of the OBA requirements should specify independent access to match the description in the MCL Operations and Safety Procedures. ▪ **MCL Operations and Safety Procedures** was updated to describe access and entry procedures into the new (b)(6); (b)(3):42 U.S.C. Action: The committee unanimously approved **MCL OSP** updates as written. 1. **SOP#4-28-25 Formaldehyde Decontamination of Animal Rooms, Airlocks and Laboratories** was updated to describe new procedures for retrieving biological indicators (BI's) now that the (b) (6) is in place. The updates include posting signs while BI's are retrieved to keep personnel out of the corridor during that time. Action: The committee unanimously approved **SOP#4-28-25 Formaldehyde Decontamination of Animal Rooms, Airlocks and Laboratories** as written.
Item 2:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Heinzen (LICP) ▪ **RD#15-123 Amend**: Identification of proteins secreted by type IV secretion machinery ▪ Reviewers: Clay Jarrett, Chris Bosio ▪ **Summary:** The amendment is to add genes from *Legionella pneumophila* that will be inserted into avirulent *Coxiella burnetii* Nine Mile phase II. ▪ Clay Jarrett summarized the amendment. The original RD describes transferring genes from *A. phagocytophilum* and *O. tsutsugamushi* into *C. burnetii*. The amendment is to add genes from *Legionella pneumophila* to that list. They will examine the importance of amino acid transporters on intracellular growth. None of these genes are expected to alter the virulence, host range, etc. so there is no concern about these new genes. ▪ Chris Bosio had no additional comments or concerns. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for studies with avirulent *C. burnetii*. ▪ No animal studies were submitted proposed or reviewed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Bob Heinzen abstained) **RD#15-123 Amend** as written.

	Research using prokaryotic hosts is approved at BSL-2 under sections III-D-1-a and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under section III-D-1-a and Appendix G-II-B of the NIH Guidelines.
Item 3:	Registration Documents for Recombinant DNA Experiments (New) ▪ Hasenkrug (LPVD) ▪ **RD#15-223**: Adeno-associated virus ▪ Reviewers: Sue Priola, Rachel LaCasse ▪ **Summary:** Adeno-associated virus (AAV) will be used with HIV to induce vascular disease in humanized mice. ▪ Sue Priola summarized the registration. The RD states that there is an increased incidence of atherosclerosis in HIV patients. Rachel LaCasse informed the committee that it is unclear at this point if the atherosclerosis is a result of the drugs used for treatment of HIV or if HIV is the cause of atherosclerosis, this study will address that question. They will use AAV infection in humanized mice to express this enzyme that will stimulate LDL cholesterol in mice over time. These mice are then expected to develop atherosclerosis. The AAV will be received from a collaborator and no cloning at RML will occur, the vector map is attached. The AAV is not pathogenic to humans and can insert into cells but cannot replicate because it needs a helper virus to replicate. ▪ Rachel LaCasse had no addition comments or concerns. ▪ George Risi pointed out a typo in the infectious dose: 5e11 should be 5 X 10e11. ▪ The committee discussed the containment requirements. Work with AAV is approved at BSL-2. ABSL-2 with 3 practices is appropriate for animal studies where HIV infection is involved. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#15-223** with minor modifications: 1. Fix the typo in the infectious dose (5e11 should be 5 X 10e11) Animal work with mice is approved under III-D-4 of the NIH Guidelines.
Item 4:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Rosa (LZP) ▪ **RD#15-314**: Leptospirosis

	▪ Reviewers: Scott Kobayashi, Bob Heinzen ▪ **Summary:** Genetic manipulation of Leptospira spp. ▪ Scott Kobayashi summarized the registration. This RD describes genetic manipulation of Leptospira spp. These Leptospira spp. will be used and genes will be taken from various species and put back into *L. biflexa* because that is the only species with a good genetic system that is well described. They will be using several plasmids with the following selectable markers, kanamycin, gentamicin, and spectinomycin, none of which are used to treat leptospirosis. The NIH Guidelines referenced are correct and there are no dual use concerns. ▪ Bob Heinzen had no additional comments or concerns. ▪ Nancy Hoe pointed out that they have an ideal system because they are putting genes from strains not expected to have any role in pathogenesis into non-pathogenic strains so they will not get any adverse effects. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for studies with Leptospira spp. ▪ No animal studies were submitted proposed or reviewed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **RD#15-314** as written. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-1-a and III-D-2-a of the NIH Guidelines.
Item 5:	<u>Registration Documents for Recombinant DNA Experiments (Renew)</u> ▪ Feldmann (LV) ▪ **RD#15-404**: VSV Replication Competent ▪ Reviewers: Sue Priola, Hideki Ebihara ▪ **Summary:** Replication competent VSV ▪ Sue Priola summarized the registration. She informed the committee that this is a renewal for using replication competent VSV to study the function of genes and generate vaccines. The VSV is just a delivery vector and expression system. They will express genes from Filo-, Bunya-, Henipa, Arena-, Retro-, and Coronaviruses. All of this work can be done at BSL-2 because they are only using individual genes from these viruses and putting them into VSV which is a RG2 agent. All the genes that will be inserted from the various viruses are glycoproteins, structural proteins, etc. These changes in VSV historically reduce the virulence of it and make VSV less pathogenic. There are several ASPs attached that include various species and routes of infection. They will need to

	add a summary page or type into the recommendations section all the animal species and routes of infection that have already been approved by the IBC. ▪ Sue Priola added that III-D-1-a should be added to the Research Product section because they are adding recombinant DNA into RG2 organisms. ▪ Hideki Ebihara had no addition comments or concerns. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for studies with replication competent VSV. ▪ Animal studies with guinea pigs, non-human primates, hamsters, pigs, and mice were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **RD#15-404** with minor modifications: 1. Add a summary of animal species and routes of inoculation. 2. Add III-D-1-a to the Research Product Section. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-1-a and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under section III-D-1-a and III-D-3-a of the NIH Guidelines.
Item 6:	<u>Registration Documents for Recombinant DNA Experiments (Renew)</u> ▪ Feldmann (LV) ▪ **RD#15-406**: Replication deficient VSV ▪ Reviewers: Karin Peterson, Chris Bosio ▪ **Summary:** To better understand viral attachment and entry with replication deficient VSV ▪ Karin Peterson summarized the registration. This RD renewal is very similar to the previous one just reviewed. This RD describes the replication deficient system, which includes insertion of genes from Filo-, Bunya-, Paramyxo-, Orthomyxo-, Flavi-, Arena-, and Coronaviruses. ▪ Chris Bosio had no addition comments or concerns. ▪ Sue Priola pointed out that under the prokaryotic host section, the minimal biosafety level statement should be re-phrased to state that, “This work will be performed at a minimum biosafety level of BSL-2”. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for studies with replication deficient VSV.

	▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#15-406** with minor modifications: 1. Add to the Prokaryotic Host section, "This work will be performed at a minimum biosafety level of BSL-2". Research using prokaryotic hosts is approved at BSL-2 under sections III-D-1-a and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under section III-D-3-a of the NIH Guidelines.
Item 7:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Caldwell (LICP) ▪ **RD#15-101**: Expression of Chlamydial proteins ▪ Reviewers: Dana Scott, Hideki Ebihara ▪ **Summary:** Expression of Chlamydial proteins for antibody generation ▪ Hideki Ebihara summarized the registration. This renewal is for the generation of plasmid constructs that express Chlamydial proteins that will ultimately be used to generate antibodies. All vector maps are attached and appropriate ASPs are attached for the animal work. ▪ Dana Scott was not present, but notified Hideki Ebihara that he had no additional comments or concerns. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for studies expressing Chlamydial proteins. ▪ Animal studies with mice and rabbits were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#15-101** as written. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Animal studies are approved under III-D-4 of the NIH Guidelines.
Item 8:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Caldwell (LICP) ▪ **RD#15-105**: Genetic Modification of Chlamydia by plasmid transformation

	▪ Reviewers: Bob Heinzen, Clay Jarrett ▪ **Summary:** Genetically modifying Chlamydia by replacing Chlamydia's cryptic plasmid. ▪ Bob Heinzen summarized the registration. He stated that they will renew their registration for the genetic transformation of Chlamydia. They will use the endogenous Chlamydia plasmid as a shuttle vector. They will select with ampicillin, and they have received approval to use beta-lactams for selection and the specific caveats for strains are detailed in the RD. They will use ampicillin with certain serovars, with chloramphenicol as an alternative which is fine to do. The NIH Guidelines for the prokaryotic host section need to include III-D-1-a. ▪ Sue Priola questioned that the vector map that is uploaded has an intact Tet gene in it. Bob Heinzen clarified that they clone the Chlamydia plasmid into the Tet gene so it inactivates the tetracycline resistance. They have tested in the past to ensure they have removed the tetracycline resistance. He clarified that the pBR322 does not need to be uploaded because it is a parent plasmid map and they have changed it so there is no Tet resistance, the committee understands the changes and is ok with the map remaining attached as written. ▪ Clay Jarrett had no additional comments or concerns. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for studies with Chlamydial transformation studies. ▪ No animal studies were submitted proposed or reviewed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#15-105** with minor modifications: 1. Add III-D-1-a to the Prokaryotic Host Section. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-1-a and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under section III-D-2-a of the NIH Guidelines.
Item 9:	**Standard Operating Procedure: SOP for Animal Biosafety Level 3 (BSL-3): West Nile Virus (New)** ▪ Sue Priola informed the committee that this was a new SOP for the Building (b)(6) ▪ Marshall Bloom pointed out that Powassan Virus was noted in several places and should be changed to West Nile Virus.

	▪ Sue Priola pointed out that Training 3.2 should be changed to, "designated by Dr. Rachel LaCasse". ▪ Clay Jarrett pointed out that 6.3.1 should say flood with disinfectant and allow to sit for the appropriate contact time. Delete spill kit and 4 hour time reference. Also at the end of 6.3.2, state that the PAPR will be removed and is disinfected after leaving the room. All disposable waste will be autoclaved. ▪ The committee had no additional comments or concerns. Action: The committee unanimously approved **SOP for Animal Biosafety Level 3 (BSL-3): West Nile Virus (New)** with the following minor modifications: 1. Remove references to Powassan virus and replace with West Nile Virus. 2. Training 3.2 should be changed to, "designated by Dr. Rachel LaCasse". 3. 6.3.1 should say flood with disinfectant and allow to sit for the appropriate contact time. Delete spill kit and 4 hour time reference. 4. 6.3.2, state that the PAPR will be removed and is disinfected after leaving the room. All disposable waste will be autoclaved.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Reviewed the BSO report. ▪ Two incident reports were summarized for the committee.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ Nothing to report.
Report	**IRF Biosafety Manager Report/Megan Morgan** ▪ (b)(6) nnual shutdown is complete. ▪ (b)(6) shutdown will begin next week. ▪ (b)(6) annual shutdown will occur the week of March 11-20 and the (b)(6) annual shutdown will be the following week, March 23-26.
Report	**Associate Director Report/Marshall Bloom** ▪ The previously described needle stick did result in convening of the BEAP as a result of discussion with OMS. This meeting included the county health officer and the head of the Ravalli County Health Department. The group discussed that the risk was negligible, and the same as a risk from a person returning from Africa working on the Ebola outbreak. This person was monitored in the same way as those individuals and the county and state health department were

	notified so all relevant parties were properly notified.
Around the room	▪ None

Other issues	▪ None

Next Meeting:

- Date: 3/19/15
- Place: Bldg A Seminar Room
- Time: 1:00 PM

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1) ***Requests approved by BSO since last meeting:***
   a) *None*
2) ***New requests approved by committee via electronic review:***
   a) *None*
3) ***New requests***
   a) *Registration Documents for Recombinant DNA Experiments*
      i) ***Amend***
         (a) *Heinzen (LICP)*
            (a) ***RD-15-123:*** *Understanding the mechanisms of pathogen vacuole biogenesis. Identification of proteins secreted by type IV secretion machinery*
               (i) Add cloning of genes from Legionella pneumophila and laboratory strains of E. coli into avirulent Coxiella burnetii Nine Mile phase II.
         (b) ***New***
            (a) *Hasenkrug (LPVD)*
               (i) RD-15-223: *study of HIV-induced vascular disease in humanized mice using an AAV vector encoding PCSK9*
         (c) ***Renew***
            (a) *Rosa (LZP)*
               (i) ***RD-15-314****: Leptospirosis, understanding the mechanisms of infection and pathogenicity*
            (b) *Feldmann (LZ)*
               (i) ***RD-15-404****: use of replication competent VSV based vectors*
               (ii) ***RD-15-406****: use of replication-deficient VSV based vectors*
            (c) *Caldwell (LICP)*
               (i) ***RD-15-101****: generation of plasmid constructs that express Chlamydia genes for antibody production*
               (ii) ***RD-15-105****: effect of DNA modification on chlamydia growth, gene regulation, and other phenotypes.*
   b) *Standard Operating Procedures*
      i) *SOP for Animal Biosafety Level 3 (ABSL-3): West Nile virus*
   c) *Service Corridor Packet*
      i) *Responses to OBA requirements*
      ii) *Updated MCL Operations and Safety Procedures*
      iii) *Updated SOP-4-28-25: Formaldehyde Decontamination of Animal Rooms, Airlocks, and Laboratories*

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4) ***Animal Study Protocols Review***

Title	*Associated HPRD*	*Associated RD*	*Reviewer*
Production of TKO-BLT mice	*12-104 (HBBF, tissues)*	*N/A*	*N. Hoe*
Friend virus infection and antigen presenting cell functionality in mice	*N/A (Friend virus)*	*N/A*	*N.Hoe*
Monocyte recruitment to the CNS following virus infection in mice	*12-103 (La Crosse virus) 14-162 (HSV1) 12-108 (West Nile virus)*	*N/A*	*N. Hoe*
Assessment of complement activation on prion disease and pathogenesis in mice	*N/A (rodent-adapted scrapie)*	*N/A*	*N. Hoe*
Third passage of anchored and anchorless 22L rodent scrapie in transgenic mice	*12-137 (rodent-adapted scrapie passage in tg666 mice)*	*N/A*	*N. Hoe*
Protective efficacy of a novel replication-deficient vaccine against lethal Ebola virus challenge in cynomologous macaques, Part II	*13-90 (EBOV)*	*N/A*	*N. Hoe*
Understanding the cell-type specific role of MAVS in protection of TBEV infection in the mouse model	*12-135 (TBEV)*	*N/A*	*M. Morgan*
Analysis of colonization of C. trachomatis to the lower genital tract in mice	*13-32 (C. trachomatis)*	*N/A*	*M. Morgan*
Pilot study examining the influence of eosinophils on Staphylococcus aureus pathogenesis in mice	*13-1 (S. aureus)*	*N/A*	*M. Morgan*
Evaluation of the therapeutic efficacy of recombinant soluble thrombomodulin in Ebola hemorrhagic fever using Syrian gold hamster model	*13-90 (Ebola)*	*N/A*	*M. Morgan*
The development of atherosclerosis in HIV-infected humanized mice	*12-55 (HIV) 15-170 (AAV) 12-104 (HBBF)*	*N/A*	*M. Morgan*
Efficacy of consecutive vaccinations with rVSV vectors against Sudan and Zaire Ebola viruses in nonhuman primates	*13-90 (EBOV) 13-82 (rVSV)*	*13-404 (rVSV)*	*M. Morgan*
Evaluation of T-705 for the treatment of Ebola hemorrhagic fever in Syrian hamsters	*13-90 (EBOV)*	*N/A*	*M. Morgan*
Regulation of cell recruitment to the murine central nervous system during neurovirulent viral infection	*N/A*	*15-101*	*M. Morgan*
Antibody production in rabbits to antigens of C. trachomatis	*N/A*	*15-101*	*B. Anderson*

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5) ***Biosafety Training Performed – Megan Morgan, Becky Anderson***

Type of Training	***Number of Sessions***	***Number of Employees Trained***
Select Agent Initial Training	***1***	***2***
BSL-3 Visitor Training	***1***	***3***
BSL-3 Laboratory Biosafety Training	***1***	***1***
BSL-4 Laboratory Biosafety Training	***1***	***1***
BSL-4 Annual Refresher	***2***	***2***

6) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
a) *Biological Incident Report:*
   i) *Dropped cage of F. tularensis-infected mice*
   ii) *Needlestick with clean needle in ABSL-4*

7) ***Select Agent Issues***
a) *White House Office of Science and Technology Policy Listening Session: Impact of Select Agent Regulations on Science, Technology, and National Security, February 17, 2015*

8) ***Other Issues***
a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 3/19/15
Meeting Time: 1:02 PM **Adjourned:** 1:43 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Paul Carlson	☒	☐	Kevin Mora	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Megan Morgan	☒	☐
Becky Anderson (EO)	☒	☐	Frank DeLeo (EO)	☐	☒	Karin Peterson	☐	☒
Alan Applebury	☐	☒	Hideki Ebihara	☐	☒	George Risi	☒	☐
Chris Bosio	☒	☐	Heinz Feldmann (EO)	☐	☒	Dana Scott	☒	☐
Marshall Bloom (EO)	☒	☐	Nancy Hoe	☒	☐	Alexandra Scranton	☐	☒
Teresa Borino	☒	☐	Clay Jarrett	☒	☐			
Jeff Burrows	☐	☒	Josh Kellar (EO)	☐	☒			
Carol Calderwood	☐	☒	Scott Kobayashi	☒	☐			
Harlan Caldwell (EO)	☐	☒	Rachel LaCasse	☒	☐			
Marcie Caldwell (EO)	☐	☒	Alida Merritt	☒	☐			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 2/19/15 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** Action: Meeting minutes for 2/19/15 were approved with minor modifications: 1. Page 2, Item 2, change "*C. burnetii*" to "avirulent *C. burnetii*" 2. Page 4 bullet 5, delete, "from pathogenic strains" and change to "not expected to have any role in pathogenesis" 3. Page 4, delete final sentence, "animal studies are approved . . ." in Item 4. 4. Throughout Item 4, change Leptospirosis to Leptospira. 5. Page 4, Item 5 change "use with replication competent VSV" to "using replication competent VSV". 6. Page 5, Item 5, add to the Minor Modifications section, "Add III-D-1-a to the Research Product Section". 7. Page 6, delete "submitted" from the first line. 8. Page 7, third bullet, delete "there are cases of genital tract infection that are

	treatable with ampicillin." 9. Page 7, Item 8, 6th bullet, change Chlamydial "gene" to "plasmid". 10. Page 8, Item 9, change "say" to "state". 11. Page 8, Item 9, change "infected" to "disinfected". 12. Change Alida Merritt from "Absent" to "Present".

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans (Amendment) ▪ de Leo (LHBP) ▪ **HPRD#13-1 Amend: *Staphylococcus aureus*** and attached list of human bacterial pathogens ▪ Becky Anderson presented the risk assessment. This amendment is to add mice to the current HPRD. Frank de Leo previously had approval from the IBC to work with mice, however that information was not included in the last renewal of the HPRD, this amendment is to add work with mice again. An animal study proposal is attached that describes work with mice. Studies with these human pathogens will be conducted in the human pathogen wing of (b)(6) All personnel must wear the lab coats, gloves, and masks. ▪ For studies with K. pneumonia carbapenemase producing bacteria (KPC), immunocompromised persons are restricted from working with this material. All personnel must be informed of the risks of working with antibiotic resistant strains and the risk of infection for immunocompromised persons. ▪ BSL-2 is appropriate for animal work with Staphylococcus aureus and the other described human bacterial pathogens. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Scott Kobayashi abstained) **HPRD#13-1 Amend** as written.
Item 2:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Steele-Mortimer (LICP) ▪ **RD#14-126 Amend**: Salmonella cancer vaccine ▪ Reviewers: Clay Jarrett, Rachel LaCasse ▪ **Summary:** The amendment is to add the Lassa virus glycoprotein to the vaccine platform.

	▪ Clay Jarrett summarized the registration. The original RD describes using a recombinant attenuated Salmonella Typhimurium vaccine (RASV) for treatment of breast cancer. The current amendment is to use the RASV, but test the system with the Lassa virus glycoprotein. All the described work will be the same as in the original RD. Clay Jarrett had no dual use concerns or other concerns with the proposed work. ▪ Rachel LaCasse pointed out that the amendment mentions animal work after the cloning and testing phase of the RASV constructs. She questioned if this amendment also gives approval for animal work. Becky Anderson clarified that they will have to submit an amendment to the IBC for approval to conduct animal work as they have not submitted a draft animal study proposal with this amendment. Sue Priola suggested that the recommendations section should be updated to state that "No animal work is approved at this time" to ensure there is no confusion about animal work approvals. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for studies with the recombinant attenuated Salmonella Typhimurium vaccine. ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **RD#14-126 Amend** with minor modifications: 1. Add to the recommendations section, "No animal work is approved at this time." Research using prokaryotic hosts is approved at BSL-2 under sections III-D-1-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under section III-D-1-a of the NIH Guidelines.
Item 3:	<u>Registration Documents for Recombinant DNA Experiments (New)</u> ▪ Peterson (LPVD) ▪ **RD#15-224**: Use of recombinant Adenovirus and inducible gene expression to examine mechanisms of La Crosse Virus infection and cell death. ▪ Reviewers: Sue Priola, Hideki Ebihara ▪ **Summary:** The study of SARM1 and SARM1-associated proteins in LACV-induced neuronal cell death. ▪ Sue Priola summarized the registration. Karin Peterson's group wants to identify the role of SARM1 during La Crosse virus infection. They will express SARM1 and other proteins in cell lines and infect with La Crosse virus to see what happens to innate immune mediators during infection. They will use

	transposable elements as well as adenoviral vectors to express their genes of interest. The genes of interest are all host derived. The adenoviral vectors are non-replicative and non-oncogenic. In order to propagate these adenoviruses, they will use the HEK293 cell line to contribute the E1a and E1b genes that have been removed from the adenovirus. ▪ Sue Priola stated that the Research Product section should include III-D-1-a and III-D-3-a for the NIH Guidelines and the Eukaryote Cells section should include III-D-1-a and III-D-3-a for the NIH Guidelines. ▪ Hideki Ebihara was not present. The committee had no additional comments or concerns with the registration. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for studies with recombinant adenovirus. ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **RD#15-224** with minor modifications: 1. In the research product section, add III-D-1-a and III-D-3-a to the NIH Guidelines. 2. In the Eukaryotic cell section, add III-D-1-a and III-D-3-a to the NIH Guidelines. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-1-a, III-D-2-a, and III-D-3-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under section III-D-1-a, III-D-2-a, and III-D-3-a of the NIH Guidelines.
Item 4:	<u>Registration Documents for Recombinant DNA Experiments (New)</u> ▪ Feldmann (LV) ▪ **RD#15-446**: Malaria speciation in human samples ▪ Reviewers: Dana Scott, Bob Heinzen ▪ **Summary:** To identify the presence or absence of various species of the malaria parasite in human samples through multiplex qPCR. ▪ Dana Scott summarized the registration. This registration describes having a commercial source generate different plasmodium species plasmids for use as a positive control in qPCR. These plasmids will be used as controls on human samples in studies in Africa where they have a lot of concomitant infections with Ebola and Malaria. Dana Scott had no concerns with the registration. ▪ Bob Heinzen had no additional comments or concerns.

	▪ The committee discussed the containment requirements. BSL-2 is appropriate for studies using Plasmodium species plasmid generation. ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#15-446** as written. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-2-a of the NIH Guidelines.
Item 5:	Registration Documents for Recombinant DNA Experiments (New) ▪ Feldmann (LV) ▪ **RD#15-447**: Modified Vaccinia virus Ankara (MVA) ▪ Reviewers: Chris Bosio, Scott Kobayashi ▪ **Summary:** MVA will be used as a vaccine platform for a variety of viral pathogens. ▪ Chris Bosio summarized the registration. This RD describes testing a vaccine platform of an attenuated vaccinia strain, MVA. In this RD, they will clone genes from different pathogens (listed in the RD) and assess the ability to immunize vertebrate hosts against disease. All the recombinant work will be done by a collaborator, they will receive the viruses, which they will propagate in eukaryotic cells and then immunize animals and challenge to test the efficacy of the vaccine candidates. They will only be inserting one or two genes into MVA so there are no dual use issues. The MVA vaccine is almost completely attenuated so it is a safe vaccine to work with. ▪ Chris Bosio pointed out that in the Research Product section, there is an X where the NIH Guidelines should be, that should be changed to III-D-2-a. ▪ Sue Priola stated that they should add what types of cell lines they will use to propagate MVA in. This should be added to the Eukaryote Cell section. ▪ George Risi asked if there is any need for vaccination for people working with vaccinia virus. Nancy Hoe clarified that when working with MVA, there is no vaccination requirement. ▪ Scott Kobayashi had no additional comments or concerns. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for studies with MVA in non-human primates. ▪ Animal studies with non-human primates were proposed. ▪ The committee discussed the dual-use potential of these experiments as

	described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#15-447** with minor modifications: 1. Add III-D-2-a to the Research Product section. 2. Specify cell lines that will be used to propagate MVA in the Eukaryote Cell section Research using eukaryotic cells is approved at BSL-2 under sections III-D-2-a of the NIH Guidelines. Research with animals is approved under III-D-4 of the NIH Guidelines.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Reviewed the BSO report. ▪ Summarized the CDC DSAT BSL-4 inspection that occurred March 3-11th.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ (b)(6) had a false fire alarm due to dust from maintenance work. ▪ A security guard twisted their knee on loose gravel on campus. ▪ An employee working with Chlamydia samples in an ice bucket received a splash to their eye when the tubes became frozen inside the bucket and they were trying to remove them. There was a very minor risk of Chlamydia being present on the outside of the tube. To mitigate the risk of this occurring again, the employee is advised to wear eye protection.
Report	**IRF Biosafety Manager Report/Megan Morgan** ▪ BSL-3 annual shutdown is wrapping up in (b)(6) now. (b)(6) lab was reactivated this morning and the other labs are scheduled to reactivate tomorrow. ▪ The BSL-3 annual shutdown in (b)(6) starts tomorrow.
Report	**Associate Director Report/Marshall Bloom** ▪ Marshall Bloom commented on the success of the BSL-4 CDC DSAT inspection.
Around the room	▪ George Risi introduced (b) (6) to the committee. He is an infectious disease physician at St. Patrick Hospital and is George Risi's backup for the CIU. He is also the Co-PI of the TBEV vaccine trial.

Other issues	▪ None

Next Meeting:

- Date: 4/16/15
- Place: Bldg A Seminar Room
- Time: 1:00 PM

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1) ***Requests approved by BSO since last meeting:***
   a) *None*
2) ***New requests approved by committee via electronic review:***
   a) *None*
3) ***New requests***
   a) *Human Pathogen Registration Documents*
      i) ***Amend***
         (a) *DeLeo (LHBP)*
            (a) ***HPRD-13-1****: Staphylococcus aureus*
               (i) Add mouse as an animal model
   b) *Registration Documents for Recombinant DNA Experiments*
      i) ***Amend***
         (a) *Steele-Mortimer (LICP)*
            (a) ***RD-14-126:*** *Salmonella cancer vaccine*
               (i) Add gene for Lassa virus glycoprotein
         (b) ***New***
            (a) *Peterson (LPVD)*
               (i) RD-15-224: *use of recombinant Adenovirus and inducible gene expression to examine mechanisms of La Crosse virus infection and cell death*
            (b) *Feldmann (LZ)*
               (i) ***RD-15-446****: identification of the presence or absence of various species of the malaria parasite in human samples*
               (ii) ***RD-15-447****: MVA vaccines*

4) ***Animal Study Protocols Review***

Title	***Associated HPRD***	***Associated RD***	***Reviewer***
Treatment of prion disease with oral statin therapy	*N/A (Rodent-adapted scrapie)*	*N/A*	*N. Hoe*
Efficacy testing of rVSV MERS-CoV vaccination in human DPP4 knock-in mice	*12-143 (MERS) VSV (13-82)*	*15-404*	*N.Hoe*
Assessing therapeutic potential of human anti-Ebola virus polyclonal IgG antibodies against development of EBD in non-human primates	*13-90 (Ebola virus)*	*N/A*	*M. Morgan*
Humanized mice as a model for Ebola virus infection	*13-90 (Ebola virus)*	*N/A*	*N. Hoe*

Title	*Associated HPRD*	*Associated RD*	*Reviewer*
Assessment of the T cell response during virulent F. tularensis infection in mice	*13-73, 13-71 (F. tularensis) 14-156 (LCMV)*	*13-125*	*B. Anderson*

5) ***Biosafety Training Performed – Megan Morgan, Becky Anderson***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
Select Agent Initial Training	***1***	***1***
BSL-3 Visitor Training	***2***	***16***
BSL-3 Laboratory Biosafety Training	***1***	***1***
BSL-4 Laboratory Biosafety Training	***1***	***2***
BSL-4 Annual Refresher	***3***	***3***

6) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
a) *Biological Incident Report:*
   i) *None*

7) ***Select Agent Issues***
a) *Annual BSL-3 Select Agent Inspection March 3-11, 2015*

8) ***Other Issues***
a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 5/14/15
Meeting Time: 1:03 PM **Adjourned:** 2:36 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Paul Carlson	☐	☒	Kevin Mora	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Megan Morgan	☒	☐
Becky Anderson (EO)	☒	☐	Frank DeLeo (EO)	☐	☒	Karin Peterson	☒	☐
Alan Applebury	☐	☒	Hideki Ebihara	☒	☒	George Risi	☒	☐
Chris Bosio	☒	☐	Heinz Feldmann (EO)	☐	☒	Dana Scott	☐	☒
Marshall Bloom (EO)	☐	☒	Nancy Hoe	☐	☒	Alexandra Scranton	☐	☒
Teresa Borino	☒	☐	Clay Jarrett	☒	☐			
Jeff Burrows	☐	☒	Josh Kellar (EO)	☐	☒			
Carol Calderwood	☐	☒	Scott Kobayashi	☒	☐			
Harlan Caldwell (EO)	☒	☒	Rachel LaCasse	☐	☒			
Marcie Caldwell (EO)	☐	☒	Alida Merritt	☒	☐			

(P=present; A=absent)

Guests: (b)(6)

Minutes: Meeting minutes from 3/19/15 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** Action: Meeting minutes for 3/19/15 were approved with minor modifications: 1. On the first bullet at the top of page 5 insert "using" after the word "studies".

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans (New) ▪ Best (LV) ▪ **HPRD#15-170: Yellow Fever Vaccine Strain 17D** ▪ Becky Anderson presented the risk assessment. The proposed studies are to

	use Yellow Fever virus to compare and contrast innate immunity to the various other Flaviviruses studied in the Best lab. Vaccination associated reactions to 17D yellow fever vaccine are typically mild. After vaccination, vaccinees have reported mild headaches, myalgia, low-grade fevers, or other minor symptoms for 5–10 days. In clinical trials, where symptoms are actively evaluated, incidence of mild adverse events has been <25%. Vaccine strain viremia after primary vaccination with yellow fever vaccine frequently occurs among healthy persons, but is usually waning or absent after the first week. Worldwide, only 23 cases of encephalitis temporally associated with or confirmed to be caused by 17D vaccine. The risk for vaccine-associated neurotropic disease has been estimated as <1/8,000,000 persons. Viscerotropic disease has also been recorded where patients have moderate illness with focal organ dysfunction to severe disease with multiple organ system failure and death. Ten cases have been reported. Primary lab hazards for working with vaccine strain 17D include accidental sharps injuries, generation of aerosols or exposure to mucous membranes. All employees should be offered the Yellow Fever vaccine. Vaccination is recommended for lab persons growing high titers or large volumes of virus. ▪ George Risi stated that the Yellow Fever vaccine is considered one of the safest vaccines ever developed, the viscerotropic disease is more common in people over age 60.(b)(6) ▪ BSL-2 is appropriate for work with the Yellow Fever Vaccine strain 17D. ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **HPRD#15-170** as written.
Item 2:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Hinnebusch (LZP) ▪ **RD#15-320**: Site Specific mutagenesis of CDC-exempt *Y. pestis* strains ▪ Reviewers: Scott Kobayashi, Dana Scott ▪ **Summary:** This RD describes expressing and mutating specific *Y. pestis* genes in order to determine their role, if any, in mediating flea-borne transmission and to introduce specific genes into the bacteria. ▪ Scott Kobayashi summarized the registration. This RD renewal describes using attenuated strains of *Y. pestis*. The strains are attenuated because they lack the virulence plasmid lcr or are pgm-. They will clone genes and express them in *E. coli* to make recombinant proteins, perform complementation studies with strains where specific genes have been knocked out, perform *in vitro* assays and infect fleas with the engineered strains, and finally will perform animal experiments with mice. The animal study proposals are attached to the

	registration and describe several imaging studies. All the antibiotics listed are appropriate and are not used clinically. The recommendations section already describes limitations on combinations of antibiotics allowed for use from the previous IBC review. The NIH Guidelines are appropriate. ▪ Sue Priola pointed out that some of the vector maps were in such low resolution they could not clearly be read, they need to be updated so we can read them. ▪ Dana Scott was not present. The committee did not have any additional comments or concerns. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for studies with CDC-exempt *Y. pestis* strains. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved (Clay Jarrett and Chris Bosio abstained) **RD#15-320** with minor modifications: 1. Update vector maps to a higher resolution so the maps can be read clearly. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-1-a and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under section III-D-1-a of the NIH Guidelines.
Item 3:	<u>Registration Documents for Recombinant DNA Experiments (Renewal)</u> ▪ Hinnebusch (LZP) ▪ **RD#15-321**: Site-specific directed mutagenesis of CDC-exempt *Yersinia pseudotuberculosis* ▪ Reviewers: Karin Peterson, Rachel LaCasse ▪ **Summary:** This study describes assessing the key genetic and molecular mechanisms that account for the inability of *Y. pseudotuberculosis* to be transmitted by fleas. ▪ Karin Peterson summarized the registration. She informed the committee that this is a renewal for the RD. This RD describes working with *Y. pseudotuberculosis* and making mutant constructs by site specific mutagenesis. Mutant strains are complemented, some genes are expressed in *E. coli* to generate recombinant proteins, and finally they perform *in vitro* assays and infect fleas with the engineered strains. The proposed antibiotics are appropriate and are not drugs of choice for treatment. There are no dual use concerns and the NIH Guidelines are appropriate.

	▪ Sue Priola pointed out that some of the vector maps were in such low resolution they could not clearly be read, they need to be updated so we can read them. She also noted that pHSG576 was not included in the RD and needs to be added. ▪ Rachel LaCasse was not present, but informed Sue Priola by email that she had no additional comments or concerns with the registration. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for studies with *Y. pseudotuberculosis*. ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Clay Jarrett and Chris Bosio abstained) **RD#15-321** with minor modifications: 1. Update vector maps to a higher resolution so the maps can be read clearly. 2. Add a map for vector pHSG576. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-1-a and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under section III-D-1-a and III-D-2-a of the NIH Guidelines.
Item 4:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Best (LV) ▪ **RD#14-420 Amend**: Langat Virus ▪ Reviewers: Sue Priola, Hideki Ebihara ▪ **Summary:** This amendment describes studies to understand the mechanisms of TRIM5 and cyclosporine mediated restriction of Langat virus. ▪ Sue Priola summarized the registration. This RD is for Langat virus only. The Best lab has shown that TRIM79 inhibits viral replication in the mouse model. Further, they have shown that human TRIM5 (hTRIM5) and rhesus TRIM5 (rhTRIM5) can inhibit Langat virus replication, which is the human TRIM with greatest homology to rodent TRIM79. Their proposed experiment is the use of directed evolution to passage Langat virus in human cells expressing rhTRIM5 to obtain a virus that is resistant to the barrier infection imposed by TRIM5. Additionally, they would like to determine the role of cyclophillin A in Langat virus infection. They have found the Langat virus required cylcophilin for efficient replication. They will use the same directed evolution to passage Langat virus in cyclosporine (a cyclophilin A/B inhibitor) to obtain a virus that is resistant to the inhibitor. They plan to take the mutants, sequence them to

	identify the mutations, and then introduce point mutations into the molecular clone of Langat virus for further study. Sue Priola stated that this is potential dual use because they may make a virus that is now more virulent and have the ability to evade the human immune system. Sue Priola informed the committee that the registration does describe what experiments they will not do, see details in the RD. Further, the RD does include a description that the Best lab will report to the BSO if unexpected results are obtained. ▪ Sue Priola stated that the main issues are: will the resulting virus be more virulent than the parent virus? If a mutation is found that increases virulence, could this information be applied to more virulent Flaviviruses like TBEV? And finally is the biosafety level appropriate for the proposed studies? The committee needs to discuss all these points. ▪ Sue Priola briefed the committee on some of the reference material that was included in the RD that described a similar system used in HIV that ended with HIV attenuation. The referenced publication stated that the researchers had to combine multiple mutations to generate a more virulent virus, all single mutations resulted in attenuation (which is what the Best lab proposes to do). Sue Priola agreed with the published material that it is unlikely to generate a more virulent virus using directed evolution. ▪ George Risi questioned if studies would change the host tropism. (b)(6) informed the committee that it is not likely because the TRIM proteins are already very species specific, in these experiments they will use rhTRIM5 so no other TRIM proteins should be altered. Further, they are not altering any receptors that would enable/restrict viral entry to a different host. ▪ Bob Heinzen asked if they did find something more virulent in the end, would that change the biosafety level. (b)(6) stated that it would be hard to assess virulence. Their virus will be resistant to rhTRIM5 so they cannot use their mouse model to assess virulence, and you should not see changes in the mouse model if you tested the resulting virus. What they will do to test the virulence is to infect non-human primate (NHP) cells with interferon and see how well the new Langat virus replicates. This should give some indication of how it would affect NHPs and humans. Becky Anderson informed the committee that the current studies will be performed at BSL-2 with additional precautions in a separate, small room within the Best lab. Personnel will wear double gloves, gown, surgical mask and safety glasses or face mask, and shoe covers. The SOP that is attached to the RD describes personal protective equipment and procedures for safe handling of Langat virus during these experiments. ▪ Alex Scranton submitted a question by email. She asked if there is an increase in virulence, should the IBC pre-determine what the level of increase would mean for this work, i.e. should work be moved to BSL-3, and if no space is available, would this alter the decision. She asked if there could be some

	planned procedures so judgment is not inadvertently swayed by inconvenience of a move of research. (b)(6) informed the committee that she already has BSL-3 space and protocols, so a move of research is not an issue if it is deemed necessary to use BSL-3. (b)(6) added that she is comfortable reporting any level of increase in replication to the IBC committee that they request. Megan Morgan added that if the virus did unexpectedly turn out to be extremely hazardous, the biosafety staff or BSO could stop work and require it to be stored in a secure location or the BSL-3 lab so a situation does not have to wait until the next IBC meeting. ▪ Alida Merritt asked if somewhere in the RD the IBC could explain that the work will be more than just standard BSL-2. Becky Anderson informed the committee that the BSL-2 with additional precautions can be added to the recommendations section. ▪ Becky Anderson asked if the committee would like to state a specific increase in viral replication that would require reporting to the BSO. Alida Merritt agreed that some level should be included, this would also cover Alex Scranton's concerns about reporting. (b)(6) said a 1 log increase or more could be reported to the BSO or anything the IBC requested. The committee agreed that a 1 log increase in viral replication in *in vitro* assays would be sufficient communication. This reporting requirement will be added to the recommendations section. ▪ Becky Anderson and Sue Priola re-iterated to the committee that the proposed biosafety level must cover the outcome of the anticipated experimental results. The committee discussed and agreed that BSL-2 with the stated additional precautions is appropriate for the proposed Langat virus studies. ▪ The committee discussed the containment requirements. BSL-2 with additional precautions is appropriate for the described Langat virus studies. The precautions include double gloves, shoe covers, disposable gowns, and mucosal protection including either surgical mask and safety glasses or face shield. ▪ Hideki Ebihara had no additional comments or concerns. ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#14-420 Amend** with minor modifications: 1. Add BSL-2 with additional precautions to the recommendation section. 2. Add to the recommendation section that any increase in viral replication

	greater than 1 log in *in vitro* assays must be reported to the BSO. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under section III-D-1-a, III-D-3-a, and III-E-1 of the NIH Guidelines.
Item 5:	<u>Registration Documents for Recombinant DNA Experiments (New)</u> ▪ Caldwell (LICP) ▪ **RD#15-129**: Selection of homologous recombinants in *C. trachomatis* genitotropic serovars. ▪ Reviewers: Bob Heinzen, Chris Bosio ▪ **Summary:** Introduction of insertion/deletion knockout mutations as well as genetically modified Chlamydial alleles via homologous recombination using the selectable aadA gene (spectinomycin resistance). These experiments include a transient Penicillin resistant step. ▪ Bob Heinzen summarized the registration. This is a new RD that describes developing an efficient system to create knock outs by allelic exchange. They would like to use penicillin selection transiently, however, penicillin is still used clinically to treat certain infections for pregnant women. The proposal describes using a shuttle vector with a deletion in the pgp6 gene. The deletion of pgp6 renders the plasmid transiently stable in *C. trachomatis*, where it confers penicillin resistance (PenR) for 1-2 passages after which the plasmid is lost. The plasmid recombines at a high frequency, but you cannot have two origins of replication so the plasmid will be incompatible with the chromosomal origin of replication so it will be a lethal event. The PenR will be transient until that plasmid is lost, the final recombinants will be spectinomycin resistant and penicillin susceptible. ▪ Bob Heinzen questioned the rate of spontaneous mutations that would render *C. trachomatis* resistant to penicillin. (b)(6) stated that they have never seen it happen in all the years of experience working with strains like L2. ▪ Bob Heinzen questioned if there could be an illegitimate recombination event. (b)(6) stated that it is very unlikely, but they will screen their end product to verify the absence of penicillin resistance. (b)(6) stated that he is in the process of creating these constructs on the L2 serovar, which could provide supportive evidence for the proposed experiments. ▪ Bob Heinzen questioned the need for RAC approval. Becky Anderson explained to the committee that the proposed experiments are a major action of Section III-A-1-a of the NIH Guidelines and require RAC review and approval. At this time the committee's role is to make sure everything is fully described so it can be submitted to the RAC. The deadline for submission to the RAC is July 14th,

	and the next RAC meeting is September 8-10, 2015. ▪ Sue Priola asked if there were alternatives they could use for antibiotic selection. (b)(6) informed the committee that other beta-lactamases may be able to be used as selectable markers, but they are not nearly as efficient and most of the time they are not even successful. Sue Priola questioned if the PenR ever goes beyond 1-2 passages. (b)(6) stated that they have never seen it last longer than 2 passages. Once they finish the 2 passages with PenR, they go directly to spectinomycin selection. The end product will always be checked to ensure that it is not PenR. ▪ Bob Heinzen and Sue Priola stated that the following information should be added to the RD to strengthen the justification for making a Penicillin resistant *C. trachomatis* during a transient step in the recombination process: add additional information on the frequency of spontaneous penicillin resistant mutants, specify why the plasmid is unstable and specifically why a co-integrant of the plasmid in the chromosome is unstable, and finally, include information on penicillin resistance being picked up by the chromosome in the L2 serovar. ▪ Chris Bosio had no additional comments or concerns. ▪ The committee discussed the containment requirements. BSL-2 with three practices is appropriate for studies with *C. trachomatis*. ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously TABLED **RD#15-129.** This RD will be sent to the September 8-10, 2015 RAC meeting. The following minor modifications should be added prior to submission to the RAC. 1. Add additional information on the frequency of spontaneous penicillin resistant mutants. 2. Specify why the plasmid is unstable and specifically why a co-integrant of the plasmid in the chromosome is unstable. 3. Include information on penicillin resistance being picked up by the chromosome in the L2 serovar. These studies are a major action of Section III-A-1-a of the NIH Guidelines requiring RAC review and approval.

Item 6:	**Standard Operating Procedure: SOP#4-28-50 Operation of the Environmental Chamber (Update)** ▪ Becky Anderson informed the committee that this SOP was updated to describe procedures for use of the environmental chamber with or without animals. ▪ The committee had no additional comments or concerns. Action: The committee unanimously approved **SOP#4-28-50 Operation of the Environmental Chamber (Update)** with the following as written.
Item 7:	**Standard Operating Procedure: Biosafety Plan for working with fleas infected with virulent *Y. pestis* (New)** ▪ Sue Priola informed the committee that this is a new biosafety plan for the (b) (6) BSL-3 and ABSL-3. This plan describes working with *Y. pestis* infected fleas. ▪ George Risi question how you know if a flea has taken a blood meal. Clay Jarrett informed the committee the fleas are visualized on a microscope and you can see blood in the abdomen, it is quite easy to tell the difference between a fed and unfed flea. George Risi also questioned if respiratory protection is used. Clay Jarrett said, yes, everyone wears N95s as described in the BSL-3 SOPs. ▪ Alex Scranton submitted questions by email. She questioned the use of Raid Flea Killer, if it is used it my hang around for long period of times and inhibit subsequent studies. Chris Bosio responded that this was a good point, however the use of Raid is a last ditch effort if you can not find a flea, and this is not used as a regular disinfectant and is not going to be used on equipment that they normally handle the fleas in or on. Chris Bosio and Clay Jarrett both informed the group that to date, they have never lost a flea. Alex Scranton also questioned if the room would be sufficiently ventilated by 2 hours after spraying the Raid. The committee discussed and agreed that the BSL-3 labs have sufficient air changes to evacuate the Raid within 2 hours. ▪ Alex Scranton asked by email how frequently the sticky mats are replaced. Clay Jarrett stated that they will be replaced at the beginning of each experiment. This will be added to the biosafety plan. ▪ Alex Scranton pointed out by email that the formatting needs to be fixed at the top of page 10. ▪ Alex Scranton pointed out by email that the use of mice and rats was not consistent in section 5. Becky Anderson will make wording consistent throughout the section. ▪ Sue Priola asked if there is a possibility that an escaped flea could get on

	street clothes and carry it out with you if you doff your PPE in the room. Clay Jarrett said it is unlikely because they would probably be on your hands or arms. The group agreed that the SOP should be updated to state that PPE is visually inspected when the Tyvek is removed. ▪ Sue Priola questioned the purpose of the sticky mats in the surrounding BSL-3 suite. Becky Anderson and Megan Morgan informed the committee that those mats are to meet the pest management requirements for the ACL-3 Guidelines. The pest management is to ensure that outside pests do not come into the lab. The use and placement of sticky mats will be consistent with the NIH Integrated Pest Management Program. An explanation should be added to Section 12.b to clarify the use of sticky mats in the BSL-3 suite (outside of the flea room). ▪ Rachel LaCasse submitted a comment by email that the ABSL-3 room was listed as (b)(6) the room is actually posted as (b)(6) Becky Anderson will put both (b)(6) to reduce confusion on the room number. ▪ Becky Anderson informed the group that the inventory record for neonatal mice needs to be updated to make it consistent with the carcass log that is maintained in the ABSL-3 for Select Agent carcasses. ▪ The committee had no additional comments or concerns. Action: The committee unanimously approved **Biosafety Plan for working with fleas infected with virulent *Y. pestis* (New)** with the following minor modifications: 1. Add to Section 8.h. to visually inspect PPE as it is removed. 2. Add to Section 12.b.ii., replace the matting at the beginning of each experiment. 3. Update the inventory record for neonatal mice to make it consistent with the ABSL-3 Select Agent Carcass log. 4. An explanation should be added to Section 12.b to clarify the use of sticky mats in the BSL-3 suit (outside of the flea room). 5. Fix formatting at the top of page 10. 6. Section 5 needs to be updated to make wording for mice and rats consistent throughout the section. 7. Page 1, ABSL-3 change (b)(6)
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Not present, the BSO report will be reviewed at the June IBC meeting.

Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ Not present.
Report	**IRF Biosafety Manager Report/Megan Morgan** ▪ SEA completed validation testing for BSL-3 and BSL-4 labs. All went well, we are currently waiting on the final report. ▪ DSAT approved our amendment to lift restriction of performing NHP studies in primary containment caging systems. So we are no longer required to house NHPs at BSL-4 in bioBubbles. Only applies to NHPs, we will work towards requesting approval for other animal species.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ None.

Other issues	▪ None.

Next Meeting:

- Date: 6/18/15
- Place: Bldg A Seminar Room
- Time: 1:00 PM

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 6/18/15
Meeting Time: 1:01 PM **Adjourned:** 2:32 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☐	☒	Paul Carlson	☒	☐	Kevin Mora	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Megan Morgan	☒	☐
Becky Anderson (EO)	☒	☐	Frank DeLeo (EO)	☐	☒	Karin Peterson	☐	☒
Alan Applebury	☐	☒	Hideki Ebihara	☒	☐	George Risi	☒	☐
Chris Bosio	☐	☒	Heinz Feldmann (EO)	☐	☒	Dana Scott	☒	☐
Marshall Bloom (EO)	☐	☒	Nancy Hoe	☒	☐	(b)(6)	☐	☒
Teresa Borino	☒	☐	Clay Jarrett	☐	☒			
Jeff Burrows	☐	☒	Josh Kellar (EO)	☐	☒			
Carol Calderwood	☐	☒	Scott Kobayashi	☒	☐			
Harlan Caldwell (EO)	☐	☒	Rachel LaCasse	☒	☐			
Marcie Caldwell (EO)	☐	☒	Alida Merritt	☐	☒			

(P=present; A=absent)

Guests: (b)(6)

Minutes: Meeting minutes from 5/14/15 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** Action: Meeting minutes for 5/14/15 were approved with minor modifications: 1. Page 2, first paragraph change "elicited" to "evaluated". 2. Page 8, Item 5, in the second bullet, last sentence change "penicillin" to "penicillin resistance". Similarly, change the corresponding sentence in the Action items. 3. Item 7, page 10, update the Action item to state the appropriate SOP.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans (New)

	▪ Race (LPVD) ▪ **HPRD#15-171: Chronic Wasting Disease (CWD)** ▪ Becky Anderson presented the risk assessment. This is a new registration for ongoing work that was started in 2003. The registration describes studies in which non-human primates (NHP) were infected with CWD in 2003 and have been evaluated ever since. These studies were initiated in the ABSL-3 because of loss of available space at ABSL-2 for prion animal work at RML following renovations. The space provided for prion work was a dedicated space in the ABSL-3 facility. Animal studies using CWD, which is classified as a BSL-2 infectious organism, have therefore been conducted in (b)(6) for the past several years at a higher biosafety level. The current registration is to request approval to move the remaining NHPs into the (b)(6) in (b)(6) for the duration of the study. The description included in the HPRD states that the likelihood of CWD crossing the species barrier from NHPs to human is expected to be unlikely. Becky Anderson reminded the committee that previously the committee approved the move of all rodent TSE work from ABSL-3 to ABSL-2 for similar reasons. ▪ Dana Scott questioned if the necropsies could still be performed at BSL-2, on a backdraft/downdraft table. Nancy Hoe agreed that those procedures would also be allowed at ABSL-2. ▪ Nancy Hoe pointed out that two of the dual use questions were marked yes, both of the questions are related to changing the host range. She pointed out that the purpose of the study was to identify the natural host range. The committee discussed and agreed there were no dual use concerns. ▪ Nancy Hoe pointed out under manipulation techniques for the HBBF section, aerosolization procedures were marked yes. Nancy Hoe pointed out that normally in the recommendations section the PI discusses how they mitigate the risk from aerosolization procedures. Becky Anderson will follow-up with Brent Race to determine what the procedures are and add a description of the mitigation procedures in the recommendations section. ▪ The committee discussed the containment requirements. The committee agreed that ABSL-2 is appropriate for NHP studies with CWD. ▪ Studies with non-human primates were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **HPRD#15-171** with the following minor modifications: 1. Follow-up with Brent Race to determine what the aerosolization procedures are and add a description of the mitigation procedures in the recommendations section.

Item 2:	Registration of Material (Potentially) Infectious for Humans (New) ▪ De Leo (LHBP) ▪ **HPRD#15-172: Chlamydia spp.** ▪ Becky Anderson presented the risk assessment. This HPRD was submitted for a change in PI on the registered work. Harlan Caldwell will be leaving RML in a couple weeks and has some personnel that will remain at RML and will finish up projects with Chlamydia spp. After Harlan Caldwell leaves, Frank de Leo will be the onsite PI for the remaining projects. The scope of work and animal work remains unchanged. The changes to the registration are the personnel lists, PI, and associated laboratories. ▪ Nancy Hoe pointed out that the NIH Guidelines should be deleted from the HPRD, they are only necessary on the RD. She also pointed out that the reference to the Class I BSC should be removed, they do not have a Class I BSC. ▪ Bob Heinzen pointed out that the accession number needs to be updated. Becky Anderson will fix it. ▪ Scott Kobayashi pointed out that Chlamydia was spelled wrong in the Description section on page 1. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for work with the Chlamydia spp. ▪ Studies with non-human primates and mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Scott Kobayashi abstained) **HPRD#15-172** with the following minor modifications: 1. Delete the NIH Guidelines from the Eukaryote Cell section. 2. Delete reference to Class I BSC. 3. Fix the accession number. 4. Correct spelling of Chlamydia in the Description section on page 1.
Item 3:	Registration of Material (Potentially) Infectious for Humans (New) ▪ Hinnebusch (LZP) ▪ **HPRD#15-174: Diphtheria toxin** ▪ Becky Anderson presented the risk assessment. The proposed studies include the use of diphtheria toxin to deplete specific cell types from transgenic mice. These mice express an inducible DTR, treatment of mice with diphtheria toxin ablates specific cell types so they can study how various cell types affect bacterial pathogenesis. The toxin, when absorbed, affects organs and tissues distant from the site of invasion. The most frequent complications of diphtheria

	are myocarditis and neuritis. The overall case-fatality rate for diphtheria is 5%–10%. Treatment with hyperimmune antiserum has been shown to reduce mortality from 7 to 2.5 percent. Antibodies only neutralize toxin before its entry into cells, so rapid treatment is essential. The primary lab hazards include: contact with skin, inhalation, and accidental needle sticks. The lethal dose of toxin is < 0.1 ug/kg of body weight in humans. To mitigate the risks of working with diphtheria toxin, BSL-2 is recommended. Preparative work with the toxin should be done in a ducted BSC or chemical fume hood at BSL-2 with proper PPE (lab coat/gloves). Refer to the BMBL Appendix I for more details on working with toxins. This information should be added to the recommendations section. ▪ George Risi asked if it should be recommended that an up to date DTP or DTap vaccination be added. Nancy Hoe agreed, since we added vaccination to the Hasenkrug HPRD as well. ▪ Nancy Hoe pointed out that the LD_{50} is less than 100 ng/kg question in the Pathogen/Toxin section should be marked yes. Nancy Hoe also informed the committee that the researcher would need to inject themselves with a full milliliter at this concentration to reach the lethal dose, the concentrations they are working with are low. ▪ Nancy Hoe also pointed out that the volume to inject in the HPRD is different than the volume in the animal study proposal. Becky Anderson will follow-up with Jeff Shannon to determine the correct dose. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for work with the diphtheria toxin. ▪ Studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **HPRD#15-174** with the following minor modifications: 1. Add to the recommendations section the precautions for working with diphtheria toxin including the recommendation for an up to date DTP vaccination. 2. Follow-up with the researcher to determine the appropriate volume and update the HPRD. 3. Change the LD50 less than 100 ng/kg question from “no” to “yes”.
Item 4:	<u>Registration of Material (Potentially) Infectious for Humans (New)</u> ▪ Ebihara (LV) ▪ **HPRD#15-175: Tick-borne Orthomyxoviruses** ▪ Becky Anderson presented the risk assessment. The proposed studies are to

understand the molecular basis for tick-borne orthomyxovirus viral life cycle, pathogenesis, and mechanisms of virulence acquisition and evolution. The HPRD lists several viruses, all listed in an attached table. The disease depends on virus, the viruses on the list are known or suspected to be human pathogens. Some individuals presented with mild febrile illness that led to the isolation of Quaranfil virus. Other individuals infected with Dhori virus developed acute febrile illness characterized by headache, retro-orbital pain, myalgia, general weakness, and a prolonged period of convalescence; two of these people also developed mild symptoms of cranial nerve involvement with radicular syndrome. Other patients with Bourbon virus presented with fever, tiredness, rash, body aches, nausea, and vomiting. In a fatal case the patient had persistent thrombocytopenia, leukopenia, and devolved multi-organ failure (symptoms were similar to Heartland virus infection). With some of the viruses listed, no human disease has been reported, however local populations had neutralizing antibodies to specific viruses. Treatment for infections with Orthomyxoviruses is supportive care, there are no specific treatments or vaccines available.

- The primary lab hazards include accidental sharps injuries, ingestion, or generation of aerosols. The committee discussed the containment requirements. To mitigate the risks of working with Orthomyxoviruses, the BSL-2 viruses will be worked with in the restricted access (b)(6) according to the attached SOP. PPE in this room includes disposable gown, surgical mask, face shield, double gloves, and shoe covers. Work with BSL-3 viruses will be according to the attached BSL-3 SOP. PPE in this lab includes disposable gown, Tyvek coveralls, shoe covers, N95 or PAPR, and double gloves.
- Nancy Hoe pointed out that the human blood and body fluid statement needs to be added to the recommendations section. She also noted in the Organism Listing "orthobunyaviruses" was listed instead of "orthomyxoviruses", this needs to be corrected.
- Nancy Hoe also noted that in the attachment material for the HPRD at the bottom of the first page, it references "nairoviruses" where it should state "orthomyxoviruses".
- The infectious work room SOP also needs to be updated to include Orthomyxoviruses.
- Bob Heinzen pointed out that Jos virus was listed as a BSL-3 agent on the Nature of Experiment section. Becky Anderson indicated that was a typo and needs to be fixed.
- No animal studies were submitted, proposed, or reviewed.
- The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.

Action: The committee approved (Hideki Ebihara abstained) **HPRD#15-175** with the following minor modifications:

	▪ The human blood and body fluid statement needs to be added to the recommendations section. ▪ In the Organism Listing "orthobunyaviruses" was listed instead of "orthomyxoviruses", this needs to be corrected. ▪ In the attachment material for the HPRD at the bottom of the first page, it references "nairoviruses" where it should state "orthomyxoviruses". ▪ The infectious work room SOP also needs to be updated to include Orthomyxoviruses. ▪ Remove Jos virus from the list of BSL-3 viruses in the Nature of Experiment section.
Item 5:	<u>Registration Documents for Recombinant DNA Experiments (Amendment)</u> ▪ Hackstadt (LICP) ▪ **RD#14-110 Amend**: Virulence determinants of spotted fever group rickettsia ▪ Reviewers: Clay Jarrett, Bob Heinzen ▪ **Summary:** The current registration is to define the molecular determinants of virulence in spotted fever group rickettsia. ▪ Bob Heinzen summarized the amendment. The amendment to the RD is to add spectinomycin resistance as a selectable marker. This antibiotic is not used clinically to treat Rickettsia spp. He further stated the *Rickettsia rickettsii* is no longer a Select Agent so approval is now only required from the IBC. ▪ Nancy Hoe asked if George Risi had any concerns with this antibiotic. He stated that he did not have any concerns and that it is not used often in the US at all. ▪ Clay Jarrett was not present, but informed Bob Heinzen by email that he had no additional comments or concerns. ▪ The committee discussed the containment requirements. BSL-2 or BSL-3 is appropriate for the specific strains worked with. See recommendations section for biosafety levels for each strain. ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **RD#14-110 Amend** as written. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-1-a, III-D-1-b, and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-3 under Appendices G-II-B and G-II-C of the NIH Guidelines.

Item 6:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Steele-Mortimer (LICP) ▪ **RD#14-126 Amend**: Salmonella cancer vaccine ▪ Reviewers: Dana Scott, Clay Jarrett ▪ **Summary:** Use of recombinant attenuated *Salmonella typhimurium* vaccine (RASV) as an infectious disease vaccine. ▪ Dana Scott summarized the amendment. This amendment is to add a new animal species to the RD. They want to add work with Mastomys natalensis. Dana Scott informed the committee that all the work would be done in the BSL-4 where they already have experience working with the mastomys. ▪ Nancy Hoe requested that the sentence in the amendment description be changed to state, "We wish to be approved to submit an animal protocol using the Recombinant Attenuated Salmonella Vaccine against Lassa fever in Mastomys natalensis." ▪ Clay Jarrett was not present, but informed Bob Heinzen by email that he had no additional comments or concerns. ▪ The committee discussed the containment requirements. BSL-4 is appropriate for animal studies where the mastomys are challenged with Lassa virus. ▪ Animal studies with Mastomys natalensis were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#14-126 Amend** with the following minor modifications: 1. Reword the sentence in the amendment description to state, "We wish to be approved to submit an animal protocol using the Recombinant Attenuated Salmonella Vaccine against Lassa fever in Mastomys natalensis." Research using prokaryotic hosts is approved at BSL-2 under sections III-D-1-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under section III-D-1-a of the NIH Guidelines.
Item 7:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Feldmann (LV) ▪ **RD#14-447 Amend**: Modified Vaccinia Ankara (MVA) Vaccines ▪ Reviewers: Chris Bosio, Rachel LaCasse ▪ **Summary:** Modified Vaccinia Ankara virus vaccines as a platform against viral

	pathogens. ▪ Rachel LaCasse summarized the amendment. The amendment is to add two new animal species: guinea pigs and hamsters. She has no concerns with the amendment, the Feldmann lab is already performing similar studies with NHPs in the BSL-4. ▪ Chris Bosio was not present, but informed Bob Heinzen by email that he had no additional comments or concerns. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for work with MVA vaccines. Studies where animals are challenged with Ebola virus will be conducted at BSL-4, and are covered under a separate HPRD. ▪ Animal studies with guinea pigs and hamsters were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#14-447 Amend** as written. Research using eukaryotic cells is approved at BSL-2 under Section III-D-1-a of the NIH Guidelines.
Item 8:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Feldmann (LV) ▪ **RD#15-442**: Cytomegalovirus (CMV) ▪ Reviewers: Hideki Ebihara, Chris Bosio ▪ **Summary:** This registration describes using CMV based vaccines against infectious pathogens including hemorrhagic fever or other highly virulent pathogens. ▪ Hideki Ebihara summarized the registration. This is a renewal of the CMV RD. No new work was added to the previously approved RD. The RD describes using recombinant CMV to develop vaccines against a variety of viruses including influenza virus. They have attached an ASP for animal work. They have checked dual use question B yes because they will use synthetic biology techniques. There are no other dual use concerns associated with the RD. ▪ Chris Bosio was not present, but informed Bob Heinzen by email that he had no additional comments or concerns. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for studies with Cytomegalovirus. Any study in which animals are challenged with an infectious virus must be performed at the biosafety level of that challenge virus.

	▪ Animal studies with mice and non-human primates were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#15-442** as written. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under section III-D-1-a of the NIH Guidelines.
Item 9:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Feldmann (LV) ▪ **RD#15-416**: Influenza virus ▪ Reviewers: Scott Kobayashi, Bob Heinzen ▪ **Summary:** The RD describes minigenome/replicon systems, transcription competent virus like particles, and generation of recombinant viruses. ▪ Scott Kobayashi summarized the registration. This is a renewal of recombinant work with influenza A viruses. The registration describes work generating recombinant viruses as well as using minigenome/replicon systems, and transcription-competent virus-like particles. The viruses that the RD covers are listed in the registration, the registration does not cover recombinant work with the reconstructed 1918 influenza virus. They have attached three animal study protocols for ferret, mice, and NHPs. When this RD was initially approved two years ago, the IBC requested a table that described the types of recombinants that would be generated and the corresponding biosafety level for that work. This table is included in the renewal. Additionally, the IBC set forth some restrictions on the work, those restrictions are included in the recommendations section. ▪ Bob Heinzen had no additional comments or concerns. ▪ The committee discussed the containment requirements. The biosafety level varies depending on the parent strains used. Refer to the attached table for specific biosafety levels. ▪ Animal studies with ferrets, mice, and non-human primates were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#15-416** as written. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under

	section III-D-1-a, III-D-3-a, and III-D-3-b of the NIH Guidelines.
Item 10:	Registration Documents for Recombinant DNA Experiments (New) ▪ de Leo (LHBP) ▪ **RD#15-315**: Genetic modification of Chlamydia by plasmid transformation ▪ Reviewers: Bob Heinzen, Hideki Ebihara ▪ **Summary:** This RD is for the change of PI from Caldwell to de Leo. ▪ Bob Heinzen summarized the registration. Bob Heinzen informed the committee that this is another registration that is a PI change for registrations under Harlan Caldwell. Frank de Leo will take over all work for Chlamydia from Harlan Caldwell's lab. The work described in the RD is unchanged, the only changes to the registration are the PI, associated personnel, and the research locations. ▪ Hideki Ebihara questioned whether the dual use question B should be marked yes. The question asks if synthetic biology techniques will be used to construct a pathogen, toxin, or potentially harmful product. The committee discussed extensively, but concluded that the question focuses more on entire organisms generated by synthetic biology techniques rather than specific genes. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for studies with Chlamydia spp. ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Scott Kobayashi abstained) **RD#15-315** as written. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under section III-D-2-a and III-D-1-a of the NIH Guidelines.

Item 11:	Registration Documents for Recombinant DNA Experiments (New) ▪ Heinzen (LICP) ▪ **RD#15-130**: Lentiviral-based gene expression in eukaryotic cell lines ▪ Reviewers: Rachel LaCasse, Scott Kobayashi ▪ **Summary:** Use of lentiviral systems to silence host genes. ▪ Rachel LaCasse summarized the registration. This RD describes use of lentiviral systems to silence host genes and assess the effects on *Coxiella burnetii* exempt infection. They will use CRISPER editing and siRNA to silence host genes. The lentiviral system that will be used is a third generation system that is replication defective. The antibiotics that will be used are not clinically relevant for treatment of *C. burnetii* exempt infections and the antibiotic resistance genes will not be acquired by *C. burnetii* from the mammalian cells. ▪ Scott Kobayashi had no additional comments or concerns. ▪ Clay Jarrett asked by email if the antibiotics used for selection of the Lentiviral constructs should be mentioned in the context of *Coxiella burnetii* infection. Bob Heinzen informed the committee that the antibiotics used for selection would never be present at the same time as the Coxiella infection of mammalian cells. ▪ Nancy Hoe informed the committee that in the Eukaryotic Cell section, Nature of Experiment subsection, the "various eukaryotic genes" statement should include, "no known oncogenes". ▪ Bob Heinzen pointed out that in the Eukaryote Cell section the NIH Guidelines should be changed from III-D-3-a to III-D-2-a. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for studies with the proposed Lentiviral vectors and *C. burnetii* exempt. ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Bob Heinzen abstained) **RD#15-130** with the following minor modifications: 1. In the Eukaryote Cell section, the NIH Guidelines should be changed from III-D-3-a to III-D-2-a. 2. In the Eukaryotic Cell section, Nature of Experiment subsection, the "various eukaryotic genes" statement should include, "no known oncogenes". Research using prokaryotic hosts is approved at BSL-2 under sections III-D-2-a and of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under

	section III-D-2-a of the NIH Guidelines.
Item 12:	**Standard Operating Procedure: SOP BSL-3 Bunyaviruses (Update)** ▪ Becky Anderson informed the committee that the SOP is being updated to include tick-borne orthomyxoviruses. ▪ Alex Scranton submitted comments by email, several of them were regarding formatting. All the formatting will be fixed. ▪ Throughout the SOP, there are many instances where orthomyxoviruses need to be included where the SOP only states bunyaviruses. The SOP will be updated throughout to make it consistent and include both viruses. ▪ Nancy Hoe pointed out that the section on reporting illness or exposures should be updated. ▪ Nancy Hoe noted that the biosafety cabinet section should be updated, the lab only has a Class II Type A2. ▪ Alex Scranton submitted by email that the Special Occupancy Practices section is confusing, the committee agreed that it is confusing and will update it. Becky Anderson added, in the same sections, SARS-CoV should be deleted, it is no longer present in that lab. ▪ The committee had no additional comments or concerns. <u>Action:</u> The committee approved (Hideki Ebihara) **SOP BSL-3 Bunyaviruses (Update)** with the following minor modifications: 1. Fix formatting throughout. 2. Update throughout to include both viruses. 3. Update section on reporting illnesses and exposures to the current version. 4. Update the biosafety cabinet section to state the lab has Class II Type A2 BSCs. 5. Clarify the Special Occupancy Practices Section, remove references to SARS-CoV.

Item 13:	**Standard Operating Procedure: SOP BSL-3 Powassan Virus (b)(6) Update)**

- Becky Anderson informed the committee that the Powassan virus SOP has several updates throughout. The biggest change is to allow flexibility to use either an N95 or PAPR. The current SOP states PAPR only, however, in the (b)(6) (b)(6) for Powassan virus, the SOP states N95 or PAPR, the update will make the SOPs consistent. The Bloom lab has also added two SOPs for microscopy work. Finally this lab no long has multiple pathogens in it, all the language for procedures with multiple pathogens has been removed.
- George Risi pointed out on page 5 that the SOP allows researchers to enter the lab without respiratory protection if no work is going on, he questioned if that was accurate. Bob Heinzen informed the committee that when there is no active work in the lab, personnel can enter without respiratory protection, a sign is posted on the door to indicate when there is active work. This procedures works well, especially if someone is entering the lab to do paperwork only. To ensure this procedure is clear, add that the sign will be posted on the door in section 2.4.
- Bob Heinzen questioned the benefit of spraying shoe covers immediately before removal in the Facility Exit Section. He stated that none of the other BSL-3 suites in (b)(6) follow that procedure. Becky Anderson clarified that these users previously worked in the (b)(6) where there were two labs that share a common vestibule before they exit into an anteroom and the SOPs for those rooms include spraying shoe covers before leaving the lab. The committee discussed, they agreed that spraying shoe covers immediately before removing them is not required. Becky Anderson will check with the users to see if they still want to include those procedures.
- Alex Scranton submitted a question by email, is the room number incorrect on the first page of the document. Nancy Hoe stated that the room number is correct, but can be deleted because it is confusing. The SOP will continue to state (b)(6)'.
- Megan Morgan pointed out that the order of PPE removal should be updated so the gloves are the very last item that gets removed. This will make it consistent with all the other (b)(6) SOPs.
- The committee had no additional comments or concerns.

Action: The committee unanimously approved **SOP BSL-3 Powassan Virus (b)(6) (Update)** with the following minor modifications:

1. Add that the sign for active work will be posted on the door in section 2.4.
2. Check with (b)(6) researchers to see if they want to continue to spray shoe covers before removal, update SOP accordingly.
3. Delete page numbers from the first page of SOP.

	4. Update the order that PPE gets removed so the inner gloves are the last ones to be removed.
Item 14:	**Standard Operating Procedure: BSL-4 SOP#4-28-44 Husbandry and Manipulation of Swine in Level 4 Biocontainment (Update)** ▪ Bob Heinzen informed the committee that the updates to the next two BSL-4 SOPs are to allow the optional use of open caging systems with swine and rabbits. OBA previously revised the NIH Guidelines to allow the optional use of open caging systems for NHPs if specific conditions were met. Bob Heinzen informed the committee that OBA would have to approve this change, so the IBC committee could approve pending OBA approval. ▪ Nancy Hoe informed the committee that in Appendix Q of the NIH Guidelines there is a section for loose housed animals, but the animals listed here are not loose housed, they are in cages and are up off the floor so they cannot kick the walls or floors. The loose housed animals require more containment enhancements, much like a BSL-3 Ag facility. ▪ Megan Morgan informed the committee that two items could be added to address the concerns of OBA, to ensure they understand that the integrity of the room cannot become compromised by housing these species in the room as long as they are in cages. This additional detail can be included in the letter to OBA. ▪ George Risi asked if this would cover all species so we would not have to go back to OBA when new animals are added to the RML BSL-4. Nancy Hoe agreed that the intent of the letter to OBA will cover all animal species that could be housed in cages or pens. ▪ Alex Scranton submitted by email that a picture of the bioBUBBLEs might be helpful. Rachel LaCasse stated that we do not have pictures of swine cages in bioBUBBLEs, but we could add a picture of an empty bioBUBBLEs. ▪ The committee had no additional comments or concerns. Action: The committee unanimously approved **BSL-4 SOP#4-28-44 Husbandry and Manipulation of Swine in Level 4 Biocontainment (Update) PENDING OBA APPROVAL** with the following minor modifications: 1. Add a picture of the bioBUBBLEs to the SOP. 2. Submit a letter to OBA to request the optional use of bioBUBBLEs for all animal species.

Item 15:	**Standard Operating Procedure: BSL-4 SOP#4-28-53 Husbandry and manipulation Procedures for Rabbits in Level 4 Biocontainment (Update)** ▪ This SOP was reviewed and commented at the same time as BSL-4 SOP4-28-44. ▪ The committee had no additional comments or concerns specific to this SOP. Action: The committee unanimously approved **BSL-4 SOP#4-28-53 Husbandry and manipulation Procedures for Rabbits in Level 4 Biocontainment (Update) PENDING OBA APPROVAL** with the following minor modifications: 1. Add a picture of the bioBUBBLEs to the SOP. 2. Submit a letter to OBA to request the optional use of bioBUBBLEs for all animal species
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Nancy Hoe presented the BSO report.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ Next Friday June 26th, the Quad will be on generator power for the day. There will be no back-up power so plan your work accordingly. ▪ An ambulance responded on Tuesday to a non-work related incident. A visitor onsite fainted after donating blood earlier in the day. ▪ On Monday this week a different visitor onsite passed out, no medical response was required.
Report	**IRF Biosafety Manager Report/Megan Morgan** ▪ The ABSL-3 will be shutdown at the end July for a large project including replacement of the cage wash, painting hallways, and installing paneling in animal holding rooms. The HVAC system controls and monitors will also be updated during the project. DOHS is working with all parties to bring down the facility to hand over to the contractors.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ None.

Other issues	▪ None.

Next Meeting:

- Date: 7/16/15
- Place: Bldg A Seminar Room
- Time: 1:00 PM

RML Biosafety Committee Meeting
June 18, 2015
Biosafety Officer/Responsible Official Report

1) Requests approved by BSO since last meeting:

a) Summer Student Projects

i) *DeLeo*

(1) (b)(6) *molecular analysis of Klebsiella pneumonia and Staphylococcus aureus*

ii) *Feldmann (*(b)(6)*)*

(1) (b)(6) *cloning Arenavirus protein genes*

iii) *Hackstadt (Noriea)*

(1) (b)(6) *epitope mapping of Rickettsia rickettsia surface proteins (BSL-2)*

iv) *Munster*

(1) (b)(6) *determining immune response and evolution of Ebolavirus (BSL-2)*

(2) (b)(6) *general microbiology and molecular biology techniques*

2) ***New requests approved by committee via electronic review:***

a) *None*

3) ***New requests***

a) *Human Pathogen Registration Documents*

i) ***New***

(a) *Race (LPVD)*

(a) ***HPRD-15-171****: Chronic Wasting Disease*

(b) *DeLeo (LHBP)*

(a) ***HPRD-15-172****: Chlamydia spp.*

(c) *Hinnebusch (LZP)*

(a) ***HPRD-15-174****: Diphtheria toxin*

(d) *Ebihara (LV)*

(a) ***HPRD-15-175****: tick-borne orthomyxoviruses*

b) *Registration Documents for Recombinant DNA Experiments*

i) ***Amend***

(a) *Hackstadt (LCIP)*

(a) ***RD-14-110:*** *Virulence determinants of spotted fever group rickettsia*

(i) Add spectinomycin resistance as selectable marker

(b) *Steele-Mortimer (LICP)*

(a) ***RD-14-126:*** *Salmonella cancer vaccine*

(i) Add mastomys rodent

(c) *Feldmann (LV)*

(a) ***RD 15-447****: MVA vaccines*

(i) Add hamsters and guinea pigs

ii) ***Renewal***

(a) *Feldmann (LV)*

(a) ***RD 15-442****: Cytomegalovirus-based vaccines*

(b) ***RD 15-416****: Generation of recombinant influenza A viruses*

iii) ***New***

(a) *DeLeo (LHBP)*

(i) RD-15-315:

(b) *Heinzen (LICP)*

(i) ***RD-15-130:*** *Lentiviral-based gene expression in eukaryotic cell lines*

c) *Standard Operating Procedures*

i) *Updates*

(a) *BSL-3 Bunyaviruses 7 Tick-borne orthomyxoviruses*

(b) *Powassan Virus BSL-3 SOP Suite D*

(c) *4-28-44 Swine Husbandry and manipulation*

(d) *4-28-53 Husbandry and manipulation of rabbits*

4) ***Animal Study Protocols Review***

Title	***Associated HPRD***	***Associated RD***	***Reviewer***
The role of NK cells in IFNα17, and IFNα21-mediated protection from HIV in humanized mice	*12-55 (HIV) 12-104 (HBBF)*	*N/A*	*M. Morgan*
Efficacy of modified Vaccinia Ankara (MVA) vectored Middle East respiratory syndrome coronavirus vaccine in NHPs	*12-143 (MERS) 14-159 (MVA)*	*15-447*	*N.Hoe*
Protective efficacy of an inactivated Ebola whole virus vaccine against ZEBOV Guinea and analysis of host signatures associated with protection in NHPs	*13-90 (Ebola virus)*	*N/A*	*B. Anderson*
Efficacy testing of a vaccine candidate for MERS-CoV in rhesus macaques	*12-143 (MERS-CoV)*	*15-404*	*B. Anderson*
Efficacy of a monoclonal antibody treatment against Ebola virus in mice	*13-90 (Ebola virus)*	*N/A*	*B. Anderson*
Virulence determinants off spotted fever group rickettsia in guinea pigs	*14-38 (Rickettsia spp. (exempt))*	*14-110*	*B. Anderson*
The role of T follicular regulatory cells in Inhibiting B cell responses against Friend Virus	*N/A (Friend virus)*	*N/A*	*N. Hoe*

RML Biosafety Committee Meeting
June 18, 2015
Biosafety Officer/Responsible Official Report

Title	*Associated HPRD*	*Associated RD*	*Reviewer*
Treatment of chronic HIV infection in humanized mice with different subtypes of human interferon alpha	*12-55 (HIV) 12-104 (HBBF)*	*N/A*	*M. Morgan*
The mechanism of Treg suppression of B cell responses during Friend virus infection in mice	*14-161 (Diphtheria toxin)*	*N/A*	*M. Morgan*
Contributions of IL10 to disease in humanized mice infected with Ebola virus	*13-90 (Ebola)*	*N/A*	*M. Morgan*
Identification of immune cells required for protection against tularemia in mice	*13-73 (F. tularensis LVS) 13-71 (F. tularensis)*	*N/A*	*M. Morgan*
Innate immunity and retrovirus-induced neurological disease in mice	*N/A (murine polytropic retrovirus)*	*13-214*	*M. Morgan*
The effect of interleukin-1 receptor antagonist (AnaKinra) on Ebola infection in rodent models	*13-90 (Ebola)*	*N/A*	*M. Morgan*
Efficacy of IFN-α treatment against Ebola virus in guinea pigs	*13-90 (Ebola)*	*N/A*	*B. Anderson*
Evaluation of Amodiaquine and Artesuntle for the treatment of Ebola hemorrhagic fever	*13-90 (Ebola)*	*N/A*	*B. Anderson*
Testing of recombinant attenuated Salmonella vaccines (RASV) against Lassa virus infection in Mastomys natalensis	*12-44 (Salmonella) 13-94 (Lassa)*	*14-126 (RASV)*	*M. Morgan*
Therapeutic vaccination against trachoma in cynomolgus monkeys	*13-32 (C. trachomatis)*	*N/A*	*B. Anderson*
Determining the role of subcapsular sinus macrophages in Y. pestis infection of mice	*13-04 (Y. pestis (vir)) 14-66 (Y. pestis (atten))*	*13-303*	*N. Hoe*
Determining the effects of psoriasis on progression of Y. pestis infection in mice	*13-04 (Y. pestis (vir))*	*N/A*	*N. Hoe*
The role of B cells and CD86 in regulatory T cell responses during persistent viral infection in mice	*N/A (Friend virus)*	*N/A*	*M. Morgan*
Treatment of relapsed HIV infection in humanized mice with different subtypes of human interferon alpha	*12-55 (HIV) 12-104 (HBBF)*	*N/A*	*B. Anderson*
Antisense oligonucleotides to delay or prevent onset of prion disease in mice	*N/A (rodent scrapie)*	*N/A*	*B. Anderson*
Activation of glia and neurons by virus infection and innate immune stimulation in mice	*N/A*	*N/A*	*M. Morgan*
Role of the kinesin motor during prion spread ina mouse model	*N/A (rodent scrapie)*	*N/A*	*M. Morgan*
Efficacy testing of neutralizing monoclonal antibodies against MERS-CoV in common marmosets	*12-143 (MERS-CoV)*	*N/A*	*B. Anderson*
Species barrier to EVD in humanized mice infected with Reston virus or mouse-adapted Ebola virus	*13-90 (Ebola)*	*N/A*	*N. Hoe*
Efficacy of a Modified Vaccinia Ankara (MVA)-based vaccine against Ebola virus in rodent models	*13-90 (Ebola) 14-159 (MVA)*	*15-447*	*M. Morgan*

RML Biosafety Committee Meeting
June 18, 2015
Biosafety Officer/Responsible Official Report

5) ***Biosafety Training Performed – Megan Morgan, Becky Anderson, Nancy Hoe***

Type of Training	***Number of Sessions***	***Number of Employees Trained***
RML Employee Annual Refresher (with Paul Carlson)	***6***	***259***
Select Agent Initial Training	***2***	***4***
BSL-3 Visitor Training	***5***	***10***
BSL-4 Laboratory Biosafety Training	***8***	***4***

6) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
   a) *Biological Incident Report:*
      i) *None*

7) ***Select Agent Issues***
   a) *DSAT BSL-3 inspection report*
   b) *USDA AgSAS BSL-4 inspection report*

8) ***Other Issues***
   a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 7/16/15
Meeting Time: 1:01 PM **Adjourned:** 1:28 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Paul Carlson	☒	☐	Kevin Mora	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Megan Morgan	☐	☒
Becky Anderson (EO)	☒	☐	Frank DeLeo (EO)	☐	☒	Karin Peterson	☒	☐
Alan Applebury	☐	☒	Hideki Ebihara	☒	☐	George Risi	☐	☒
Chris Bosio	☐	☒	Heinz Feldmann (EO)	☐	☒	Dana Scott	☒	☐
Marshall Bloom (EO)	☐	☒	Nancy Hoe	☐	☒	Alexandra Scranton	☐	☒
Teresa Borino	☐	☒	Clay Jarrett	☒	☐			
Jeff Burrows	☒	☐	Josh Kellar (EO)	☐	☒			
Carol Calderwood	☐	☒	Scott Kobayashi	☒	☐			
Harlan Caldwell (EO)	☐	☒	Rachel LaCasse	☒	☐			
Marcie Caldwell (EO)	☐	☒	Alida Merritt	☐	☒			

(P=present; A=absent)

Guests: (b)(6)

Minutes: Meeting minutes from 6/18/15 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** Action: Meeting minutes for 6/18/15 were approved with minor modifications: 1. Clay Jarrett asked why the Hasenkrug HPRD for diphtheria toxin was referenced on page 4 second bullet. Becky Anderson clarified that the reference is because the Hasenkrug HPRD for diphtheria included a recommendation for DTAP vaccination, Nancy Hoe wanted to ensure consistency between the documents. 2. Hideki Ebihara informed the committee that his HPRD#15-175 for Tick-borne Orthomyxoviruses did not include animal studies with mice. 3. Bob Heinzen stated that RD#15-130 should be clarified to state "exempt" strains of *C. burnetii*.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans (New) ▪ Feldmann (LV) ▪ **HPRD#15-173: Sendai Virus** ▪ Becky Anderson presented the risk assessment. This HPRD has two study purposes. First, the Best lab will use Sendai virus as a potent activator of innate immune responses leading to production of Type I interferon in tissue culture models. The second use is for the Feldmann lab to use Sendai virus as a vaccine vector to express genes of interest. In this initial study, Sendai virus will be used to express an Ebola glycoprotein in hamsters. The vaccine was generated and prepared by a collaborator so no recombinant work will be performed at RML. The Sendai vaccine is a replication incompetent virus. Sendai virus causes respiratory disease in rodents and sometimes swine. There is limited evidence of zoonotic transmission to humans, but the virus is capable of infecting human cell lines, and is similar to human parainfluenza virus type 1. There are no specific treatments or vaccines available. The primary lab hazards include generation of aerosols, parenteral inoculation, and accidental needle sticks. For these reasons, work with Sendai virus is classified as BSL-2. ▪ The committee discussed the containment requirements. The committee agreed that BSL-2/ABSL-2 is appropriate for studies with Sendai virus. ▪ Becky Anderson informed the committee that the synopsis section states two purposes for this "RD" which should be changed to "HPRD". ▪ Becky Anderson also stated that the HPRD had dual use question B marked yes for the use of synthetic biology techniques. She asked if the committee agreed that it should be changed to no since no recombinant work will be performed at RML. The committee agreed that question B should be changed from yes to no. ▪ Alex Scranton submitted questions by email. She questioned the biosafety level listed in the animal use section, containment BSL comments. Her concern was that in this HPRD, they state "typically BSL-4" she wondered if it should be specific until there is an amendment for a different challenge virus. The committee discussed and proposed the comment section sentence be reworded to, "Sendai virus is a BSL-2 virus. However, in challenge experiments vaccinated animals will be housed at the biosafety level of the challenge virus". ▪ Studies with hamsters were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **HPRD#15-173** with the following minor modifications: 1. In the synopsis section, change "There are two purposes for this RD" to "HPRD".

	2. In the animal use section, Containment BSL; change the comments sentence to, "Sendai virus is a BSL-2 virus. However, in challenge experiments vaccinated animals will be housed at the biosafety level of the challenge virus." 3. Change dual use question B from "yes" to "no".
Item 2:	<u>Registration of Material (Potentially) Infectious for Humans (New)</u> ▪ Gardner (RMVB) ▪ **HPRD#15-176: Human and Non-human primate (NHP) blood and body fluids** ▪ Becky Anderson presented the risk assessment. This HPRD is to cover RMVB staff. RMVB staff either independently collect NHP samples or assist PIs in the collection of NHP samples. Typically samples are handed off to PIs at the time of collection, sometimes they are temporarily stored in (b)(6) Histopathology usually works with fixed tissue samples. However, on occasion may work with fresh frozen human or NHP tissue until they process and fix onsite for further analysis. The three most common human blood borne pathogens include: Hepatitis B, Hepatitis C, and HIV. All RML employees are offered Hepatitis B vaccine free of charge. Currently there is no vaccine for prevention of HIV or Hepatitis C. All RML employees are given annual training on blood borne pathogens. The risks of working with NHP blood or body fluids include risk of exposure to Herpes B virus (specifically if working with old world NHP). Infection in humans is rare, but can often result in severe neurologic impairment or fatal encephalomyelitis if the patient is not treated soon after exposure (approx. 70% mortality). Immediate diagnosis and treatment with antiviral drugs is critical. Valcyclovir is maintained in all the animal facilities where NHPs are housed and RML employees are directed to contact OMS immediately prior to taking the valcyclovir if they have had an exposure. The primary lab hazards include inhalation, ingestion, contact with mucous membranes, and accidental sharps injuries. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for work with human and non-human primate blood and body fluids. ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved (Rachel LaCasse and Dana Scott abstained) **HPRD#15-173** as written.
Item 3:	**Exposure Control Plan (Annual Review)** ▪ Sue Priola informed the committee that this is the annual review of the Exposure Control Plan. There are minor edits throughout and all changes were tracked. ▪ Alex Scranton submitted several questions by email:

	▪ On page 8, under Response for Biohazard Exposures Requiring Immediate Medical Attention, it states, "accident". Should this be changed to "injury or incident" to be consistent with the rest of the document? The committee agreed that it should be changed. ▪ On pages 8-10, it is not clear who fills out the Exposure Risk Assessment Guide and the flow of documentation is not clear except in Appendix 3. Becky Anderson informed the committee that it is always the OHSM/IRFBSM that fills out the Exposure Risk Assessment Guide. The committee discussed that the flow chart in Appendix 3 should stay where it is, but should be referenced on pages 8-10. ▪ On Page 10 Alex Scranton questioned why the section for Post-Exposure Clinical Evaluation and Follow-up did not include BSL-2 exposures. Becky Anderson informed the committee that only in the case of BSL-3 or BSL-4 exposures does care transfer from OMS to the Infectious Disease Advisor. In the event of a BSL-2 exposure, OMS maintains care of the exposed individual. ▪ On page 15, the plan states that Select Agents are not entered into PI Dashboard and are submitted by paper form only. Alex Scranton questioned if this was still accurate. Becky Anderson informed the committee that PI Dashboard is still not secure enough to put Select Agent registrations on it. ▪ On page 19, the URL listed for the BMBL is outdated. Becky Anderson will update with the current link. ▪ Page 37, Appendix 3 the "IR" and "EG" are not defined, are they the same as the Injury and Exposure Risk Assessment Guide? Becky Anderson will update Appendix 3 to make the chart consistent with the rest of the wording. ▪ The committee had no additional comments or concerns. Action: The committee unanimously approved the **Exposure Control Plan (Annual Review)** with the following minor modifications: 1. On page 8, under Response for Biohazard Exposures Requiring Immediate Medical Attention, it states, "accident". Change to "injury or incident". 2. On pages 8-10, state that the OHSM/IRFBSM fills out the Exposure Risk Assessment Guide. Reference the flow chart in Appendix 3 on pages 8-10. 3. On page 19, the URL listed for the BMBL needs to be updated. 4. Update Appendix 3 to make the chart consistent with the rest of the document.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Not present. BSO report attached.

Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ Annual fire drills will take place next week. Reminder emails will be sent out. ▪ A medical transport occurred last week on campus. It was not due to a work related injury.
Report	**IRF Biosafety Manager Report/Megan Morgan** ▪ Not present.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ None.

Other issues	▪ None.

Next Meeting:

- Date: 8/20/15
- Place: Bldg A Seminar Room
- Time: 1:00 PM

RML Biosafety Committee Meeting
July 16, 2015
Biosafety Officer/Responsible Official Report

1) Requests approved by BSO since last meeting:

a) Summer Student Projects

i) *Hackstadt (b)(6)*

(1) (b)(6) epitope mapping of Rickettsia rickettsia surface proteins (BSL-2)

ii) *Hinnebusch (b)(6)*

(1) (b)(6) cloning and mutagenesis of Y. pestis (Select Agent exempt) (BSL-2)

iii) *Rosa (multiple)*

(1) (b)(6) screen colonies or isolate genomic DNA from cultures of Borrelia burgdorferi and Leptospira biflexa (non-infectious saprophyte).

2) ***New requests approved by committee via electronic review:***

a) *None*

3) ***New requests***

a) *Human Pathogen Registration Documents*

i) ***New***

(a) *Feldmann (LV)*

(a) ***HPRD-15-173****: Sendai virus*

(b) *Gardner (RMVB)*

(a) ***HPRD-15-176****: Human/non-human primate blood and body fluids*

b) *Registration Documents for Recombinant DNA Experiments*

i) ***None***

c) *Standard Operating Procedures*

i) *Exposure Control Plan Annual Review*

4) ***Animal Study Protocols Review***

Title	***Associated HPRD***	***Associated RD***	***Reviewer***
The mechanism of CD86 induction in Friend virus-infected B cells in mice	*N/A*	*N/A*	*M. Morgan*
Assessing T-705 as a post exposure countermeasure to Lujo virus infection in strain 13 guinea pigs	*13-94 (Lujo virus/Arenaviride)*	*N/A*	*N.Hoe*
Pathobiological role of macrophages/monocytes in Ebola virus pathogenesis in mice	*13-90 (Ebola virus)*	*14-426*	*N. Hoe*
Pathogenicity of Zaire ebolavirus isolates from West Africa 2014 in IFNAR -/- mice	*13-90 (Ebola virus)*	*N/A*	*M. Morgan*
Assessment of CWD transmission to humans using tow transgenic mouse models	*N/A*	*N/A*	*B. Anderson*
Assessment of prion disinfectants by RT-QuIC analysis and mouse bioassay	*N/A*	*N/A*	*B. Anderson*

Title	*Associated HPRD*	*Associated RD*	*Reviewer*
Further development of hDPP4 mice MERS-CoV animal model	*12-143 (MERS)*	*N/A*	*M. Morgan*
Production of antibodies against great ape pathogens in rabbits	*N/A*	*N/A*	*N. Hoe*

5) ***Biosafety Training Performed – Megan Morgan, Becky Anderson, Nancy Hoe***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
New Security Guards	***1***	***6***
Annual Employee Refresher Training	***1***	***15***
Select Agent Initial Training	***1***	***2***
BSL-3 Laboratory Biosafety Training	***2***	***3***
BSL-4 Laboratory Biosafety Training	***2***	***2***
BSL-4 Annual Refresher Training	***1***	***1***

6) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
a) *Biological Incident Report:*
i) *None*

7) ***Select Agent Issues***
a) *None*

8) ***Other Issues***
a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 8/20/15
Meeting Time: 1:01 PM **Adjourned:** 2:39 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Paul Carlson	☒	☐	Kevin Mora	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Megan Morgan	☒	☐
Becky Anderson (EO)	☒	☐	Frank DeLeo (EO)	☐	☒	Karin Peterson	☒	☐
Alan Applebury	☐	☒	Hideki Ebihara	☒	☐	George Risi	☒	☒
Chris Bosio	☒	☐	Heinz Feldmann (EO)	☐	☒	Dana Scott	☒	☐
Marshall Bloom (EO)	☒	☐	Nancy Hoe	☒	☐	Alexandra Scranton	☐	☒
Teresa Borino	☒	☐	Clay Jarrett	☒	☐			
Jeff Burrows	☐	☒	Josh Kellar (EO)	☐	☒			
Carol Calderwood	☐	☒	Scott Kobayashi	☐	☒			
Harlan Caldwell (EO)	☐	☒	Rachel LaCasse	☐	☒			
Marcie Caldwell (EO)	☒	☐	Alida Merritt	☒	☐			

(P=present; A=absent)

Guests (b)(6)

Minutes: Meeting minutes from 7/16/15 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** Action: Meeting minutes for 6/18/15 were approved with minor modifications: 1. Sue Priola pointed out a couple of minor typos. **Caldwell RD#15-129**: ▪ Sue Priola reminded the committee that Harlan Caldwell's RD to transiently express penicillin resistance in *Chlamydia trachomatis* was tabled at the May IBC meeting. The committee agreed that the RD should be submitted to the RAC for review as the studies proposed were a major action of Section III-A-1-a of the NIH Guidelines. ▪ Nancy Hoe submitted the proposal to the RAC, and on July 21, 2015 a response was received. The RAC's determination was that if the expression of penicillin resistance is only transient, then these experiments are not considered a major

	action of Section III-A-1-a of the NIH Guidelines. Action: The committee unanimously approved **RD#15-129** as written.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans (Amendment) ▪ Steele-Mortimer (LB) ▪ **HPRD#12-44 Amend: *Salmonella typhimurium*** ▪ Becky Anderson presented the risk assessment. The proposed amendment is to perform cell sorting of Salmonella cultures and Salmonella infected cells. The primary lab hazard for this work is the generation of aerosols. To mitigate the risk of cell sorting, RML recently purchased a Class II BSC to enclose the BD Facs Aria. The BD Facs Aria is located in a dedicated room for cell sorting (b)(6) (b)(6) The BD Facs Aria is equipped with an Aerosol Management system that rapidly evacuates aerosolized particles that are produced inside the sort chamber. The AMS creates a negative pressure inside the sort chamber and draws aerosolized particles into a four stage 0.01 um HEPA filter. An SOP for sorting infected cells has been developed and is referenced in the amendment. The SOP will be reviewed separately from this amendment. ▪ The committee discussed the containment requirements. BSL-2 with additional precautions is appropriate for cell sorting of Salmonella infected cells. Gloves and a lab coat must be worn at all times. Double gloves must be worn when handling samples or touching any potentially contaminated surfaces. ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **HPRD#12-44 Amend** approved as written.
Item 2:	Registration of Material (Potentially) Infectious for Humans (Amendment) ▪ Feldmann (LV) ▪ **HPRD#12-131 Amend: Reconstructed 1918 Influenza virus** ▪ Becky Anderson presented the risk assessment. The amendment is to add animal studies with mice. The primary lab hazards include bites and/or scratches. To mitigate the hazards of working with mice in the ABSL-4, the following SOPs are already in place: • 4-28-16 Husbandry procedures for rodents in Level 4 biocontainment

	• 4-28-21 ABSL-4 Rodent Inhalant Anesthesia • 4-28-41 Recapture of Escaped Rodents in Level 4 Containment • 4-28-48 Inoculation/Infection and Blood Collection Procedures in Rodents in Level 4 Biocontainment ▪ The proposed studies will also follow the SOP for Influenza Viruses (including Highly Pathogenic Avian Influenza and Reconstructed 1918 Influenza virus). This SOP outlines additional precautions including, work with reconstructed 1918 virus will always be physically and/or temporally separated from work with HPAI, and also recommends seasonal influenza vaccination. ▪ The committee discussed the containment requirements. BSL-3 enhanced is appropriate for work with reconstructed 1918 Influenza virus, however RML cannot meet those requirement in the normal BSL-3 labs. Instead the work will either be performed at BSL-4 or in a BSL-4 lab that is lowered to enhanced BSL-3 containment. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **HPRD#12-131 Amend** as written.
Item 3:	<u>Registration Documents for Recombinant DNA Experiments (New)</u> ▪ Best (LV) ▪ **RD#15-448**: Vesicular Stomatitis virus (VSV) ▪ Reviewers: Chris Bosio, Sue Priola ▪ **Summary:** This study describes using reverse genetics to determine which VSV protein is targeted by MxA and how this affects virus replication. ▪ Chris Bosio summarized the registration. This RD describes using VSV to look at interactions of viral proteins with MxA. MxA is an interferon stimulating protein. The Best lab wants to look specifically at two mutations in the NA protein that were previously associated with virus strains resistant to MxA inhibition so they can test those mutations in combination or independently. This work will generate infectious VSV, but all the manipulations will be performed in the BSL-2 enhanced lab as described in the attached SOP. Chris Bosio questioned why the figures referenced glycoproteins from other viruses that were not described in the RD. (b)(6) informed the committee that it was a carryover from Heinz Feldmann's figures, she will not use any foreign glycoproteins, only that of VSV. The figures will be updated and references to foreign glycoproteins will be removed. ▪ Chris Bosio had no dual use concerns with the proposed work. For the biosafety of the proposed studies, the RD states that an increase in virus replication by 1 log will be reported to biosafety staff. This seems appropriate

	and is consistent with the IBC decision on a previous RD with similar studies. ▪ Sue Priola questioned if dual use question A2 should be marked yes. This question refers to disrupting immunity. She stated that this virus could potentially avoid the innate immune response if it is now resistant to MxA. The committee extensively discussed the potential results of the experiments and the effects on host immunity. The committee agreed that these experiments could result in a resistant virus but agreed with Dr. (b)(6) that the experiments were not dual use research of concern (DURC). The RD includes risk mitigation steps including reporting to biosafety of any increase in viral replication of 1 log. The committee agreed that question A2 should remain no. ▪ The committee discussed the containment requirements. BSL-2 with additional precautions is appropriate for the proposed studies with VSV. The additional precautions include experiments being performed in Room 2A147C and the use of the following PPE: double gloves, shoe covers, disposable gown, and mucous membrane protein (surgical mask and safety glasses or face shield). ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that this was not dual-use research of concern. <u>Action:</u> The committee unanimously approved **RD#15-448** with minor modifications: 1. Remove references in the attached figures about insertion of foreign glycoproteins. Research using eukaryotic cells is approved at BSL-2 under section III-D-1-a and III-D-2-a of the NIH Guidelines.
Item 4:	<u>Registration Documents for Recombinant DNA Experiments (New)</u> ▪ Steele-Mortimer (LB) ▪ **RD#15-131**: Adenoviral Expression Systems ▪ Reviewers: Hideki Ebihara, Chris Bosio ▪ **Summary:** This study describes using adenovirus expression systems to transiently express proteins in mammalian cells, infect the cells with Salmonella, and determine the specific importance of host cell genes in Salmonella pathogenesis. ▪ Hideki Ebihara summarized the registration. The studies outlined in the RD describe an adenoviral vector that is replication incompetent. The system will only produce viral particles in 293 cells. They will use commercial systems as described in the RD. Their goal is to understand the importance of specific host

	cell genes in Salmonella pathogenesis. The listed NIH Guidelines are correct and there were no dual-use questions answered yes. Hideki Ebihara had no dual use concerns. ▪ Chris Bosio had no additional comments or concerns. ▪ Sue Priola pointed out that III-D-3-a should be added to the Research Product section. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for studies with the adenoviral vector systems proposed. ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#15-131** with minor modifications: 1. Add III-D-3-a to the Research Product Section. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under section III-D-1-a and III-D-3-a of the NIH Guidelines.
Item 5:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Steele-Mortimer (LB) ▪ **RD#15-124**: Lentiviral system ▪ Reviewers: Karin Peterson, Clay Jarrett ▪ **Summary:** This study describes using lentiviruses to deliver RNAs (short hairpin or full length cDNAs) to various cell lines and primary cells to induce RNA interference or over-expression of cellular and foreign genes. ▪ Karin Peterson summarized the registration. The RD is a renewal with no changes from the last RD submission. They will use a commercial lentiviral system to knock down host proteins in different cell lines and see what their effect is on Salmonella infection. They will use a four plasmid system which is safe and mitigates risk of production of replication competent lentivirus. ▪ Clay Jarrett had no additional comments or concerns with the registration. ▪ Sue Priola pointed out that III-D-3-a should be added to the Research Product section. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for the proposed studies with lentiviruses.

	▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#15-124** with minor modifications: 1. Add III-D-3-a to the Research Product Section. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under section III-D-1-a and III-D-3-a of the NIH Guidelines.
Item 6:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Hinnebusch (LZP) ▪ **RD#15-303**: Mutagenesis of *Yersinia pestis* for plague pathogenesis studies ▪ Reviewers: Scott Kobayashi, Dana Scott ▪ **Summary:** This study describes identifying and characterizing specific genes of *Y. pestis* that are important for the pathogenicity of plague. ▪ Dana Scott summarized the registration. The RD describes generating mutations in specific genes in *Y. pestis* in order to study the pathogenesis of plague. The RD also describes using mutant and wild type *Y. pestis* strains in animal models of bubonic plague. The RD outlines the use of ampicillin and kanamycin resistance, Joe Hinnebusch already has DSAT approval for those antibiotics and the approval letter is attached to the RD. Dana Scott had no dual use concerns or issues with the RD. ▪ Scott Kobayashi was not present, but informed Sue Priola by email that he had no additional comments or concerns with the registration. ▪ Sue Priola pointed out that 2 vector maps were missing: pACYC177 and pTAC-MAT-Tag2. ▪ The committee discussed the containment requirements. BSL-3/ABSL-3 is appropriate for studies with virulent *Y. pestis*. ▪ Animal studies with mice and rats were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Clay Jarrett and Chris Bosio abstained) **RD#15-303** with minor modifications: 1. Attach the missing vector maps, pACYC177 and pTAC-MAT-Tag2.

	Research using prokaryotic hosts is approved at BSL-2 and BSL-3 under sections III-D-1-b and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-3 under section III-D-1-a of the NIH Guidelines.
Item 7:	<u>Registration Documents for Recombinant DNA Experiments (Renewal)</u> ▪ Feldmann (LV) ▪ **RD#15-433**: Reconstructed 1918 Influenza virus ▪ Reviewers: Sue Priola, Karin Peterson ▪ **Summary:** This study describes generating reconstructed 1918 Influenza virus ▪ Sue Priola summarized the registration. Sue Priola informed the committee that the RD is a renewal with no changes from the previously approved version. The RD describes generating live 1918 Influenza virus using a series of plasmids. She informed the committee that if they already have the plasmids, Section A should be changed from "We will receive plasmids . . ." to "We have plasmids . . ." ▪ Sue Priola questioned if dual use questions A7 and B should be changed to yes. They both refer to techniques of synthetic biology being used. Question A7 could potentially be marked yes because they are making an eradicated pathogen. The committee discussed the dual use potential comprehensively, and agreed that 1918 is a non-circulating influenza virus so it is not extinct or eradicated. The committee also discussed that other labs have already reconstructed 1918 Influenza with the same techniques, the research will be performed in a highly regulated manner, and the Feldmann lab already has approval with DSAT to work with reconstructed 1918 Influenza virus. The committee agreed that these reasons are why the dual use questions do not need to be marked yes. The committee also agreed that the RD does not need to include a description of why the answers should be no. The committee does not want to set a precedent for explaining why there is a no answer. ▪ Karin Peterson noted that the attached ASP is old and expired. Becky Anderson informed the committee that we typically allow the use of older ASPs to keep an animal species up to date on a registration. If we do not include the older ASP, they would have to amend the registration at a later date for an animal species that was previously approved. The committee agreed it is ok to use an older ASP. ▪ The committee discussed the containment requirements. BSL-3 enhanced is appropriate for work with reconstructed 1918 Influenza virus, however RML cannot meet those requirement in the normal BSL-3 labs. Instead the work will either be performed at BSL-4 or in a BSL-4 lab that is lowered to enhance BSL-3 containment. ▪ Animal studies with mice and ferrets were proposed.

	▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#15-433** with minor modifications: 1. In section A, change "We will receive. . ." to "We have received . . ." Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-3 enhanced under sections III-D-7-c and III-D-1-a of the NIH Guidelines.
Item 8:	**Standard Operating Procedures: Sorting Infected Samples (New)** ▪ Sue Priola informed the committee that the Sorting Infected Samples SOP is to be used for cell sorting of any BSL-2 infectious agents. The standardized SOP will allow the BSO to approve amendments for cell sorting because the procedures have already been reviewed and approved. ▪ Alex Scranton submitted several questions by email: a. Several typos were mentioned and will be fixed. b. She also questioned when the door is locked to prevent entry. Is it during the pre-sort or during the sort and post sort cleanup? Becky Anderson stated that the door does not need to be locked during pre-sort, only when the infectious sample is being sorted and during clean up. The wording in the SOP will be updated to be clearer. c. She wrote that 2.4 is confusing because it describes that PPE must be worn while the sort is in progress, but 2.3 makes it sound like PPE must be worn prior to any sorting. The committee agreed that 2.4 should be deleted. d. Alex Scranton pointed out that the organization of the sections is confusing and could be reorganized to make it easier to read. The committee agreed the sections could be rearranged as described by (b)(6) e. She questioned section 4.1 as to when the barriers be closed, before or after the samples are placed in the chamber. Karin Peterson stated that the tubes have to be set up first so the barriers have to be closed after the samples are placed in the chamber. f. She pointed out that Section 4.2 states that samples must be filtered prior to sorting, but where and when does this occur, it is not described. Becky Anderson stated that samples are filtered in the PI's lab prior to bringing to (b)(6) for cell sorting. This can be mentioned in a different section to avoid confusion.

	g. (b)(6) mentioned sections 2.5 and 4.4 to 4.6 are duplicated but with some different details. The committee agreed these issues will be cleared up with reorganizing the sections. h. She also questioned 4.5 and 2.5.3 on letting waste decontaminate in bleach overnight before discarding. Both sections refer to bleach waste, again the reorganization will reduce the redundancy in the SOP. ▪ The committee had no additional comments or concerns. Action: The committee unanimously approved the **Sorting Infected Samples (New)** with the following minor modifications: 1. Clarify section 2.2 to better describe when the door is locked. 2. Section 2.4 should be deleted. 3. Reorganize several sections described above to reduce redundancy and make the order of steps more clear. 4. Section 4.2, state that the samples should be filtered prior to cell sorting in (b)(6)
Item 9:	**Annual IBC Training was presented by Nancy Hoe**
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ BSO report attached.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ DOHS is currently performing safety inspections of the BSL-2 labs for the next 2-3 weeks. ▪ The RML Safety Committee will be walking through offices, BSL-1 labs, and corridors. ▪ Charcoal filters have been installed on the air intakes to buildings on campus. We are continuing to monitor the forest fire smoke and responding according to RML's Smoke Management Plan. ▪ Three injuries on campus have resulted in outside medical treatment.
Report	**IRF Biosafety Manager Report/Megan Morgan** ▪ The (b)(6) facility is currently under construction to install new cage wash units, wall panels and apply new coatings, upgrade the BAS and air handling controls, and will also install wireless data points to allow personnel to capture and transmit data electronically from the suites. The project is

	currently on schedule and is estimated to be completed by the end of October.
Report	**Associate Director Report/Marshall Bloom** ▪ Informed the committee that the progress on the ABSL-3 is impressive and can arrange for anyone to go on a tour if they are interested.
Around the room	▪ None.

Other issues	▪ None.

Next Meeting:

- Date: 9/17/15
- Place: Bldg A Seminar Room
- Time: 1:00 PM

RML Biosafety Committee Meeting
August 20, 2015
Biosafety Officer/Responsible Official Report

1) ***Requests approved by BSO since last meeting:***
   a) *None*
2) ***New requests approved by committee via electronic review:***
   a) *None*
3) ***New requests***
   a) *Human Pathogen Registration Documents*
      i) ***Amend***
         (a) *Steele-Mortimer (LB)*
            (a) ***HPRD-15-448****: Salmonella typhimurium*
               (i) Add cell sorting
         (b) *Feldmann (LV)*
            (a) ***HPRD-12-131****: 1918 influenza*
               (i) Add mice, intranasal route of infection
   b) *Registration Documents for Recombinant DNA Experiments*
      i) ***New***
         (a) *Best (LV)*
            (a) ***RD-15-448****: Vesicular stomatitis virus*
         (b) *Steele-Mortimer (LB)*
            (a) ***RD-15-131****: Adenovirus expression systems*
      ii) ***Renewal***
         (a) *Steele-Mortimer (LB)*
            (a) ***RD-15-124****: Lentivirus delivery of either shRNAs for RNA-mediated RNA interference or full-length mRNAs for overexpression of genes in the study of Salmonella pathogenesis*
         (b) *Hinnebusch (LZP)*
            (a) ***RD-15-303****: Identification and characterization of specific genes of Y. pestis that are important for pathogenesis.*
         (c) *Feldmann (LV)*
            (a) ***RD-15-433****: Reconstitution of 1918 influenza using reverse genetics*
   c) *Standard Operating Procedures*
      i) *Sorting Infected Samples on the BDFacsAria*

4) ***Animal Study Protocols Review***

Title	***Associated HPRD***	***Associated RD***	***Reviewer***
The mechanism of CD86 induction in Friend virus-infected B cells in mice	*N/A*	*N/A*	*M. Morgan*

Title	*Associated HPRD*	*Associated RD*	*Reviewer*
Understanding the cell-type specific role of MAVS in protection from Ebola virus infection in the mouse model	*13-90 (Ebola virus)*	*N/A*	*B. Anderson*
Determining the role of MAVS in host susceptibility to 1918 influenza virus in the mouse model	*12-131 (1918 influenza)*	*12-433*	*B. Anderson*
Efficacy testing of a new neutralizing mAb (LEA60) against MERS-CoV in common marmosets	*12-143 (Coronaviridae)*	*N/A*	*B. Anderson*
Infection of several transgenic mouse strains expressing human prion protein using human TSE agents	*12-151 (human TSE)*	*12-211 (tg mice)*	*N. Hoe*
Optimization of spike SynCon DNA Vaccines for MERS-CoV in the rhesus macaque model	*12-143 (Coronaviridae)*	*N/A*	*N. Hoe*
Cell-specific MAVS responses and LACV pathogenesis in mice	*12-103 (LACV)*	*N/A*	*N. Hoe*

5) ***Biosafety Training Performed – Megan Morgan, Becky Anderson***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
Full-length clone lab annual refresher	***2***	***14***
BSL-3 Visitor	***2***	***19***
BSL-3 Laboratory Biosafety	***1***	***2***
BSL-4 Laboratory Biosafety	***1***	***2***
BSL-4 Annual Refresher	***3***	***3***

6) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
a) *Biological Incident Report:*
   i) *None*

7) ***Select Agent Issues***
a) *None*

8) ***Other Issues***
a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 9/17/15
Meeting Time: 1:01 PM **Adjourned:** 2:16 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Paul Carlson	☐	☒	Kevin Mora	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Megan Morgan	☒	☐
Becky Anderson (EO)	☒	☐	Frank DeLeo (EO)	☐	☒	Karin Peterson	☒	☐
Alan Applebury	☐	☒	Hideki Ebihara	☒	☐	George Risi	☒	☐
Chris Bosio	☒	☐	Heinz Feldmann (EO)	☐	☒	Dana Scott	☒	☐
Marshall Bloom (EO)	☒	☐	Nancy Hoe	☒	☐	Alexandra Scranton	☐	☒
Teresa Borino	☒	☐	Clay Jarrett	☒	☐			
Jeff Burrows	☐	☒	Josh Kellar (EO)	☐	☒			
Carol Calderwood	☐	☒	Scott Kobayashi	☒	☐			
Harlan Caldwell (EO)	☐	☒	Rachel LaCasse	☐	☒			
Marcie Caldwell (EO)	☐	☒	Alida Merritt	☐	☒			

(P=present; A=absent)
Guests (b)(6)

Minutes: Meeting minutes from 8/20/15 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** Action: Meeting minutes for 8/20/15 were unanimously approved as written.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Heinzen (LB) ▪ **RD#14-106 Amend**: Genetic transformation of virulent *Coxiella burnetii* ▪ Reviewers: Scott Kobayashi, Clay Jarrett ▪ **Summary:** The amendment is to add experiments introducing *argF*, *argG*, and

	argH from *Legionella pneumophila* into virulent Coxiella. Additional experiments include converting virulent phase I Coxiella to attenuated phase II and vice versa by genetic transformation. ▪ Scott Kobayashi summarized the amendment. The amendment is to add experiments introducing *argF*, *argG*, and *argH* from *Legionella pneumophila* into virulent Coxiella. This methodology provides a strong, non-antibiotic selection method. Additional experiments include converting virulent phase I Coxiella to attenuated phase II and vice versa by genetic transformation. These experiments will help determine the role of specific genes in LPS truncation. The NIH Guidelines are appropriate, the biosafety levels are clearly indicated, and there are no dual use concerns. ▪ George Risi questioned if they are making a strain that would no longer require arginine, does that constitute an increase in fitness of the bacteria? Would this be addressed by one of the dual use questions? Bob Heinzen stated that this is more applicable to growing in media rather than *in vivo* or in cell culture. They already have experiments with attenuated *C. burnetii* auxotrophs and they are no more fit than wild type, and have a similar growth rate to wild type. Bob Heinzen also stated that the virulent auxotrophs may be less fit because they now have to express more genes. The committee discussed the dual use potential of these experiments further and agreed that there is no overall dual use concerns with the proposed experiments. ▪ Clay Jarrett had no additional comments or concerns. ▪ The committee discussed the containment requirements. BSL-3 is appropriate for work with virulent *C. burnetii*. BSL-2 is appropriate for work with lab strains of *E. coli* and avirulent C*. burnetii* phase II clone 4 (Select Agent exempt). ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved (Bob Heinzen abstained) **HPRD#14-106 Amend** as written. Research using prokaryotic hosts is approved at BSL-2 and BSL-3 under sections III-D-1-a, III-D-1-b, and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 and BSL-3 under III-D-1-a and Appendix G-II-C of the NIH Guidelines.
Item 2:	<u>Registration Documents for Recombinant DNA Experiments (Amendment)</u> ▪ Ebihara (LV) ▪ **RD#14-419 Amend**: Characterization of viral protein functions in viral life cycle and identification of virulence determinants of human pathogenic

	orthobunyaviruses by reverse genetics systems. ▪ Reviewers: Karin Peterson, Sue Priola ▪ **Summary:** The amendment is to clarify the descriptions of genetic manipulations of full-length clones and replicon/minigenomes and to add novel strategies to express foreign genes from recombinant orthobunyaviruses. ▪ Karin Peterson summarized the amendment. The RD describes generating genetic reassortants of three different groups of Orthobunyaviruses and generating ancestral viruses of some of the strains. The amendment is to provide a better description of the genetic manipulations of clones. The second part provides information for how they are making the clones. The amendment does not change the fundamentals of the protocol very much. The first question is answered yes on the dual use questionnaire because they are making recombinants between virulent and avirulent strains. The avirulent strains will become more virulent, but are not expected to be more than the parent. She pointed out that most of the sections in the dual use description included a description of the biosafety level, but not all do. The biosafety level should be added to each paragraph (missing in paragraphs 1 and 2). ▪ Sue Priola questioned if the mutations would be made in the newly reassorted viruses. The committee discussed and agreed that there is no dual use concern with mutations in the reassortants for the same reasons as the non-reassortants. Hideki Ebihara stated that a description could be included in the dual use listing. ▪ The committee discussed the containment requirements. BSL-2 enhanced or BSL-3 is appropriate for the specific strains worked with. See recommendations section for biosafety levels for each strain. ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved (Hideki Ebihara abstained) **HPRD#14-419 Amend** with the following minor modifications: 1. Add a description of the biosafety level to paragraphs 1 and 2 in the dual use discussion section. 2. Add to the dual use discussion section a description of why mutations in the reassortants are not a dual use concern. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-1-a, III-D-1-b, III-D-3-a and III-D-3-b of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 or BSL-3 under section III-D-1-a, III-D-3-a, III-D-3-b, III-E-1-a, and III-D-1-b of the NIH Guidelines.

Item 3:	Registration Documents for Recombinant DNA Experiments (New) ▪ Ebihara (LV) ▪ **RD#15-449**: Molecular biology and pathogenesis of tick-borne orthomyxovirus ▪ Reviewers: Sue Priola, Chris Bosio ▪ **Summary:** The RD describes development of a reverse genetics system including virus rescue system for generation of recombinant tick-borne orthomyxovirus from cloned cDNA. ▪ Sue Priola summarized the RD. The RD describes development of a reverse genetics system including virus rescue system for generation of recombinant tick-borne orthomyxovirus from cloned cDNA. Their work is focused on getting a better understanding of the viral life cycle and the molecular basis of pathogenesis so ultimately they can develop vaccines. These viruses have 6-7 segments and some of the experiments will generate live virus and some will be mutated with similar methods as discussed in the previous RD today. They will also make a cell line that stably expresses several segments of the virus as well as minigenomes. The end cell line will have 6 segments but two of the segments will be minigenomes so they will be incomplete. Sue Priola questioned if there is any risk for recombination with the minigenome to result in live virus when they add helper plasmids? Hideki Ebihara informed the committee that this has never happened with Influenza virus which has been used extensively. By design of these experiments, homologous recombination cannot occur. Nancy Hoe added that you would need to have the entire genome present in the cell and this is not the case in the proposed experiments. ▪ Sue Priola stated that the NIH Guidelines are appropriate. She did note that the Foreign Gene list was not attached and needs to be added. ▪ Sue Priola also indicated that on the top of page 6 in the Eukaryote Cells section, on the second line, the three should be changed to a six for the number of full length genomic plasmids. ▪ Chris Bosio pointed out that there were a few copy/paste errors where phleboviruses were mentioned instead of orthmyxoviruses. This should be updated. ▪ The committee discussed the containment requirements. BSL-2 or BSL-3 is appropriate for the specific strains worked with. See recommendations section on the RD for biosafety levels for each strain. ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns

	with the proposal. Action: The committee approved (Hideki Ebihara abstained) **HPRD#15-449** with the following modifications: 1. Attach the foreign gene list. 2. On the top of page 6 in the Eukaryote Cells section, on the second line, the three should be changed to a six for the number of full length genomic plasmids. 3. Anywhere Phlebovirus is mentioned it should be changed to Orthomyxovirus. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-1-a, III-D-1-b, and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-3 under Appendices G-II-B and G-II-C of the NIH Guidelines.
Item 4:	**Standard Operating Procedure: BSL-3 Operations and Safety Procedures (Annual Review)** ▪ Sue Priola informed the committee that this SOP is being updated for the annual review. There are only a couple of minor changes to the document and all changes were tracked for easy review. ▪ Alex Scranton submitted comments by email, she found the following changes: a. Page 20, the 42 CFR 73.4 should be updated to 42 CFR 73.3. b. Page 22 42 CFR 73.5 should be updated to 42 CFR 73.4. c. She also questioned if the list of livestock agents was correct. Becky Anderson informed the committee that the list in the document is current, possibly Alex Scranton was looking at an older version. Several of those agents she listed have been dropped from the list by DSAT. d. She also pointed out that on page 56, the purpose of the SOP does not make sense, the committee agreed it needs to be updated. e. She also questioned if the SOP needed to be validated like all the other inactivation procedures. Megan Morgan pointed out that room decontamination by paraformaldehyde is an industry standard, but that some wording could be added to make that clear. ▪ The committee had no additional comments or concerns. Action: The committee unanimously approved **BSL-3 Operations and Safety Procedures (Annual Review)** with the following minor modifications: 1. Page 20, the 42 CFR 73.4 should be updated to 42 CFR 73.3. 2. Page 22 42 CFR 73.5 should be updated to 42 CFR 73.4. 3. Update the Purpose for SOP BSL-3-25-7.

	4. Add a reference to the paraformaldehyde room decontamination SOP to state that it is an industry standard.
Item 5:	**Standard Operating Procedure: ABSL-3 Operations and Safety Procedures (Annual Review)** ▪ Sue Priola informed the committee that the SOP is being updated for the annual review. There are only a couple of minor changes to the document and all changes were tracked for easy review. ▪ The committee had no comments or concerns. Action: The committee unanimously approved **ABSL-3 Operations and Safety Procedures (Annual Review)** as written.
Item 6:	**Standard Operating Procedure: (b)(6) SOP, (b)(6) (New)** ▪ Sue Priola informed the committee that the SOP is a new SOP for Ted Hackstadt's lab and will be added to the (b)(6) SOP. ▪ Clay Jarrett pointed out that the wording is inconsistent for the parts of the SOP where the rotor or buckets are disinfected and removed from the BSC. Sometimes it says to disinfect the tubes as well, but is inconsistent. Perhaps a general statement could be added to describe how to handle the rotor/buckets when removed from the BSC to then place in the centrifuge. The committee agreed, the SOP will be updated with a statement at the beginning of the SOP to describe procedures for the rotor/buckets. ▪ The committee had no additional comments or concerns. Action: The committee unanimously approved (b)(6) **SOP, (b)(6) (New)** with the following minor modification: 1. Add a description at the beginning of the SOP to describe procedures for removing the rotor/buckets from the BSC.
Item 7:	**Working Group Summaries for Inactivation Studies** ▪ Sue Priola informed the committee that two IBC Working Groups met with the following four PI's: Catharine Bosio, Bob Heinzen, Ted Hackstadt, and Joe Hinnebusch. The PI's presented their data for the inactivation of their respective agents. The summary lists what the working group reviewed. ▪ For all four labs, the working group agreed that the procedures presented and listed in the SOPs clearly demonstrated inactivation of the specific biological

	agent. ▪ The committee agreed and approved the conclusions of the Working Groups for the inactivation procedures. See Working Group Summaries.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Nancy Hoe presented the BSO report.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ Not present.
Report	**IRF Biosafety Manager Report/Megan Morgan** ▪ The ABSL-3 shutdown in (b)(6) is on schedule and will likely be reactivated in early November.
Report	**Associate Director Report/Marshall Bloom** ▪ Hugh Auchincloss, the acting director of DIR was here earlier this week. Nancy and Sue met with him to discuss IBC and the biosafety program. He was very pleased with our programs at RML.
Around the room	▪ None.

Other issues	▪ None.

Next Meeting:

- Date: 10/15/15
- Place: Bldg A Seminar Room
- Time: 1:00 PM

RML Biosafety Committee Meeting
September 17, 2015
Biosafety Officer/Responsible Official Report

1) ***Requests approved by BSO since last meeting:***
   a) *None*
2) ***New requests approved by committee via electronic review:***
   a) *None*
3) ***New requests***
   a) *Human Pathogen Registration Documents*
      i) *None*
   b) *Registration Documents for Recombinant DNA Experiments*
      i) ***New***
         (a) *Ebihara (LV)*
            (a) ***RD 15-449:*** *Molecular biology and pathogenesis of tick-borne Orthomyxoviruses*
      ii) ***Amend***
         (a) *Heinzen (LB)*
            (a) ***RD-14-106****: Genetic transformation of Coxiella burnetii*
               (i) Introduct argF, argG, argH from Legionella pneumophila into virulent Coxiella
               (ii) Convert virulent phase I Coxeilla to attenuated phase II Coxiella (and vice versa) by genetic transformation)
         (b) *Ebihara (LV)*
            (a) ***RD 14-419****: Characterization of viral protein functions in viral life cycle and identification of virulence determinants of human pathogenic orthobunyaviruses by reverse genetics systems*
               (i) To clarify the descriptions of genetic manipulations of full-length clones and replicon/minigenome.
               (ii) To add the novel strategies to express foreign genes from recombinant orthobunayviruses.
   c) *Standard Operating Procedures*
      i) ***Annual Review***
         (a) *BSL-3 Operations and Safety Procedures*
         (b) *ABSL-3 Operations and Safety Procedures*
      ii) ***New***
         (a) *Suite A BSL-3-Rick-3 Purification of Rickettsia spp.*

4) ***Animal Study Protocols Review***

Title	***Associated HPRD***	***Associated RD***	***Reviewer***
Efficacy of prophylactic and therapeutic MERS-CoV MAbs in the transgenic hDPP4 mouse model	*12-143 (MERS-CoV)*	*N/A*	*M. Morgan*

RML Biosafety Committee Meeting
September 17, 2015
Biosafety Officer/Responsible Official Report

Title	***Associated HPRD***	***Associated RD***	***Reviewer***
Efficacy of a MVA-based vaccine against Ebola virus in the macaque model	*13-90 (Ebola virus) 14-159 (MVA)*	*15-447*	*B. Anderson*
Treatment of hDPP4 mice with mycophenolic acid, cyclosporine A, or favipiravir against MERS-CoV	*12-143 (MERS-CoV)*	*N/A*	*N. Hoe*

5) ***Biosafety Training Performed – Megan Morgan, Becky Anderson, Nancy Hoe***

Type of Training	***Number of Sessions***	***Number of Employees Trained***
Select Agent Annual Refresher	***4***	***106***
BSL-3 Visitor	***2***	***6***
BSL-4 Laboratory Biosafety	***2***	***1***
BSL-4 Annual Refresher	***10***	***41***
Biosafety Brief	***1***	***LV WIP***

6) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
a) *Biological Incident Report:*
   i) *None*

7) ***Select Agent Issues***
a) *None*

8) ***Other Issues***
a) *Upcoming visit of RML DOHS by Director, Office of Laboratory Science and Safety, CDC.*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 10/15/15
Meeting Time: 1:02 PM **Adjourned:** 1:50 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Karin Peterson	☒	☐
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	George Risi	☒	☐
Becky Anderson (EO)	☒	☐	Hideki Ebihara	☒	☐	Dana Scott	☒	☐
Alan Applebury	☐	☒	Heinz Feldmann (EO)	☐	☒	Alexandra Scranton	☐	☒
Chris Bosio	☐	☒	Nancy Hoe	☒	☐			
Marshall Bloom (EO)	☒	☐	Clay Jarrett	☒	☐			
Teresa Borino	☐	☒	Josh Kellar (EO)	☐	☒			
Jeff Burrows	☐	☒	Scott Kobayashi	☒	☐			
Carol Calderwood	☐	☒	Alida Merritt	☒	☐			
Marcie Caldwell (EO)	☐	☒	Kevin Mora	☐	☒			
Paul Carlson	☒	☐	Megan Morgan	☒	☐			

(P=present; A=absent)

Guests: (b)(6)

Minutes: Meeting minutes from 9/17/15 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** Action: Meeting minutes for 9/17/15 were unanimously approved with the following minor modificatinos: ▪ Sue Priola pointed out on page 3, on the Action item, instead of, "as written", it should read, "with the following minor modifications". ▪ Sue Priola also noted that on page 7 the summary of the working group should state that the IBC agreed and approved the procedures reviewed by the working group. ▪ Nancy Hoe informed the committee that the way bullet 4 on page 3 reads makes it sound like the committee did not discuss the dual use concerns of generating mutations in reassortants viruses. Sue Priola pointed out that it was discussed at the last meeting, but that an additional sentence could be added to the minutes, such as, "The committee discussed and agreed that there is no dual use concern with mutations in the reassortants for the same reasons as

	the non-reassortants." ▪ Scott Kobayashi pointed out that Harlan Caldwell is no longer at RML and should be removed from the Member list.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans (Amendment) ▪ Bosio (LB) ▪ **HPRD#14-157 Amend: *Listeria monocytogenes*** ▪ Becky Anderson presented the risk assessment. This amendment is to add animal work with *Listeria monocytogenes*. They will use *L. monocytogenes* to help assess antigen specific T cells during *F. tularensis* infection. The primary lab hazards include rodent bites or scratches. To mitigate these hazards they will perform all animal work in the human pathogen wing of (b)(6) All personnel must wear the minimum PPE of a lab coat, gloves, and face mask. All personnel must be informed of the risks of working with *L. monocytogenes*, specifically women who are pregnant or thinking of becoming pregnant are encouraged to notify the Lab supervisor and RML OMS Nurse. This is in order to assure that they are aware of any potential risks to themselves or the fetus and determine if any additional risk reduction measures should be taken. All work with infectious materials is conducted in a BSC, centrifugation of infectious materials must be carried out in sealed safety cups or removable rotors that can be loaded and unloaded in a BSC. ▪ ABSL-2 is appropriate for work with *L. monocytogenes*. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. ▪ Action: The committee unanimously approved **HPRD#14-157 Amend** as written.
Item 2:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Feldmann (LV) ▪ **RD#15-412**: Hantavirus reverse genetics system ▪ Reviewers: Karin Peterson, Sue Priola ▪ **Summary:** This RD describes generating a reverse genetics system for the preparation of recombinant Hantaviruses. ▪ Karin Peterson summarized the RD. The RD describes developing a reverse

genetics system for Hantavirus. The system uses transfection of cells with six plasmids to get infectious viral particles. They will mutate structural and regulatory genes to see what the effects are and study virus-host interactions. The RD also describes generating reassortants. For the dual use form, they stated that any reassortants or mutants generated are not expected to be more virulent than wild type. This is well described in the comments section. The committee agreed that there were no dual use concerns with the proposed research.

- Bob Heinzen noted that Question B was marked yes for synthetic biology, but questioned if it was necessary to be marked yes. Bob Heinzen stated that they are using standard molecular biology techniques. The committee discussed that historically the PI's have marked the question yes, but then include rationale as to why the work is not dual use of concern.
- Nancy Hoe stated that she will talk to the BSO at NIH and see how they interpret Question B on the dual use form.
- Karin Peterson questioned if the virus list needed to be in the form or if it was alright to be attached. Sue Priola stated that as long as it is associated with the RD it is fine.
- Nancy Hoe pointed out in the Recombinant DNA Section and the Eukaryote Cell Section that the following sentence should be deleted because they will not perform large scale virus preparation and they do not have animal work currently associated with the RD, "Large scale virus preparation (not currently planned) and animal experiments conducted in susceptible species will be conducted at BSL-4)".
- The committee discussed the containment requirements. BSL-3 is appropriate for laboratory work with Hantavirus
- No animal studies were submitted, proposed, or reviewed.
- The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal.

Action: The committee unanimously approved **HPRD#15-412** with the following minor modifications:

1. Remove in 2 places the following sentence, "Large scale virus preparation (not currently planned) and animal experiments conducted in susceptible species will be conducted at BSL-4)". This was in the Recombinant DNA section and the Eukaryote Cell Section.

Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-3 under sections III-D-1-b and III-D-3-b of the NIH Guidelines.

Item 3:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Steele-Mortimer (LB) ▪ **RD#15-108**: Salmonella Host Cell Interactions ▪ Reviewers: Clay Jarrett, Chris Bosio ▪ **Summary:** The RD describes using deletion mutants as well as strains in which deletions are complemented by wild type or mutant genes expressed from a plasmid or inserted into the chromosome of *Salmonella enterica* serovar *typhimurium*. ▪ Clay Jarrett summarized the RD. He informed the committee that this was a renewal for the Steele-Mortimer lab for their general work with Salmonella to determine pathogenicity. They will make mutations in the typhimurium strain and complement the mutations. Most of the studies will be performed in cell culture, all of their methods are very standard. They have an ASP attached for the animal work with mice. There are no dual use questions marked yes and Clay Jarrett did not see any dual use issues with the proposed research. Clay Jarrett questioned the NIH Guidelines in the Research Product and Prokaryote Host section, Nancy Hoe informed him they were all correct. ▪ George Risi asked about using ampicillin resistance in *S. enterica* because it can be used clinically. Nancy Hoe pointed out that many strains are naturally resistant to ampicillin so it does not meet the definition of a major action. The committee discussed that the wording should be updated to acknowledge that some strains are already resistant to ampicillin. On page 4 in the Prokaryote Host Section, Description subsection, the following sentence will be added, "Because ampicillin resistance is commonly found in *S. enterica* strains in nature, ampicillin is not clinically used for treatment." ▪ Chris Bosio was not present, the committee had no additional comments or concerns. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for studies with *Salmonella typhimurium*. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#15-108** with the following modifications: 1. On page 4 in the Prokaryote Host Section, Description subsection, the following sentence will be added, "Because ampicillin resistance is commonly found in *S. enterica* strains in nature, ampicillin is not clinically used for treatment. "

	Research using prokaryotic hosts is approved at BSL-2 under sections III-D-1-a and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-3 under Appendices G-II-B and G-II-C of the NIH Guidelines.
Item 4:	**Standard Operating Procedure: SOP#4-28-55 Husbandry and Manipulation of Sheep and Goats in Level 4 Biocontainment (NEW)** ▪ Sue Priola informed the committee that this SOP was tabled at the April 2014 IBC meeting because of concerns about the pig caging being appropriate for sheep and goats. The request was that LV did a training period with sheep and goats to ensure the caging was sufficient. They completed the training and the current caging works well. ▪ Nancy Hoe questioned if a size or weight restriction should be added to the SOP. Dana Scott pointed out that size will already meet the animal welfare requirements which dictates the largest animals they can put in the caging. The committee agreed that nothing needs to be added for size restrictions. ▪ Sue Priola pointed out that after 6.5.a.i, there should be a sentence that states, "Use the swing gate to keep animals to the other side of the pen." ▪ Sue Priola also questioned 6.11.a and 6.11.b, should they be required to spray their entire suit? Megan Morgan pointed out that they just need to check for soiled areas, spraying the entire suit gets the immediate area wet and very slippery in the animal holding rooms. Dana Scott pointed out that the language from 6.9.g could be used to state that the suit, hand, and foot decontamination procedures need to be performed. ▪ The committee had no additional comments or concerns. Action: The committee unanimously approved **SOP#4-28-55 Husbandry and Manipulation of Sheep and Goats in Level 4 Biocontainment (NEW)** with the following minor modifications: 1. Add to 6.5.a.i that there should be a sentence added that states, "Use the swing gate to keep animals to the other side of the pen." 2. Reword 6.11.a and 6.11.b to include language from 6.9.g for suit decontamination procedures.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Nancy Hoe presented the BSO report.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ Paul Carlson reported a few incidents over the last two months: ▪ An employee in a BSL-2 animal quarantine room received a small bite from a marmoset when they were opening the cage. When the cage opened the

	marmoset ran up their arm and onto the shoulder when the marmoset bit the employee's neck. Different cages are used with infectious studies where the opening to the cage is much smaller. ▪ An employee was cleaning cages with high pressure hoses when the spray hit the edge of a catch pan and sprayed back at the employee and up and under their face shield and safety glasses. The employee was advised to wear goggles instead of safety glasses. ▪ An employee was cutting fixed rabbit tissue with a microtome when the cut their fingertip while trying to clean the equipment. They were advised to use proper tools for cleaning like a paintbrush type device. ▪ An employee has a herniated disc, it is not clear if it is a work related at this point. There is an investigation and they are awaiting information from the personal physician. ▪ There are two construction projects coming up, the HAZMAT truck shed and the library remodel will begin soon. Expect areas to be blocked off at different times during construction.
Report	**IRF Biosafety Manager Report/Megan Morgan** ▪ The ABSL-3 shutdown in (b)(6) is on schedule and will likely be reactivated in early November.
Report	**Associate Director Report/Marshall Bloom** ▪ Hugh Auchincloss, the acting director of DIR was here earlier this week. Nancy and Sue met with him to discuss IBC and the biosafety program. He was very pleased with our programs at RML.
Around the room	▪ None.

Other issues	▪ None.

Next Meeting:

- Date: 10/15/15
- Place: Bldg A Seminar Room
- Time: 1:00 PM

RML Biosafety Committee Meeting
August 20, 2015
Biosafety Officer/Responsible Official Report

1) ***Requests approved by BSO since last meeting:***
   a) *Registration Documents for Recombinant DNA Experiments*
      i) ***Amend***
         (a) *Feldmann (LV)*
            (a) ***RD 15-442****: Cytomegalovirus-based vaccine vectors*
               (i) Add additional rodent species, Mastomys natalensis

3) ***New requests approved by committee via electronic review:***
   a) *None*

4) ***New requests***
   a) *Human Pathogen Registration Documents*
      i) ***Amend***
         (a) *Bosio (LB)*
            (a) ***HPRD 14-157****: Listeria monocytogenes*
               (i) Add animal work, mice, intranasal
   b) *Registration Documents for Recombinant DNA Experiments*
      i) ***Renewal***
         (a) *Feldmann (LV)*
            (a) ***RD 15-412****: Hantavirus reverse genetics*
         (b) *Steele-Mortimer (LB)*
            (a) ***RD-15-108****: Salmonella/Host Cell Interactions*
   c) *Standard Operating Procedures*
      i) ***Second Review***
         (a) *SOP# 4-28-55: Husbandry and Manipulation of Sheep and Goats in level 4 Biocontainment*

5) ***Animal Study Protocols Review***

Title	***Associated HPRD***	***Associated RD***	***Reviewer***
Infectious Cycle of relapsing fever spirochetes	*14-03 (Borrelia hersmii)*	*14-319*	*B. Anderson*
Ornithodoros tick colony feeding and maintenance	*N/A*	*N/A*	*B. Anderson*
Ixodes tick colony feeding and maintenance	*N/A*	*N/A*	*B. Anderson*
Investigating the mechanisms of development and progression of Salmonella meningitis in mice	*12-44 (Salmonella typhimurium)*	*N/A*	*M. Morgan*
Modeling Salmonella typhimurium infection in the mouse gallbladder	*12-44 (S. typhimurium)*	*12-108*	*M. Morgan*
Immunotherapeutic blockade of PD-1 and SIRPα to restore immune cell function in a model of murine retrovirus infection	*N/A (Friend virus)*	*N/A*	*M. Morgan*

RML Biosafety Committee Meeting
August 20, 2015
Biosafety Officer/Responsible Official Report

Title	***Associated HPRD***	***Associated RD***	***Reviewer***
T cell responses to Lassa virus in mastomys natalensis	*13-94 (Lassa virus)*	*N/A*	*B. Anderson*
Transmission of MERS-CoV in hΔPP4 transgenic mice	*12-143 (MERS-CoV)*	*N/A*	*B. Anderson*
IFN-ART cure of HIV infection in TKO BLT mice	*12-105 (HBBF) 12-55 (HIV)*	*N/A*	*B. Anderson*

6) ***Biosafety Training Performed – Megan Morgan, Becky Anderson, Nancy Hoe***

Type of Training	***Number of Sessions***	***Number of Employees Trained***
Select Agent Initial	***1***	***4***
Select Agent Annual Refresher	***2***	***39***
BSL-3 Laboratory Biosafety	***2***	***8***
BSL-4 Annual Refresher	***1***	***5***
Biosafety Brief	***1***	***RMVB Staff***

7) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
a) *Biological Incident Report:*
i) *None*

8) ***Select Agent Issues***
a) *None*

9) ***Other Issues***
a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 11/19/15
Meeting Time: 1:03 PM **Adjourned:** 2:02 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Karin Peterson	☒	☐
Bob Heinzen, Vice Chair	☐	☒	Frank DeLeo (EO)	☐	☒	George Risi	☒	☐
Becky Anderson (EO)	☒	☐	Hideki Ebihara	☐	☒	Dana Scott	☒	☐
Alan Applebury	☐	☒	Heinz Feldmann (EO)	☐	☒	Alexandra Scranton	☐	☒
Chris Bosio	☒	☐	Nancy Hoe	☒	☐			
Marshall Bloom (EO)	☒	☐	Clay Jarrett	☒	☐			
Teresa Borino	☒	☐	Josh Kellar (EO)	☐	☒			
Jeff Burrows	☐	☒	Scott Kobayashi	☒	☐			
Carol Calderwood	☐	☒	Alida Merritt	☐	☒			
Marcie Caldwell (EO)	☐	☒	Kevin Mora	☐	☒			
Paul Carlson	☒	☐	Megan Morgan	☒	☐			

(P=present; A=absent)

Guests: (b)(6)

Minutes: Meeting minutes from 10/15/15 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** Action: Meeting minutes for 10/15/15 were unanimously approved as written.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans (Amendment) ▪ Feldmann (LV) ▪ **HPRD#13-91 Amend: Paramyxoviridae (Hendra, Nipah, Cedar virus)** ▪ Becky Anderson presented the risk assessment. This amendment is to add animal work with mice. The primary lab hazards include bites or scratches from infected mice. To mitigate these lab hazards, the following SOPs have been

	developed: ▪ SOP#4-28-16 Husbandry procedures for rodents in Level 4 biocontainment ▪ SOP#4-28-21 ABSL-4 Rodent Inhalant Anesthesia ▪ SOP#4-28-41 Recapture of Escaped Rodents in Level 4 Containment ▪ SOP#4-28-48 Inoculation/Infection and Blood Collection Procedures in Rodents in Level 4 Biocontainment ▪ ABSL-4 is appropriate for work with Paramyxoviridae (Hendra, Nipah, Cedar viruses) ▪ Becky Anderson pointed out that the statement, "Species to be used include all viruses in the Subfamily Paramyxoviridae, Genus Henipavirus, such as Nipah Hendra, and Cedar viruses." should be changed to the statement in the original HPRD, "This HPRD to include the following virus species belonging to the fmily Paramyxoviridae, Subfamily Paramyxovirinae, Genus Henipavirus: 1. Nipah virus, 2. Hendra virus, 3. Cedar virus (not a Select Agent)." ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. ▪ <u>Action:</u> The committee unanimously approved **HPRD#13-91 Amend** with the following minor modifications: 1. The sentence "Species to be used include all viruses in the Subfamily Paramyxoviridae, Genus Henipavirus, such as Nipah Hendra, and Cedar viruses." should be changed to the statement in the original HPRD, "This HPRD to include the following virus species belonging to the fmily Paramyxoviridae, Subfamily Paramyxovirinae, Genus Henipavirus: 1. Nipah virus, 2. Hendra virus, 3. Cedar virus (not a Select Agent)."
Item 2:	<u>Registration of Material (Potentially) Infectious for Humans (Amendment)</u> ▪ Feldmann (LV) ▪ **HPRD#13-92 Amend: Bunyaviridae (Crimean-Congo haemorrhagic fever, CCHF)** ▪ Becky Anderson presented the risk assessment. This amendment is to add animal work with non-human primates (NHP). The primary lab hazards include bites or scratches from infected NHPs. To mitigate these lab hazards, the following SOPs have been developed: ▪ SOP#4-28-17 Husbandry Procedures for NHP in Level 4 Biocontainment ▪ SOP#4-28-18 Recapture of Escaped Primates in Level 4 Biocontainment ▪ SOP#4-28-22 Immobilization and Anesthesia of NHP in Level 4 Biocontainment ▪ SOP#4-28-49 NHP primate manipulation ▪ SOP#4-28-51 Intratracheal and intrabronchial Inoculation Procedures

	for NHPs ▪ ABSL-4 is appropriate for work with CCHF. ▪ Animal studies with NHPs were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. ▪ Action: The committee unanimously approved **HPRD#13-92 Amend** as written.
Item 3:	Registration of Material (Potentially) Infectious for Humans (New) ▪ Munster (LV) ▪ **HPRD#15-177: Copenhagen virus** ▪ Becky Anderson presented the risk assessment. The Munster lab proposes to use Copenhagen virus as a vector to express proteins from viral pathogens of interest: filo-, bunya, arena, paramyxo, orthomyxo and coronaviruses. They will use this vector as a vaccine platform. The Copenhagen strain the Munster lab proposes to use, the tyrosine kinase gene has been knocked out and replaced with the viral protein of interest (in this case MERS-CoV Spike protein). Copenhagen virus is classified as a non-highly attenuated vaccinia virus. Lab acquired infections from non-highly attenuated vaccinia viruses have been documented. Several cases have been from accidental needle sticks, which have caused symptoms ranging from swelling at the site of fingertip up past the first finger joint with no associated malaise or fever to swelling at the site of needle stick, necrotic areas on the lesion, including fever and malaise. There are limited treatments for vaccinia virus infections, cidofovir an antiviral used off label can be used as well as VIG, an isotonic sterile solution of the Ig fraction of plasma from vaccinated persons. The primary lab hazards for working with Copenhagen virus include, ingestion, parenteral inoculation, droplet or aerosol exposure to mucous membranes, and exposure to broken skin. ▪ Typically the biosafety level is BSL-2/ABSL-2, however NIH OMS and the ACIP Smallpox Vaccine Recommendations indicate successful vaccinia vaccination for personnel working with Copenhagen virus. NIH OMS has waived the requirement for vaccination if all work with Copenhagen virus is conducted in the BSL-4 lab. Dr. Munster has agreed to keep all experiments, stocks and samples in the BSL-4 lab. ▪ BSL-4/ABSL-4 is appropriate for work with Copenhagen virus. ▪ Sue Priola pointed out that in the Synopsis section the Description section states there are no plans to propagate the virus or do any manipulations. This should be deleted because it contradicts the next section. ▪ Sue Priola stated that III-D-3-c should be added to the Eukaryote Cell section. ▪ Sue Priola noted that the comment about the biosafety level should be deleted. It makes the biosafety level confusing since everything must be performed at

	ABSL-4. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **HPRD#15-177** with the following minor modifications: 1. In the Synopsis section, Description subsection, delete statement that there are no plans to propagate the virus or do any manipulations. 2. III-D-3-c should be added to the Eukaryote Cell section. 3. Delete comment in the biosafety level section of the Animal Use section.
Item 4:	Registration of Material (Potentially) Infectious for Humans (New) ▪ Priola (LZP) ▪ **HPRD#15-178: Bovine Spongiform Encephalopathy (BSE)** ▪ Becky Anderson presented the risk assessment. The proposed studies are to understand how different proteins contribute to pathogenesis in complex proteinopathies. These studies are aimed at elucidating how complex proteinopathies develop in humans. BSE has been causally linked to new variant Creutzfeldt-Jakob disease (CJD) in humans. CJD is a very rare and incurable degenerative neurological disorder (brain disease) that is ultimately fatal, with the first symptom of CJD being rapidly progressive dementia, which then leads to progressive memory loss, personality changes and hallucinations. This is accompanied by physical problems such as speech impairment, jerky movements (myoclonus), balance and coordination dysfunction (ataxia), changes in gait, rigid posture and seizures. The duration of the disease varies greatly and in some people the symptoms can persist for years. There are no treatments available, only supportive care. Primary lab hazards include: exposure of broken skin with infected tissues, blood, etc. ▪ BSL-2 with additional precautions (work is performed in a restricted access lab where gown and gloves are required and a face mask should be worn, use of a respirator is optional) is appropriate for work with BSE. ▪ Mass spec analysis will be conducted in (b)(6) samples will be prepared in (b)(6) and transported in a durable/leak proof container. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Sue Priola abstained) **HPRD#15-178** as written.

Item 5:	Registration of Material (Potentially) Infectious for Humans (New) ▪ Bosio (LB) ▪ **HPRD#15-179: Pichinde Virus** ▪ Becky Anderson presented the risk assessment. The proposed studies are to use Pichinde virus as a control for LCMV infections (both Arenaviruses) to assess the T cell responses to the gp61 T cell epitope. Pichinde virus is not a human pathogen and does not normally infect humans. However, there have been 2 reports of lab acquired infection. In one case, the infection included a 1- month period of mild dysuria, myalgia, and a localized vesicular eruption of one hand, which could represent the portal of entry. Both cases have been associated with generation of aerosols with high concentrations of virus. Routine work with cell cultures and animal subjects are not subject to chronic infections. Primary lab hazards include: accidental sharps injuries, ingestion, or generation of aerosols with high concentrations. ▪ BSL-2/ABSL-2 is appropriate for work with Pichinde virus. No work with high concentrations is approved, comments in the HPRD state they will not work with high concentrations. ▪ George Risi questioned if high concentrations were defined. Nancy Hoe stated that there is not a specific definition. Becky Anderson pointed out that the lab acquired infection occurred when they had concentrated Pichinde virus, the Bosio lab will not be concentrating the virus. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Chris Bosio abstained) **HPRD#15-179** as written.
Item 6:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Feldmann (LV) ▪ **RD#15-447 Amend**: MVA Vaccines ▪ Reviewers: Sue Priola, Dana Scott ▪ **Summary:** The amendment is to add experiments with Copenhagen virus as a vaccine platform, similar to MVA. ▪ Sue Priola summarized the amendment. The original RD described work with modified Vaccinia Ankara (MVA). The purpose was to express proteins from specific viruses like Ebola or MERS-CoV and use MVA as a vaccine platform. The amendment describes using Copenhagen virus instead of MVA as the vaccine platform. The Copenhagen strain will have the MERS-CoV spike protein inserted and they expect to generate an antibody response to the spike protein.

	▪ Sue Priola informed the committee that the same recommendations listed on the Copenhagen HPRD were listed on the RD, but it is important to reiterate that information on the Amendment Description so it is clear that all work will be performed at BSL-4. To alleviate confusion, the statement, "All other information for this section is the same as for MVA" should also be deleted. ▪ Sue Priola also pointed out that the Eukaryotic Cell section should include III-D-3-a of the NIH Guidelines added. ▪ Dana Scott had no additional comments or concerns. ▪ Animal studies with mice were proposed. ▪ The committee discussed the containment requirements. BSL-4/ABSL-4 is appropriate for work with Copenhagen virus to waive the vaccinia virus vaccination requirement. See discussion in Item 3 for Copenhagen HPRD. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **RD#15-447 Amend** with the following minor modifications: 1. Spell out the biosafety level again in the Amend Registration section. 2. Delete the following sentence, "All other information for this section is the same as for MVA" 3. Add III-D-3-a to the Eukaryotic Cell Section. Research using eukaryotic cells is approved at BSL-2* under III-D-3-a and III-D-2-a of the NIH Guidelines. *All work is approved at BSL-4 in order to waive the requirement for vaccinia virus vaccination.
Item 7:	<u>Registration Documents for Recombinant DNA Experiments (Renewal)</u> ▪ Hasenkrug (LPVD) ▪ **RD#15-220**: HIV DNA Vaccines ▪ Reviewers: Hideki Ebihara, Sue Priola ▪ **Summary:** These studies are aimed at determining if the mA3 gene is responsible for mutating DNA vaccines and making them ineffective. ▪ Sue Priola summarized the registration. She stated that this is a renewal for an HIV vaccine for the Hasenkrug lab. The HIV based vaccine expresses T cell reactive epitopes that should generate a T cell immune response. The attached ASP describes testing the role of mA3 in introducing mutations in DNA and see if mA3 decreases the immune response. ▪ Hideki Ebihara informed Sue Priola by email that he questioned if the RD

	needed a Prokaryotic Host section. Becky Anderson stated that they do not because they will not perform any work with Prokaryotic Hosts, they will receive the vaccine from a collaborator. Hideki Ebihara did not have any additional concerns. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for work with HIV DNA vaccines. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#15-220** as written. Animal use is approved under section III-D-4 of the NIH Guidelines.
Item 8:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ de Leo (LB) ▪ **RD#15-313**: Understanding Pathogen-PMN Interactions ▪ Reviewers: Bob Heinzen, Clay Jarrett ▪ **Summary:** The RD describes enhancing the current understanding of the pathogen-PMN interface at both the cell and molecular level. ▪ Clay Jarrett summarized the registration. This is a renewal for the general RD for the de Leo lab. They study the host-pathogen interaction of S. aureus with a focus on PMNs. They use molecular techniques to analyze several genes, some encode toxins, but they have an LD_{50} of less than 100 ng/kg. ▪ Clay Jarrett pointed out that dual use question 3 is answered yes, however that is for the use of tetracycline resistance, which can be naturally occurring as described on the dual use questionnaire. ▪ Sue Priola pointed out that 2 vector maps are missing, the pQE and pET-15b. Scott Kobayashi stated that they will not use those vectors, just delete the references to them in the Recombinant DNA section. ▪ Sue Priola also noted that the beta lactamase gene is in several of the vector maps, but the RD states that beta lactamase is the primary treatment for methicillin sensitive strains. George Risi and Scott Kobayashi clarified that those strains are resistant to ampicillin, but would still be sensitive to methicillin. Most strains are resistant to ampicillin now. Sue Priola proposed that the wording could be changed to make it clear which beta lactams are used clinically. The Prokaryotic Host section and the dual use section (in two places) need to be updated. ▪ Sue Priola pointed out that III-D-2-a should be added to the Research Product

	Section. ▪ Bob Heinzen informed Sue Priola by email that he had no comments or concerns. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for work with *S. aureus* strains. ▪ Animal studies with rabbits and mice were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Scott Kobayashi abstained) **RD#15-313** with the following modifications: 1. Remove reference in the Recombinant DNA section to pQE and pET-15b. 2. Add III-D-2-a to the Research Product Section. 3. Clarify clinical usage of beta lactamases in the Prokaryotic Host section and in both sections of the dual use questionnaire. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-1-a, III-D-1-b, and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a of the NIH Guidelines.
Item 9:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Munster (LV) ▪ **RD#15-441**: Baculovirus expression system ▪ Reviewers: Chris Bosio, Scott Kobayashi ▪ **Summary:** The registration describes using a baculovirus expression system to express viral proteins in their native state. ▪ Chris Bosio summarized the registration. This is a renewal for using a baculovirus system to express proteins from viruses for diagnostic tests, generation of antibodies, etc. This system has been around for over 20 years, they transfect insect cells to generate the proteins, then purify the proteins. There are ASPs attached for using the proteins to make antibodies in rabbits and to use proteins to generate an immune response in mice. Chris Bosio had no concerns with the RD. ▪ Scott Kobayashi pointed out a typo in the first sentence of the Synopsis, Purpose subsection, “the is” should be “this”. Scott Kobayashi had no additional comments or concerns. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for work with baculovirus.

	▪ Animal studies with mice and rabbits were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#15-441** with the following minor modifications: 1. Correct a typo in the first sentence of the Synopsis, Purpose subsection. "the is" should be "this". Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a and III-D-3-e of the NIH Guidelines.
Item 10:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Bloom (LV) ▪ **RD#15-443**: Vector borne Flavivirus genetic analysis ▪ Reviewers: Karin Peterson, Hideki Ebihara ▪ **Summary:** The RD describes performing genetic analysis of vector borne Flaviviruses. ▪ Karin Peterson summarized the registration. Karin Peterson informed the committee that this is also a renewal. The RD describes work where they are not generating a replication competent virus. They will work with Tick Borne Encephalitis virus or West Nile Virus and generate a reporter system to study virus replication. ▪ Hideki Ebihara informed Sue Priola by email that he had no additional comments or concerns. ▪ Sue Priola pointed out that VBFV is not spelled out anywhere in the document. It appears in the first line of the Synopsis section, Purpose subsection. ▪ The committee discussed the containment requirements. BSL-2 is appropriate for work with Vector borne Flaviviruses. ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#15-443** with the following minor modification: 1. Spell out VBFV in the first line of the Synopsis section, Purpose subsection. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-2-a of

	the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a of the NIH Guidelines.
Item 11:	**Standard Operating Procedure: Maximum Containment Laboratory Operations and Safety Procedures (MCL OSP) (Annual Review)** ▪ Becky Anderson informed the committee that the MCL OSP was due for annual review. The changes are tracked in red, and the updates were listed on page 9 of the document. ▪ George Risi asked if there is only one courier for the shipment of Select Agents. Nancy Hoe replied that previously there had been only one, but she was recently informed that there are a few more companies trying to provide that service. She will look into their availability for shipping and receiving from RML. ▪ Sue Priola pointed out that the chain of custody forms were missing from the document and need to be replaced. ▪ The committee had no additional comments or concerns. Action: The committee unanimously approved **Maximum Containment Laboratory Operations and Safety Procedures (MCL OSP) (Annual Review)** with the following minor modifications: 1. Add the Chain of Custody forms back to the MCL OSP.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Nancy Hoe presented the BSO report.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ Paul Carson informed the committee that there was a medical transport that was not work related on Tuesday. ▪ On Friday there will be a drill with St. Patrick hospital. There will be an ambulance on site.
Report	**IRF Biosafety Manager Report/Megan Morgan** ▪ The (b)(6); (b)(3):42 annual shutdown started this week. ▪ The ABSL-3 was reactivated this week. The first studies will start tomorrow.
Report	**Associate Director Report/Marshall Bloom** ▪ Nothing to report.

Around the room	▪ None.

Other issues	▪ None.

Next Meeting:

- Date: 12/17/15
- Place: Bldg A Seminar Room
- Time: 1:00 PM

RML Biosafety Committee Meeting
November 19, 2015
Biosafety Officer/Responsible Official Report

1) ***Requests approved by BSO since last meeting:***
   a) *Request for Student to Work with Human Pathogens*
      i) (b)(6) ***(LZP)***
         (i) understanding of the arginine pathway in Borrelia burgdorferi
3) ***New requests approved by committee via electronic review:***
   a) *None*
4) ***New requests***
   a) *Human Pathogen Registration Documents*
      i) ***Amend***
         (a) *Feldmann (LZ)*
            (a) ***HPRD 13-91****: Paramyxoviridae, Henipavirus*
               (i) Add animal work, mice, all DSAT-approved routes of infection
            (b) ***HPRD 13-92:*** *Bunyaviridae*
               (i) Add animal work, non-human primates, all DSAT-approved routes of infection
      ii) ***New***
         (a) *Munster (LV)*
            (a) ***HPRD 15-177****: Modified Vaccinia – Copenhagen*
         (b) *Priola (LPVD)*
            (a) ***HPRD 15-178****: Bovine Spongiform Encephalopathy*
         (c) *Bosio (LB)*
            (a) ***HPRD 15-179****: Pichinde virus*
   b) *Registration Documents for Recombinant DNA Experiments*
      i) ***Amend***
         (a) *Feldmann (LV)*
            (a) ***RD 15-447:*** *MVA vaccines*
               (i) *Addition of Modified Vaccinia – Copenhagen*
      ii) ***Renewal***
         (a) *Hasenkrug (LPVD)*
            (a) ***RD 15-220****: use of DNA vaccines to determine role of mA3 gene*
         (b) *DeLeo (LB)*
            (a) ***RD-15-313****: understanding the pathogen-PMN interface*
         (c) *Munster (LV)*
            (a) ***RD 15-441****: creation of baculovirus expression system*
         (d) *Bloom (LV)*

(a) *RD **15-443**: creation of WNV and Toro TBEV replicons*

c) *Standard Operating Procedures*

i) ***Annual Review***

(a) *MCL Operations and Safety Procedures*

5) ***Animal Study Protocols Review***

Title	***Associated HPRD***	***Associated RD***	***Reviewer***
Determination of the presence of infectivity in prion samples prepared for mass spectrometry analysis	*12-51 (SCJD)*	*N/A*	*N. Hoe*
In vivo imaging of Yersinia pestis dissemination in mice after infection by flea bite	*13-04 (Y. pestis)*	*15-303*	*N. Hoe*
Protective efficacy of VSV-CCHF vaccine in IFNAR -/- mice	*13-92 (CCHF) 13082 (VSV)*	*13-404 (VSV)*	*B. Anderson*
The mobilization of endogenous retroviruses in mice during Friend57 muLV infection	*N/A*	*N/A*	*B. Anderson*
Defining the role of distinct host genetic backgrounds in Ebola virus pathogenicity in collaborative cross mice	*13-90 (EBOV)*	*N/A*	*N. Hoe*
Defining the role of distinct host genetic backgrounds in Nipah virus pathogenicity in CC mice	*13-91 (Nipah virus)*	*N/A*	*B. Anderson*
Investigating the requirement of monocytes for the dissemination of S. enterica serovar Typhimurium in infected mice	*12-44 (S.*	*N/A*	*B. Anderson*

6) ***Biosafety Training Performed – Megan Morgan, Becky Anderson, Nancy Hoe***

Type of Training	***Number of Sessions***	***Number of Employees Trained***
Select Agent Initial	***1***	***5***
BSL-3 Laboratory Biosafety	***1***	***2***
BSL-3 Visitor Training	***1***	***2***
BSL-4 Annual Refresher	***1***	***1***
Full-length clone lab Annual Refresher	***1***	***2***

7) ***Safety Audits and Inspections***

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

a) *Biological Incident Report:*

i) *None*

8) ***Select Agent Issues***

a) *None*

9) ***Other Issues***

a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 12/17/15
Meeting Time: 1:00 PM **Adjourned:** 1:40 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Karin Peterson	☒	☐
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	George Risi	☒	☐
Becky Anderson (EO)	☒	☐	Hideki Ebihara	☒	☐	Dana Scott	☒	☐
Alan Applebury	☐	☒	Heinz Feldmann (EO)	☐	☒	Alexandra Scranton	☐	☒
Chris Bosio	☒	☐	Nancy Hoe	☒	☐			
Marshall Bloom (EO)	☒	☐	Clay Jarrett	☒	☐			
Teresa Borino	☐	☒	Josh Kellar (EO)	☐	☒			
Jeff Burrows	☐	☒	Scott Kobayashi	☒	☐			
Carol Calderwood	☐	☒	Alida Merritt	☐	☒			
Marcie Caldwell (EO)	☐	☒	Kevin Mora	☐	☒			
Paul Carlson	☒	☐	Megan Morgan	☒	☐			

(P=present; A=absent)

Guests: (b)(6)

Minutes: Meeting minutes from 11/19/15 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** Action: Meeting minutes for 11/19/15 were unanimously approved as written.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans (Amendment) ▪ de Leo (LB) ▪ **HPRD#13-1 Amend: *Staphylococcus aureus* and various BSL-2 agents** ▪ Becky Anderson presented the risk assessment. This amendment is to add *Enterobacter aerogenes*. The de Leo lab will compare *E. aerogenes* to *Klebsiella pneumoniae* in multiple *in vitro* assays including work with human neutrophils.

	Both pathogens are closely related by taxonomy. *Enterobacter* is a frequent cause of infection in immunocompromised individuals, low birth weight and premature babies, and those with serious underlying health conditions. It has frequently been implicated in urinary tract infections (UTIs), skin and soft tissue infections, respiratory infections, GI infections, adult meningitis, wound infections and bacteremia. Particular risk factors for *E. aerogenes* infection include prolonged hospital stay, intravenous catheter use, invasive surgical procedures and previous antibiotic usage. For treatment, no vaccines are available although infections can be treated with antibiotics, however, strains frequently have a broad spectrum of antimicrobial resistance and can produce extended-spectrum beta-lactamases (enzymes that confer resistance to most *beta*-lactam antibiotics). Of the beta-lactams, the fourth generation cephalosporins and carbapenems are the best options. Aminoglycosides retain good activity but usually require combination therapy. Quinolones are highly active against most strains, but emerging resistance is a major concern. The primary lab hazards include parenteral inoculation, generation of aerosols, and exposure to broken skin. Immunocompromised persons should be informed of the risks of working with *E. aerogenes*. ▪ BSL-2/ABSL-2 is appropriate for work with *E. aerogenes*. All employees should be informed of the risks of working with *E. aerogenes*. ▪ Alex Scranton submitted questions to Sue Priola by email. Alex Scranton questioned at what point should the addition of a new agent be a new HPRD, this HPRD has been amended several times. Nancy Hoe agreed that it was probably time to split current HPRD into two separate ones. A new HPRD could be made that covers *K. pneumoniae* and *E. aerogenes* and that will be separate from the current HPRD#13-1. The committee agreed that the addition of *E. aerogenes* could be approved by the IBC this meeting and biosafety could administratively work to split the HPRD as discussed. ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. ▪ <u>Action:</u> The committee unanimously approved **HPRD#13-1 Amend** with the following minor modifications: 1. Split HPRD#13-1 into two separate HPRDs. HPRD#13-1 should continue to cover *S. aureus*, and the new one should include *K. pneumoniae* and *E. aerogenes*.
Item 2:	<u>Registration Documents for Recombinant DNA Experiments (Amendment)</u> ▪ Ebihara (LV) ▪ **RD#14-431 Amend**: Molecular characterization of Viral proteins

	▪ Reviewers: Sue Priola, Chris Bosio ▪ **Summary:** The amendment is to add experiments from Feldmann RD 11-405, Feldmann RD 12-408, and Ebihara RD 14-430 and inactivate those RDs. Work from Feldmann RD 12-409 will be added to the RD, but it will not be inactivated at this time. ▪ Sue Priola summarized the amendment. She informed the committee that the amendment is to combine multiple RDs into one. The RD describes using different viral proteins from different viruses and expressing them in eukaryotic cells to study their function. All the listed experiments are BSL-2 because they are not dealing with live viruses. The additions to this RD are Flavivirus protein studies from RD 12-408 and RD 11-405. ▪ Nancy Hoe informed the committee that only Sonja Best and Marshall Bloom are approved for work with TBEV, she questioned whether Hideki Ebihara's personnel will be working with RNA or cDNA clones from TBEV. Hideki Ebihara said his group will not be involved with any handling of any form of TBEV. Nancy Hoe pointed out that RNA from Flaviviruses will not be Select Agent Flaviviruses because those have to be handled at BSL-4. Clarification should be added to (8) Part B Research Using Eukaryotic Cells stating, "Non-select agent Flaviviruses". ▪ Sue Priola pointed out that the dual use form needs to be signed by Hideki Ebihara. ▪ Chris Bosio had no additional comments or concerns. ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved (Hideki Ebihara abstained) **RD#14-431 Amend** with the following minor modifications: 1. Hideki Ebihara needs to sign the dual use form. 2. Add to Part B Research Using Eukaryotic Cells, "Non-select agent Flaviviruses". Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-2-a and III-E-1 of the NIH Guidelines.
Item 3:	<u>Registration Documents for Recombinant DNA Experiments (Renew)</u> ▪ Feldmann (LV) ▪ **RD#15-417**: Marburg virus reverse genetics ▪ Reviewers: Clay Jarrett, Bob Heinzen

	▪ **Summary:** The RD describes the use of a reverse genetics system for work with Marburg virus. ▪ Clay Jarrett summarized the RD. The renewal of the RD is for a reverse genetics system for Marburg virus. All of the cloning will be in *E. coli* at BSL-2 in accordance with the RAC determination. The RAC approval letter is attached to the RD as well. Any work to generate live virus will be performed at BSL-4. ▪ Bob Heinzen had no additional comments or concerns. ▪ Alex Scranton submitted questions by email to Sue Priola. She asked if the complete RAC approval letter was attached. Sue Priola informed the group that the entire letter is indeed attached. She also questioned if the biosafety level should be re-evaluated given the note in the dual use survey indicating that the potential does exist for enhanced virulence from the new experiments. Sue Priola stated that the type of work where enhanced virulence could be observed is already performed at BSL-4, so that should be covered. Finally, Alex Scranton questioned what "restricted BSL-2" meant, she asked if more information should be added to describe it in the RD? Sue Priola pointed out that it is in the attached SOP that is part of the RD. Sue Priola informed the committee that Alex Scranton had trouble opening the complete file so maybe some of this information was not available to her. ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **RD#15-417** as written. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-4 under III-D-3-c, III-D-1-a, and III-D-1-c of the NIH Guidelines.
Item 4:	<u>Registration Documents for Recombinant DNA Experiments (New)</u> ▪ Hinnebusch (LZP) ▪ **RD#15-322**: Retroviral Vectors for Transduction of Murine Cells ▪ Reviewers: Karin Peterson, Hideki Ebihara ▪ **Summary:** The RD describes using retroviral vectors to introduce foreign DNA into mouse cells. ▪ Karin Peterson summarized the RD. This RD describes the use of a retroviral packaging system that is commercially available. They will generate non-replicating virions to transduce murine bone marrow progenitor cells to generate immortalized cell lines. These cells are immortal until they differentiate them *in vitro* to make neutrophils or macrophages. Cells will later

	be infected with *Y. pestis* virulent and avirulent strains. ▪ Hideki Ebihara had no additional comments or concerns. ▪ No animal studies were submitted, proposed, or reviewed. ▪ Sue Priola questioned if the antibiotic resistance genes are ok, is there a concern with Yersinia getting into a cell that has resistance markers in the cell and taking that up? The committee discussed that this does not happen with these intracellular bacteria. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Chris Bosio, Clay Jarrett abstained) **RD#15-322** as written. Research using prokaryotic hosts is approved at BSL-2 under section II-A-3 of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under II-A-3 of the NIH Guidelines.
Item 5:	**Working Groups for Disinfectant Review:** ▪ Sue Priola informed the committee that the disinfectant used in several of the BSL-3 labs is no longer being manufactured so these labs have tested a replacement product called Earth Sense Disinfectant. They have verified that it is effective against their agents. ▪ The IBC needs to set up working groups to review the data as has been done for the past inactivation procedures. Scott Kobayashi, Karin Peterson, and Hideki Ebihara will be selected because other committee members are either PI's for those groups or work in those labs. The working groups will be scheduled to meet sometime between January 12 and the 15 to review the data.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Nancy Hoe presented the BSO report. ▪ GAO and OIG both have ongoing engagements with the NIH, including RML.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ The speed limit was increased on site from 10-15 mph and we have seen more near misses of pedestrians almost getting hit. Please pay attention for pedestrians when driving and when walking and stepping out onto the street, be careful.
Report	**IRF Biosafety Manager Report/Megan Morgan** ▪ (b)(6) annual shutdowns for 2016 are being planned. The

	shutdowns will be two weeks for each suite and they will be staggered so they are not shutdown at the same time. Megan Morgan is working with lab groups to get these scheduled between February and May.
Report	**Associate Director Report/Marshall Bloom** ▪ GAO and OIG engagements that are ongoing demonstrate the need for clear documentation. Everyone complains about documentation and the number of records required, but it has been clear through these engagements that the more straightforward we can make these things, the easier it is to deal with these types of situations and inspectors. ▪ This committee does a great job making sure we keep our documents clear and in order.
Around the room	▪ None.

Other issues	▪ None.

Next Meeting:

- Date: 1/21/15
- Place: Bldg A Seminar Room
- Time: 1:00 PM

RML Biosafety Committee Meeting
December 17, 2015
Biosafety Officer/Responsible Official Report

1) ***Requests approved by BSO since last meeting:***
   a) ***None***
3) ***New requests approved by committee via electronic review:***
   a) *None*
4) ***New requests***
   a) *Human Pathogen Registration Documents*
      i) ***Amend***
         (a) *DeLeo (LB)*
            (a) ***HPRD 13-1****: Staphylococcus aureus (and additional BSL-2 pathogens)*
               (i) Add Enterobacter aerogenes
   b) *Registration Documents for Recombinant DNA Experiments*
      i) ***Amend***
         (a) *Ebihara (LV)*
            (a) ***RD 15-447:*** *Characterization of the rolls played by viral proteins in viral replication cycle and pathogenesis using in vitro systems*
               (i) *Consolidation of RDs 11-405, 12-408, 14-430*
               (ii) *Clarifications and updates to text as a result of consolidation*
      ii) ***Renewal***
         (a) *Feldmann (LV)*
            (a) ***RD 15-417****: Marburg virus reverse genetics*
      iii) ***New***
         (a) *Hinnebusch (LZP)*
            (a) *RD* ***15-322****: Use of retroviral vectors to introduce foreign DNA into mouse cells*

5) ***Animal Study Protocols Review***

Title	***Associated HPRD***	***Associated RD***	***Reviewer***
Tracking ISG expression in HIV infected humanized mice treated with IFNα	*12-55 (HIV) 12-104 (HBBF)*	*N/A*	*B. Anderson*
Efficacy of rVACV-COP/MERS-S vaccine using transgenic DPP4 mice	*12-143 (MERS-CoV) 15-177 (VACV-COP)*	*15-447 (recomb. Vaccinia Copenhagen)*	*M. Morgan*
Development of a non-human primate model for Crimean-Congo hemorrhagic fever (CCHF)	*13-92 (CCHF)*	*N/A*	*M. Morgan*
Modulation of inflammation by synthetic PE:PC liposomes in mice	*13-71 (F. tul) 12-108 (West Nile virus)*	*N/A*	*N. Hoe*

Title	***Associated HPRD***	***Associated RD***	***Reviewer***
Establishment of a lethal model (mouse) for Ebola infection suitable for both vaccine and therapeutic treatments	*13-90 (EBOV)*	*14-407 rEbola*	*B. Anderson*
Assessing T705 as a post-exposure countermeasure to Lassa virus infection in cynomolgous macaques	*13-94 (Lassa virus)*	*N/A*	*N. Hoe*

6) ***Biosafety Training Performed – Megan Morgan, Becky Anderson, Nancy Hoe***

Type of Training	***Number of Sessions***	***Number of Employees Trained***
BSL-3 Laboratory Biosafety	***1***	***2***
BSL-4 Medical Extraction Refresher	***6***	***30***

7) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
a) *Biological Incident Report:*
   i) *None*

8) ***Select Agent Issues***
a) *None*

9) ***Other Issues***
a) *GAO engagement: "High Containment Laboratories: Inactivation and Attenuation"*
b) *OIG engagement: Review of the National Institutes of Health's Controls Over the Preparation and Receipt of Select Agent Shipments"*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 1/21/16
Meeting Time: 1:00 PM **Adjourned:** 1:40 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Megan Morgan	☒	☐
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Karin Peterson	☐	☒
Becky Anderson (EO)	☒	☐	Hideki Ebihara	☒	☐	George Risi	☐	☒
Alan Applebury	☐	☒	Heinz Feldmann (EO)	☐	☒	Dana Scott	☒	☐
Chris Bosio	☒	☐	Nancy Hoe	☒	☐	Alexandra Scranton	☐	☒
Marshall Bloom (EO)	☒	☐	Clay Jarrett	☒	☐			
Teresa Borino	☒	☐	Josh Kellar (EO)	☐	☒			
Jeff Burrows	☐	☒	Scott Kobayashi	☒	☐			
Carol Calderwood	☒	☐	Jamie Lovaglio	☒	☐			
Marcie Caldwell (EO)	☐	☒	Alida Merritt	☐	☒			
Paul Carlson	☒	☐	Kevin Mora	☐	☒			

(P=present; A=absent)
(b)(6)

Minutes: Meeting minutes from 12/17/15 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** Action: Meeting minutes for 12/17/15 were unanimously approved with the following minor modifications: 1. Page 3, bullet 5, change Sue Priola to Nancy Hoe. 2. Becky Anderson informed the committee that the NIH Guidelines approved for RD#15-322 were not correct and should be updated to III-E in the minutes. The RD in PI Dashboard will have comments added to correct the NIH Guidelines listed in the RD. 3. In the Working Group section, bullet two, change Hideki Ebihara to Dana Scott.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans (Amendment) ▪ Hackstadt (LB) ▪ **HPRD#12-37 Amend: *Chlamydia trachomatis*** ▪ Becky Anderson presented the risk assessment. The amendment is to add mice. The Hackstadt lab will test the virulence of chlamydia that is genetically modified to knock out expression of specific genes believed to be important to Chlamydial disease. The primary lab hazards include rodent bites or scratches. To mitigate these hazards, all animal studies with *C. trachomatis* will be conducted in the Human Pathogen wing of (b)(6) All infection and control solutions will be prepared and administered by laboratory personnel wearing protective clothing, gloves, and safety goggles or a face shield. ▪ ABSL-2 is appropriate for animal work with *C. trachomatis*. All studies will be conducted in the Human Pathogen wing of (b)(6) ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **HPRD#12-37 Amend** with the following minor modifications: 1. Add the following statement "All infection and control solutions will be prepared and administered by laboratory personnel wearing protective clothing, gloves, and safety goggles or a face shield" to the recommendation section.
Item 2:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Bloom (LV) ▪ **RD#14-445 Amend**: Analysis of molecular signaling pathways in tick-borne Flavivirus persistence. ▪ Reviewers: Hideki Ebihara, Sue Priola ▪ **Summary:** The amendment is to add pGEM-T vector to the current RD. ▪ Hideki Ebihara summarized the amendment. The amendment is to add a commercial vector (pGEM-T) to the current RD. They will use the vector to generate ds RNA that will be transfected into cells for knockdown/gene silencing experiments. This RNA will be used as a control for the knockdown of various tick genes. The NIH Guidelines are appropriate and Hideki Ebihara did not have any dual use concerns. ▪ Sue Priola had no additional comments or concerns. ▪ No animal studies were submitted, proposed, or reviewed.

	▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#14-445 Amend** as written. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-2-a of the NIH Guidelines.
Item 3:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Hackstadt (LB) ▪ **RD#14-120 Amend**: Genetic modification of Chlamydia spp. ▪ Reviewers: Dana Scott, Scott Kobayashi ▪ **Summary:** The amendment is to add animal work with mice. ▪ Dana Scott summarized the amendment. The amendment is to add animal work with mice. The animal work and precautions were described by Becky Anderson earlier in the meeting for HPRD 12-37 Amend. ▪ Becky Anderson pointed out that the same precautions need to be added to the recommendation section as were added to HPRD 12-37 Amend, "All infection and control solutions will be prepared and administered by laboratory personnel wearing protective clothing, gloves, and safety goggles or a face shield." ▪ Scott Kobayashi had no additional comments or concerns. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#14-120 Amend** with the following minor modifications: 1. Add to the recommendations section, "All infection and control solutions will be prepared and administered by laboratory personnel wearing protective clothing, gloves, and safety goggles or a face shield" Research using prokaryotic hosts is approved at BSL-2 under section III-D-1-a and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a of the NIH Guidelines.

Item 4:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Hackstadt (LZP) ▪ **RD#16-126**: Development of expression vectors for *Chlamydia trachomatis* ▪ Reviewers: Bob Heinzen, Clay Jarrett ▪ **Summary:** The RD describes transforming Chlamydia in order to study the cellular interactions of Chlamydia with host cells. ▪ Bob Heinzen summarized the RD. This is a renewal for the Hackstadt lab's genetic transformation of Chlamydia spp. They use beta-lactams as a selectable marker in their system. Attached to the RD is OBA correspondence that agreed that the use of beta lactams are not an issue for the proposed studies. There is no concern with any of the proposed antibiotics listed and the NIH Guidelines are fine. Bob Heinzen had no dual use concerns with the proposed research. ▪ Clay Jarrett questioned if vectors like pMW1650 from RD 14-120 should also be added to the RD. The committee agreed that the vectors of the Mariner-based transposon system should be added to the current RD. ▪ Sue Priola pointed out that this RD is a little confusing because it describes a specific strain, but this is not clear until you read the Prokaryote Host section. A description that this RD applies to the specific strain should be added to the recommendation section. ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#16-126** with the following minor modifications: 1. Add vectors for the Mariner-based transposon system. 2. Add to the recommendation section a description of the specific strain that the RD applies to. Research using prokaryotic hosts is approved at BSL-2 under section III-D-1-a and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a of the NIH Guidelines.
Item 5:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Feldmann (LV) ▪ **RD#16-413**: Henipavirus reverse genetics ▪ Reviewers: Sue Priola, Chris Bosio

	▪ **Summary:** The RD describes the Henipavirus reverse genetics system ▪ Sue Priola summarized the RD. This is the renewal of an old RD and includes work from RD 12-409. After this renewal is approved, RD 12-409 will be inactivated. In red, they list the new work and any new plasmids, the new work includes studies with trVLPs. They have two sets of objectives: 1) develop minigenome systems for these viruses, 2) develop reverse genetics system using cloned fragments of these viruses, then transfect full length clone of viral genomes. They have permission from OBA to do the described work. Section B describes expressing viral proteins in cells and determining how they will effect cellular processes. They will also rescue recombinant viruses by cotransfection, and this work will be conducted in the BSL-4 lab. Virus like particle work will be conducted at BSL-2. Sue Priola had no dual use concerns with the proposed work. ▪ Sue Priola pointed out that NiV, HeV, and CedPV need to be spelled out in section A. ▪ Nancy Hoe pointed out that III-E-1 should be deleted from Section A and III-D-3-b should be deleted from Section B of the NIH Guidelines. ▪ Megan Morgan pointed out in the Laboratory Building and Room Number should state (b)(6) not '(b)(6) ▪ Chris Bosio had no additional comments or concerns. ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#16-413** with the following minor modifications: 1. Spell out NiV, HeV, and CedPV in Section A. 2. Delete III-E-1 from Section A and III-D-3-b from Section B of the NIH Guidelines. 3. Change in the Laboratory Building and Room Number Section (b)(6) not (b)(6) Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 or BSL-4 under III-D-2-a, III-D-3-a, III-D-3-c and III-E-1 of the NIH Guidelines.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Nancy Hoe presented the BSO report. ▪ There will be no March IBC meeting because of the CDC DSAT BSL-4 Inspection occurring March 8-17, 2016.

Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ There was an ambulance response on campus, someone slipped and hit their head on the ice and the employee refused transport. ▪ An employee accidentally inhaled sodium bisulfate, immediately began coughing, but it subsided fairly quickly. The incident is under investigation. ▪ There was an indoor air quality issue in (b)(6) where xylene fumes went to an adjacent lab while an employee was transferring the chemical to another container. ▪ There was an incident of a sewer line not being properly vented, sewer gas vented into an employee's office, the employee sought outside medical treatment. ▪ A buffer solution leaked onto a surge protector and shorted out the protector. The short resulted in lots of smoke, but no one was injured. ▪ There was a motor vehicle collision, snow equipment that was plowing ran into a metal barrier.
Report	**IRF Biosafety Manager Report/Megan Morgan** ▪ The BSL-3 annual shutdowns are underway in (b)(6) These shutdowns include upgrades to the HVAC system in the BSL-3 labs. (b)(6) lab is down this week and next week. (b)(6) will be February 8-19, (b)(6) will be Feb 22-March 4, and (b)(6) ll be April 4-15th.
Report	**Associate Director Report/Marshall Bloom** ▪ NIAID Division of Clinical Research is starting a pre-exposure prophylaxis vaccine trial with VSV based Ebola vaccine. RML has been asked if they would like to participate in the trial. At this time RML has yet to make a decision. RML would need to work out several logistical issues.
Around the room	▪ Sue Priola informed the committee that the Working Group met to review Earth Sense Neutral Disinfectant as a replacement for Roccal-D. She wanted to thank everyone for their hard work. The final reports are not ready, but should be by the next IBC meeting.

Other issues	▪ None.

Next Meeting:

- Date: 4/21/16

- Place: Bldg A Seminar Room
- Time: 1:00 PM

RML Biosafety Committee Meeting
January 21, 2016
Biosafety Officer/Responsible Official Report

1) ***Requests approved by BSO since last meeting:***
   a) ***None***
3) ***New requests approved by committee via electronic review:***
   a) ***None***
4) ***New requests***
   a) *Human Pathogen Registration Documents*
      i) ***Amend***
         (a) *Hackstadt (LB)*
            (a) ***HPRD 12-37****: Chlamydia trachomatis*
               (i) Add animal work with mice
   b) *Registration Documents for Recombinant DNA Experiments*
      i) ***Amend***
         (a) *Bloom (LV)*
            (a) ***RD 14-445:*** *Analysis of molecular signaling pathways in tick-borne Flavivirus persistence*
               (i) *Add pGEM-T vector*
               (ii) *Create and purify dsRNA for dsRNA-mediated transcript knockdown*
      ii) ***Amend***
         (a) *Hackstadt (LB)*
            (a) ***RD 14-120****: Genetic Modification of Chlamydiae to determine virulence genes*
               (i) Add animal work with mice
      iii) ***Renew***
         (a) *Hackstadt (LB)*
            (a) ***RD 16-126****: Development of expression vector for Chlamydia trachomatis*
      iv) ***Renew***
         (a) *Feldmann (LV)*
            (a) ***RD 16-413****: Reverse genetics of Henipavirus*
               (i) Consolidate work from RD 12-409, RD 12-409 will be inactivated

5) ***Animal Study Protocols Review***

Title	***Associated HPRD***	***Associated RD***	***Reviewer***
Evaluation of the effect of Ixodid tick salivary gland extract on Powassan virus infection in Peromyscus leucopus mice	*13-75 (Powassan virus)*	*N/A*	*M. Morgan*

RML Biosafety Committee Meeting
January 21, 2016
Biosafety Officer/Responsible Official Report

Title	***Associated HPRD***	***Associated RD***	***Reviewer***
Mouse model of Chlamydia trachomatis infection	*12-37 (Chlamydia trachomatis)*	*14-120 (transformation of Chlamydia trachomatis)*	*M. Morgan*
The role of transcription factor Foxo3 on virus specific and non-specific CD4 and CD8 T cell response to a Friend retrovirus infection	*N/A (Friend virus)*	*N/A*	*B. Anderson*

6) ***Biosafety Training Performed – Megan Morgan, Becky Anderson, Nancy Hoe***

Type of Training	***Number of Sessions***	***Number of Employees Trained***
BSL-3 & BSL-4 Visitor Training	***1***	***1***
BSL-3 & BSL-4 Maintenance & Support Staff	***1***	***1***
BSL-4 Annual Refresher	***1***	***1***
Select Agent Initial	***2***	***4***
Biosafety Brief	***2***	***LV, RMVB Staff***

7) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
a) *Biological Incident Report:*
   i) *None*

8) ***Select Agent Issues***
a) *The BSL-4 CDC DSAT inspection is scheduled for March 8-17.*

9) ***Other Issues***
a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 2/18/16
Meeting Time: 1:03 PM **Adjourned:** 2:17 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Megan Morgan	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Karin Peterson	☒	☐
Becky Anderson (EO)	☒	☐	Hideki Ebihara	☒	☐	George Risi	☒	☐
Alan Applebury	☐	☒	Heinz Feldmann (EO)	☒	☐	Dana Scott	☐	☒
Chris Bosio	☒	☐	Nancy Hoe	☐	☒	Alexandra Scranton	☐	☒
Marshall Bloom (EO)	☒	☐	Clay Jarrett	☐	☒			
Teresa Borino	☒	☐	Josh Kellar (EO)	☐	☒			
Jeff Burrows	☐	☒	Scott Kobayashi	☒	☐			
Carol Calderwood	☒	☐	Jamie Lovaglio	☒	☐			
Marcie Caldwell (EO)	☐	☒	Alida Merritt	☒	☐			
Paul Carlson	☒	☐	Kevin Mora	☐	☒			

(P=present; A=absent)

Guests: (b)(6)

Minutes: Meeting minutes from 1/21/16 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** Action: Meeting minutes for 1/21/16 were unanimously approved with the following minor modifications: 1. Page 4, 7th bullet, change the sentence to, ". . . ,but this is not clear until you read . . ."

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans (New) ▪ Bloom (LV) ▪ **HPRD#16-181: Zika virus**

	▪ Becky Anderson presented the risk assessment. The proposed studies for the Bloom and Feldmann HPRDs are to elucidate mechanisms of Zika virus pathogenesis and determine medical countermeasures. About 1 in 5 people infected with Zika virus become ill. The most common symptoms of Zika are fever, rash, joint pain, or conjunctivitis. Other common symptoms include muscle pain and headache. The incubation period for Zika virus disease is not known, but is likely to be a few days to a week. The illness is usually mild with symptoms lasting for several days to a week. People usually don't get sick enough to go to the hospital, and they very rarely die of Zika. Zika virus usually remains in the blood of an infected person for about a week but it can be found longer in some people. The symptoms of Zika are similar to those of dengue and chikungunya, the diseases spread through the same mosquitoes that transmit Zika. Zika virus infection in women has been associated with microcephaly, a birth defect in which a developing baby's brain fails to grow to its usual size. Almost 4,000 Brazilian infants with microcephaly have been born since the start of the Zika epidemic, which is about 20 times the expected number. The Zika outbreak has also been associated with an increase in Guillain-Barre syndrome. Guillain-Barre syndrome (GBS) is a disorder in which the body's immune system attacks part of the peripheral nervous system. The first symptoms of this disorder include varying degrees of weakness or tingling sensations in the legs. Currently, there is no vaccine to prevent Zika infection and no specific medications for treatment of infections, they just provide treatment for the symptoms. The primary lab hazards for this work include, accidental sharps injuries, parenteral inoculation and animal bites or scratches. Zika virus is not known to be transmitted by aerosols, however generation of aerosols should be avoided. Work with Zika virus should be performed at BSL-2/ABSL-2 with the following precautions: ▪ Care should be taken to minimize worker exposure to aerosols, such as working in a certified Class II BSC at all times and using gasketed bucket covers when centrifuging infectious material. Gasketed bucket covers or sealed rotors must only be loaded/unloaded in a BSC. It is recommended if possible that work with Zika virus be performed in a small or dedicated lab away from the main lab areas. Women of child bearing years must be advised of the risks of working with this agent, please consult with OMS. ▪ Animal studies with rodents will be performed in the Human Pathogen Wing of (b)(6) (b)(6) Wing is restricted access. All manipulations must be performed in a BSC. A sign at the suite door will indicate when Zika procedures are in progress. PPE includes: Lab coat, gloves, surgical mask. Husbandry practices will include spraying used cages with disinfectant, autoclaving, and then dumping the used bedding. ▪ Animal studies with NHPs will be performed in the Non-human Primate Wing of (b)(6) Access is restricted to RMVB staff, laboratorians

	must be escorted by RMVB. While exams are in progress, a sign will be posted at the entrance to the NHP Wing indicating Zika procedures are in progress. PPE Includes: Gown/lab coat, double gloves, surgical mask, face shield/goggles. ▪ The Feldmann lab may use a BSL-4 suite decontaminated and lowered to BSL-2 for Zika virus animal studies. The same PPE and practices as described for (b)(6) will be required. Additionally, a BSL-4 suite operating at BSL-4 can be used for Zika virus animal studies. ▪ All personnel listed on the HPRD including animal caretakers, and staff working in shared lab or animal spaces must receive hazard awareness training. ▪ BSL-2/ABSL-2 is appropriate for work with Zika virus following the above stated precautions. ▪ No animal studies were submitted, proposed, or reviewed for the Bloom HPRD#16-181. ▪ Sue Priola noted that the requirement for hazard awareness training for all lab members listed on the HPRD needs to be added to the recommendations section on the HPRD. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **HPRD#16-181** with the following minor modifications: 1. Add to the recommendations section the requirement for hazard awareness training.
Item 2:	<u>Registration of Material (Potentially) Infectious for Humans (New)</u> ▪ Feldmann (LV) ▪ **HPRD#16-182: Zika virus** ▪ Becky Anderson presented the risk assessment as described in HPRD#16-181. ▪ Work with Zika virus should be performed at BSL-2/ABSL-2 with the following precautions: ▪ Care should be taken to minimize worker exposure to aerosols, such as working in a certified Class II BSC at all times and using gasketed bucket covers when centrifuging infectious material. Gasketed bucket covers or sealed rotors must only be loaded/unloaded in a BSC. It is recommended if possible that work with Zika virus be performed in a small or dedicated lab away from the main lab areas. Women of child bearing years must be advised of the risks of working with this agent, please consult with OMS. ▪ Animal studies with rodents will be performed in the Human Pathogen Wing of (b)(6) Wing is restricted access. All

	manipulations must be performed in a BSC. A sign at the suite door will indicate when Zika procedures are in progress. PPE includes: Lab coat, gloves, surgical mask. Husbandry practices will include spraying used cages with disinfectant, autoclaving, and then dumping the used bedding. ▪ Animal studies with NHPs will be performed in the Non-human Primate Wing of (b)(6). Access is restricted to RMVB staff, laboratorians must be escorted by RMVB. While exams are in progress, a sign will be posted at the entrance to the NHP Wing indicating Zika procedures are in progress. PPE Includes: Gown/lab coat, double gloves, surgical mask, face shield/goggles. ▪ The Feldmann lab may use a BSL-4 suite decontaminated and lowered to BSL-2 for Zika virus animal studies. The same PPE and practices as described for (b)(6) will be required. Additionally, a BSL-4 suite operating at BSL-4 can be used for Zika virus animal studies. ▪ All personnel listed on the HPRD including animal caretakers, and staff working in shared lab or animal spaces must receive hazard awareness training. ▪ BSL-2/ABSL-2 is appropriate for work with Zika virus following the above stated precautions. ▪ Animal studies with rodents and non-human primates were proposed. ▪ Becky Anderson pointed out that an additional route of inoculation for rodents needs to be added to the HPRD, placental. ▪ Sue Priola noted that the precautions for animal work and the requirement for hazard awareness training needs to be added to the recommendations section. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **HPRD#16-182** with the following minor modifications: 1. Add to the recommendations section the requirement for hazard awareness training. 2. Add to the recommendations section the precautions for animal studies with Zika virus in rodents and non-human primates. 3. Add to the animal section, the route of inoculation for rodents, placental.
Item 3:	<u>Registration of Material (Potentially) Infectious for Humans (Amendment)</u> ▪ Peterson (LPVC) ▪ **HPRD#12-103 Amend: LaCrosse virus** ▪ Becky Anderson presented the risk assessment. The amendment is to add the

	California serogroup Orthobunyaviruses to the current HPRD. This includes: Jamestown Canyon virus, Tahyna virus, Snowshoe hare virus, Trivittatus virus, and Inkoo virus. The additional viruses cause human illness presenting with fever, headache, and flu-like illness. Severe cases with some of the listed viruses can result in meningitis or encephalitis. None of the viruses have been documented to result in fatalities. The viruses have been isolated from the United States (Jamestown Canyon Virus), Europe, Asia Africa (Tahyna), North America (Snowshoe hare virus, Trivattatus) and Northern Europe (Inkoo). The natural route of transmission is through the bite of an infected mosquito. The primary lab hazards include accidental needle sticks, parenteral inoculation, and generation of aerosols. ▪ Sue Priola questioned if these viruses were similar to LaCrosse virus in that children under 16 were more susceptible to infection. Karin Peterson and Hideki Ebihara commented that there is no evidence to indicate the same risk for children under 16. Karin Peterson also stated that her lab is already posted to restrict entry to anyone under 16. ▪ BSL-2/ABSL-2 is appropriate for work with the California serogroup Orthobunyaviruses. ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **HPRD#12-103 Amend** as written.
	<u>Registration of Material (Potentially) Infectious for Humans (Amendment)</u> ▪ Best (LV) ▪ **HPRD#12-140 Amend: Dengue virus** ▪ Becky Anderson presented the risk assessment. The amendment is to add animal work with mice. The Best lab in coordination with Karin Peterson's lab will test the effect of a previous Dengue infection and its influence on subsequent Zika fetal infection. The primary lab hazards include rodent bites or scratches and accidental sharps injuries. To mitigate these hazards, all animal studies will be conducted in the Human Pathogen wing of (b)(6) For studies that include Zika virus, these studies will be performed in (b)(6) . All manipulations must be performed in a BSC. PPE for this work includes: a lab coat, gloves, and surgical mask. ▪ ABSL-2 is appropriate for animal work with Dengue virus. All studies will be conducted in the Human Pathogen wing of (b)(6) ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.

	Action: The committee unanimously approved **HPRD#12-140 Amend** as written.
	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Hinnebusch (LZP) ▪ **RD#15-321 Amend**: Site-specific mutagenesis of CDC-exempt *Yersinia pseudotuberculosis* ▪ Reviewers: Bob Heinzen, Hideki Ebihara ▪ **Summary:** The amendment is to add animal work with mice. ▪ Bob Heinzen summarized the RD. The amendment is to add animal work with mice to the RD. The mice are used to provide frequent blood meals to maintain their flea colony in which the fleas are infected with *Y. pseudotuberculosis*. The Hinnebusch labs uses an artificial feeding system to maintain their fleas. Bob Heinzen also reviewed the original information in the RD and confirmed that the antibiotics proposed are appropriate and all relevant vector maps are attached. ▪ Hideki Ebihara had no comments or concerns. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Chris Bosio abstained) **RD#15-321 Amend** as written. Research using prokaryotic hosts is approved at BSL-2 under section III-D-1-a and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a of the NIH Guidelines.
Item 4:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Ebihara (LV) ▪ **RD#14-431 Amend**: Molecular characterization of viral proteins of pathogenic RNA viruses ▪ Reviewers: Karin Peterson, Scott Kobayashi ▪ **Summary:** The amendment is to add Zika virus to the RD on the list of Flaviviruses

	▪ Karin Peterson summarized the RD. The amendment is to add Zika virus to Hideki Ebihara's protein expression RD. They will clone and express Zika virus proteins in eukaryotic cells similar to the other viruses listed on the RD. They will not be working with live virus in this RD. Karin Peterson had no concerns with the proposed work or dual use concerns. ▪ Scott Kobayashi had no comments or concerns. ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Hideki Ebihara abstained) **RD#14-431 Amend** as written. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-2-a and III-E-1 of the NIH Guidelines.
Item 5:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Feldmann (LV) ▪ **RD#16-436**: Arenavirus reverse genetics ▪ Reviewers: Sue Priola, Chris Bosio ▪ **Summary:** The RD describes the Arenavirus reverse genetics system ▪ Sue Priola summarized the RD. This is the renewal of their reverse genetics RD and includes work from RD 12-435 on minigenomes and trVLPs. After this renewal is approved, RD 12-435 will be inactivated. This RD describes making mutants to study live virus *in vivo* or study reverse engineered viruses in vitro in tissue culture cells. Sue Priola informed the committee that all the dual use questions are marked no, but they did include descriptions for questions 3 and 5. They described that the virulence of the chimeric viruses or the Lassa point mutation is not expected to be any more virulent than the parent virus. She stated that all the NIH Guidelines listed are appropriate and all appropriate vector maps are included. ▪ Chris Bosio had no additional comments or concerns. ▪ Animal studies with non-human primates and guinea pigs were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#16-436** as written. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the

	NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 or BSL-4 under III-D-1-a,b,c, III-D-3-a,b,c and III-E-1 of the NIH Guidelines.
	Standard Operating Procedure: BSL-3-Rick-4 *Rickettsia rickettsii* Membrane Fractionation (New SOP for (b)(6) BSL-3 Lab) ▪ Becky Anderson informed the committee that this was a new SOP for Ted Hackstadt's lab in the (b)(6) BSL-3 lab in (b)(6) This procedure specific SOP will be added to the (b)(6) SOP. ▪ Becky Anderson informed the group that "1.b.i" should be updated to state, "disinfect exterior of rotor/buckets with 70% EtOH *and wipe dry* before removing . . ." ▪ Bob Heinzen stated that in "e" the method for deconning the nitrogen line needs to be described. He also noted that "g" should be clarified, as written it sounds like the cells are being drained, but he believes the nitrogen is vented off first, then the cells are removed. ▪ Alex Scranton submitted questions by email. Alex questioned why there was a single reference to (b)(6) at the end of the SOP, is this the only place the SOP will be used? Becky Anderson clarified that this procedure specific SOP will be added to the (b)(6) SOP in the BSL-3 lab and these procedures will only be performed in (b)(6). ▪ The committee had no additional comments or concerns. Action: The committee unanimously approved **BSL-3-Rick-4 *Rickettsia rickettsii* Membrane Fractionation (New SOP for (b)(6) BSL-3 Lab)** with the following minor modifications: 1. Describe in "e" the method for deconning the nitrogen line. 2. Clarify in "g" if the nitrogen is vented off first, followed by removal of cells that have been lysed. 3. Section "1.b.i" should be updated to state, "disinfect exterior of rotor/buckets with 70% EtOH *and wipe dry* before removing . . ."
	Standard Operating Procedure: SOP#4-28-31 Removal of Specimens for Protein Analysis (Update) ▪ Sue Priola informed the committee that information from SOP#4-28-24 has been moved to the three SOPs under review today and SOP#4-28-24 will be inactivated if the proposed updates are approved. The updates are minor to each of the three SOPs and the changes are tracked in red. ▪ Alex Scranton submitted questions by email. She questioned why section "g" stated that samples could be worked on outside the BSC while "b" states that

	all infectious material must be manipulated in a BSC. Should it be made more clear when samples can be removed from the BSC. Sue Priola stated that the first step in the SOP inactivates the virus and this inactivation step has been reviewed by the IBC, no additional detail needs to be added. ▪ The committee had no additional comments or concerns. Action: The committee unanimously approved **SOP#4-28-31 Removal of Specimens for Protein Analysis (Update)** as written.
	Standard Operating Procedure: SOP#4-28-32 Removal of Specimens for Nucleic Acid Extraction (Update) ▪ Sue Priola informed the committee that information from SOP#4-28-24 has been moved to the three SOPs under review today and SOP#4-28-24 will be inactivated if the proposed updates are approved. The updates are minor to each of the three SOPs and the changes are tracked in red. ▪ Sue Priola questioned the use of RNAlater. She stated that it was not reviewed by the IBC Working Group for inactivation for the BSL-4. Hideki Ebihara stated that RNAlater is for stabilizing the RNA, not for inactivation or isolation of RNA. ▪ The committee had no additional comments or concerns. Action: The committee unanimously approved **SOP#4-28-32 Removal of Specimens for Nucleic Acid Extraction (Update)** as written.
	Standard Operating Procedure: SOP#4-28-33 Removal of Specimens for Fluorescence, Immunofluorescence, Histopathology, Immunohistopathology, and Flow Cytometry (Update) ▪ Sue Priola informed the committee that information from SOP#4-28-24 has been moved to the three SOPs under review today and SOP#4-28-24 will be inactivated if the proposed updates are approved. The updates are minor to each of the three SOPs and the changes are tracked in red. ▪ Alex Scranton submitted questions by email. She questioned if it was clear in Section "6.f" that all the following procedures could be performed outside the BSC, but no procedure prior to that. The committee agreed that the second sentence in "6.f" should be changed to, "All the *subsequent* procedures can be performed on the open bench." ▪ The committee had no additional comments or concerns. Action: The committee unanimously approved **SOP#4-28-33 Removal of Specimens for Fluorescence, Immunofluorescence, Histopathology, Immunohistopathology, and Flow Cytometry (Update)** with the following minor modification: 1. The second sentence in "6.f" should be changed to, "All the *subsequent*

	procedures can be performed on the open bench."
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Becky Anderson presented the BSO report. ▪ The CDC DSAT BSL-4 Inspection is scheduled for March 8-17, 2016. ▪ The committee is reminded to make comments on the proposed rulemaking for the Select Agent Regulations.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ Not present.
Report	**IRF Biosafety Manager Report/Megan Morgan** ▪ Not present.
Report	**Associate Director Report/Marshall Bloom** ▪ JR Iman will replace Jeff Burrows on the IBC committee. ▪ The IBC committee will consider (b)(6) as an alternate for Carol Calderwood. She is the (b)(6)
Around the room	▪ Sue Priola informed the committee that the IBC working group summaries for the review of Earth Sense Neutral Disinfectant Detergent as a replacement for Roccal-D are not ready yet. Sue Priola is waiting for Dana Scott to return from Australia so he has an opportunity to comment as well.

Other issues	▪ None.

Next Meeting:

- Date: 4/21/16
- Place: Bldg A Seminar Room
- Time: 1:00 PM

RML Biosafety Committee Meeting
February 18, 2016
Biosafety Officer/Responsible Official Report

1) ***Requests approved by BSO since last meeting:***
   a) ***None***
3) ***New requests approved by committee via electronic review:***
   a) ***None***
4) ***New requests***
   a) *Human Pathogen Registration Documents*
      i) ***New***
         (a) *Bloom (LV)*
            (a) ***HPRD-16-181:*** *Zika virus*
         (b) *Feldmann (LV)*
            (a) *HPRD-16-182: Zika virus*
      ii) ***Amend***
         (a) *Peterson (LPVD)*
            (a) ***HPRD 12-103****: La Cross virus pathogenesis*
               (i) Add other members of California serogroup of Orthobunyaviruses (Tahyna virus, Snowshoe hare virus, Trivittatus virus, Inkoo virus)
   b) *Registration Documents for Recombinant DNA Experiments*
      i) ***Amend***
         (a) *Hinnebusch (LZP)*
            (a) ***RD 15-321:*** *Site-specific mutagenesis of CDC-exempt Yersinia pseudotuberculosis*
               (i) *Add animal work with mice*
         (b) *Ebihara (LV)*
            (a) ***RD-14-431:*** *Molecular characterization of viral proteins of pathogenic RNA viruses*
               (i) *Add Zika virus*
      ii) ***Renew***
         (a) *Feldmann (LV)*
            (a) ***RD 16-436****: Arenavirus genetics (mini genome systems and trVLPs)*
               (i) Consolidate work from RD 12-435, RD 12-435 will be inactivated
   c) *Standard Operating Procedures*
      i) ***New***
         (a) *BSL-3-Rr-4 Rickettsia rickettsia Membrane Fractionation SOP*
         (b) *SOP#4-28-56 Bat Husbandry and Manipulation*
      ii) *Amend*
         (a) *SOP#4-28-31 Removal of Specimens for Protein Analysis*

(b) *SOP#4-28-32 Removal of Specimens for Nucleic Acid Extraction*

(c) *SOP#4-28-33 Removal of Specimens for Fluorescence, Immunofluorescence, Histopathology, Immunohistopathology, and Flow Cytometry*

iii) ***Inactivate***

(a) *SOP#4-28-24 Removal of Aimal Tissues or Cells from BSL-4*

(a) *Material in this SOP incorporated into SOPs 31, 32, and 33 above*

5) ***Animal Study Protocols Review***

Title	***Associated HPRD***	***Associated RD***	***Reviewer***
Evaluation of the effect of Ixodid tick salivary gland extract on Powassan virus infection in Peromyscus leucopus mice	*13-75 (Powassan virus)*	*N/A*	*M. Morgan*
Mouse model of Chlamydia trachomatis infection	*12-37 (Chlamydia trachomatis)*	*14-120 (transformation of Chlamydia trachomatis)*	*M. Morgan*
The role of transcription factor Foxo3 on virus specific and non-specific CD4 and CD8 T cell response to a Friend retrovirus infection	*N/A (Friend virus)*	*N/A*	*B. Anderson*

6) ***Biosafety Training Performed – Megan Morgan, Becky Anderson***

Type of Training	***Number of Sessions***	***Number of Employees Trained***
BSL-3 Laboratory Biosafety	***1***	***3***
BSL-4 Laboratory Biosafety	***1***	***1***
Select Agent Initial	***2***	***4***
Biosafety Brief	***1***	***LB***

7) ***Safety Audits and Inspections***

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

a) *Biological Incident Report:*

i) *None*

8) ***Select Agent Issues***

a) *Notice of proposed rulemaking to update Select Agent Regulation (Fed Register/Vol 81, No. 11/Tuesday, January 19, 2016)*

9) ***Other Issues***

a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 4/21/16
Meeting Time: 1:02 PM **Adjourned:** 2:36 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Megan Morgan	☒	☐
Bob Heinzen, Vice Chair	☐	☒	Hideki Ebihara	☐	☒	Karin Peterson	☒	☐
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	George Risi	☒	☐
Alan Applebury	☐	☒	Nancy Hoe	☒	☐	Dana Scott	☒	☐
Chris Bosio	☒	☐	JR Iman	☒	☐	Alexandra Scranton	☐	☒
Marshall Bloom (EO)	☒	☐	Clay Jarrett	☒	☐			
Teresa Borino	☒	☐	Josh Kellar (EO)	☐	☒			
Carol Calderwood	☒	☐	Scott Kobayashi	☒	☐			
Marcie Caldwell (EO)	☒	☐	Jamie Lovaglio	☒	☐			
Paul Carlson	☒	☐	Alida Merritt	☒	☐			
Bruce Chesebro (EO)	☐	☒	Kevin Mora	☐	☒			

(P=present; A=absent)

Guests: (b)(6)

Minutes: Meeting minutes from 2/18/16 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** Action: Meeting minutes for 2/18/16 were unanimously approved with the following minor modifications: 1. Page 2, 1st bullet, fix the spelling of Guillain-Barre syndrome. 2. Sue Priola submitted a couple of minor typos.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New) ▪ Bosio (LB)

	▪ **PRD#16-183: West Nile virus (WNV)** ▪ Becky Anderson presented the risk assessment. The purpose of this study is to determine the ability of novel therapeutics to inhibit WNV replication and WNV mediated inflammation *in vitro* and *in vivo*. The Bosio lab will expose mammalian cells to purified and/or synthetic versions of sugars and lipids found in *Francisella tularensis* before and/or after infection with WNV. Most individuals infected with WNV remain asymptomatic. West Nile fever is typically a mild illness lasting 3 to 6 days. The main symptoms are sudden onset of fever with chills, rash, malaise, headache, backache, arthralgia, myalgia and eye pain. Meningitis, encephalitis, and/or acute flaccid paralysis develop in less than 1% of WNV-infected individuals. Patients with neurological disease typically have a febrile phase of 1 to 7 days, which may be biphasic, before they develop neurological symptoms. A New York serological survey revealed that, of those infected, approximately 20% developed West Nile fever. The overall case fatality rate ranges from 4% to 14% in individuals exhibiting neuroinvasive disease, with a higher incidence of severe presentation and higher fatality rates in older populations. Currently, there is no specific treatment or vaccination for WNV, just supportive care is offered. The primary lab hazards include: accidental parenteral inoculation, contact with broken skin or mucous membranes, accidental needle stick. ▪ The Bosio lab submitted new SOPs for (b)(6) and an animal WNV SOP that will be reviewed later during this IBC meeting. ▪ Nancy Hoe pointed out that the recommendations section should state that animal work with WNV will be performed in (b)(6) ABSL-3 (b)(6) the animal study protocol states a different suite that is not correct. ▪ BSL-3/ABSL-3 is appropriate for work with West Nile virus. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **HPRD#16-183** with the following minor modifications: 1. Add to the recommendations section that animal work with WNV will be performed in (b)(6) ABSL-3 (b)(6) .
Item 2:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment)</u> ▪ Feldmann (LV) ▪ **HPRD#12-143 Amend: Coronaviruses** ▪ Becky Anderson presented the risk assessment. The amendment is to add work

	with bat coronaviruses: WIV1, SHC014, HKU4. None of the proposed coronaviruses are currently known to cause disease in humans. They are of interest to the Feldmann and (b)(6) labs as they have identified these bat coronaviruses from the same bats, Chinese horseshoe bats, (found in Asia & Australis) that carry SARS-CoV. It is possible even MERS-CoV originated from this bat species. The current strains have been sequenced, but have not been isolated. As these viruses are difficult to grow, the Ralph Baric lab at UNC has generated recombinant viruses that will be the source of the viruses at RML. There has been some testing of the strains to identify their pathogenic potential for humans. The SARS-like viruses are capable of infecting and replicating in human airway epithelial cells similar to SARS for (WIV1 & SHC014). The MERS-like (HKU4) virus is capable of growing and replicating in human airway cells as well. Experiments with WIV1 and SHC014 in mice compared to SARS showed no weight loss and reduced viral titers. These bat coronaviruses are similar to MERS and SARS and use similar human receptors. There is concern for the potential of bat coronavirus cross-species transmission to humans. Currently there is no treatment for bat or human coronaviruses, supportive care is offered. The primary lab hazards include: accidental sharps injuries and generation of aerosols. ▪ BSL-3/ABSL-3 is appropriate for work with the listed bat coronaviruses ▪ Sue Priola stated the biosafety level should be included in the recommendations section to avoid any confusion with the biosafety level for other coronaviruses listed on this registration. ▪ No new animal studies were proposed in the amendment. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **HPRD#12-143 Amend** with the following minor modifications: 1. Add to the recommendations section, "Laboratory work with bat Coronaviruses is approved for work at BSL-3. Animal work with bat Coronaviruses in bats is approved for work at ABSL-3, but will be performed at ABSL-4."
Item 3:	<u>Registration Documents for Recombinant DNA Experiments (New)</u> ▪ Best (LV) ▪ **RD#16-449**: Reverse Genetics of Zika virus ▪ Reviewers: Hideki Ebihara, Sue Priola ▪ **Summary:** The Best lab will develop a reverse genetics system for Zika virus. ▪ Hideki Ebihara was not present. Sue Priola summarized the RD. The RD describes developing a reverse genetics system for Zika virus to make a clone of

	the virus that they can be manipulated to study viral pathogenesis, with a focus on the innate immune responses. The goal is to develop vaccines or therapeutics. They will clone the full length genome into a plasmid and then mutate genes of interest. Zika virus is a positive sense single stranded RNA virus so the cDNA is considered infectious. All the vectors listed are attached to the registration. There is no concern with antibiotics for selection because this is a virus. The list of foreign genes is fine, nothing will increase the virulence of the virus. There are no dual use concerns and the NIH Guidelines are appropriate. ▪ The committee had no additional comments or concerns. ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **RD#16-449** as written. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-3-a of the NIH Guidelines.
Item 4:	<u>Registration Documents for Recombinant DNA Experiments (Amendment)</u> ▪ Hasenkrug (LPVD) ▪ **RD#14-219 Amend**: Adenovirus 5 vector ▪ Reviewers: Chris Bosio, Clay Jarrett ▪ **Summary:** The amendment is to add 3 vectors expressing human cytokine genes. ▪ Chris Bosio summarized the RD. The amendment is to add 3 human cytokines to the Ad5 expression system. There are no dual use concerns and there is an ASP already approved with the current registration. ▪ Clay Jarrett questioned why there are no NIH Guidelines listed in the original RD. The committee agreed it was because a company made the Ad5 vector for the Hasenkrug lab. Nancy Hoe stated that III-D-4 could be added because it covers animal work with rDNA. ▪ Sue Priola pointed out that if the Hasenkrug lab is now making the Ad5 vector, then the NIH Guidelines would need to be added to this amendment. ▪ Clay Jarrett had no additional comments or concerns. ▪ No new animal studies were proposed in the amendment. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns

	with the proposal. Action: The committee unanimously approved **RD#14-219 Amend** with the following minor modifications: 1. Determine if they are ordering the vector from the same company as before or if his lab is generating the vectors. If the lab is generating the vectors, additional sections of the NIH Guidelines need to be included. 2. Add to the recommendations section III-D-4 for animal work. Research using mice is approved under section III-D-4.
Item 5:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Hasenkrug (LPVD) ▪ **RD#15-223 Amend**: Adeno-associated virus ▪ Reviewers: Scott Kobayashi, Karin Peterson ▪ **Summary:** The amendment is to add an AAV vector expressing human B cell activating factor (BAFF). ▪ Scott Kobayashi summarized the RD. They use the AAV vector system in mice. They will insert the AAV into humanized mice. The AAV vector is replication deficient and does not insert itself, but is capable of infecting dividing or non-dividing cells. The amendment is to add an AAV vector expressing human BAFF because they do not want to inject BAFF daily into mice, which is what they currently do. The AAV vector will result in long-term expression. If an employee accidentally injected themselves, there could be an effect because of the increased BAFF expression. BAFF has been associated with excess antibody production, is also associated with autoimmune diseases and potentially makes some cancers worse. The Hasenkrug lab stated that they would follow strict adherence to sharps precautions, this should be added to the recommendations section. There were no dual use concerns and the appropriate vector maps were included. ▪ Karin Peterson had the same comment as on the previous RD, that if they are not getting the AAV vector made, NIH Guidelines should be added to the RD. ▪ Sue Priola stated that III-D-4 should be added to this RD too. ▪ No new animal studies were proposed in the amendment. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#15-223 Amend** with the following minor modifications: 1. Add to the recommendations section that they must follow strict adherence to

	sharps safety. 2. Determine if they are ordering the vector from the same company as before or if his lab is generating the vectors. If the lab is generating the vectors, additional sections of the NIH Guidelines need to be included. 3. Add to the recommendations section III-D-4 for animal work. Research using mice is approved under section III-D-4.
Item 6:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Feldmann (LV) ▪ **RD#16-440**: Development of reverse genetics system for Coronaviruses ▪ Reviewers: Karin Peterson, Sue Priola ▪ **Summary:** The RD describes developing a reverse genetics system for Coronaviruses. ▪ Karin Peterson summarized the RD. The RD describes a reverse genetics system for coronaviruses. They will generate deletions and mutations which typically attenuate the viruses. They will do some animal model studies described in the RD. The main change to this renewal is that they will be adding bats as an animal model. The bats are not expected to develop clinical signs, but the bats can shed the virus. They have also added a plasmid map in the renewal which is for a commonly used plasmid. Karin Peterson had no dual use concerns with the RD. ▪ Sue Priola questioned the biosafety level listed in the safety paragraph for SARS-CoV in Section A. The paragraph states BSL-3 or BSL-4 for SARS-CoV, she questioned if that was correct. Nancy Hoe stated that it was not correct, Feldmann only has Select Agent registered space in BSL-4. The committee agreed to delete BSL-3 in that sentence. ▪ Animal studies with mice, non-human primates, and bats were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Hideki Ebihara abstained) **RD#16-440** with minor modifications: 1. Delete "BSL-3" from the Safety paragraph in Section A, 4th line in the paragraph. Research using prokaryotic hosts is approved at BSL-2 to BSL-4 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 to BSL-4 under III-D-3-a, III-D-3-b, and III-D-1-a of the NIH Guidelines.

Item 7:	**Working Group Summaries** ▪ Sue Priola informed the committee that the IBC working groups met January 13, 2016 and April 4, 2016 to review the replacement of Roccal-D disinfectant with Earth Sense Neutral Disinfectant for Bosio, Heinzen, and Hinnebusch labs. They also met to review additional inactivation procedures for the Bosio and Ebihara labs. ▪ The Working Group summaries outline the procedures and disinfectants reviewed. ▪ The Bosio and Ebihara inactivation procedures are reflected in updated or new SOPs that will be reviewed during this meeting. ▪ The IBC approved the change in disinfectant and agreed that biosafety can update the disinfectant and appropriate concentration for all SOPs. The SOPs do not need to come back to the IBC for review. Action: The committee unanimously approved the conclusions of the working group summaries.
Item 8:	**Standard Operating Procedure: Standard Operating Procedures for Animal Biosafety Level 3 (ABSL-3) *Yersinia pestis* (Updated)** ▪ Becky Anderson informed the committee that the Hinnebusch lab included new procedures for the use of the IVIS Lumina System for real time monitoring of bacterial infection. ▪ Nancy Hoe added that the details of their SOP was taken from another lab that previously performed the same procedures with Burkholderia spp. on the IVIS system Action: The committee unanimously approved **Standard Operating Procedures for Animal Biosafety Level 3 (ABSL-3) *Yersinia pestis* (Updated)** as written.
Item 9:	**Standard Operating Procedure: Standard Operating Procedures for Animal Biosafety Level 3 (ABSL-3): West Nile virus-Bosio (New SOP)** ▪ Becky Anderson informed the committee that the Bosio lab will now be working with West Nile virus and they have added a new SOP for animal work in the ABSL-3 lab. This SOP will be separate from the Best lab's animal SOP. ▪ Remove references to (b)(6) as the facility director and replace with (b)(6) ▪ Fix the numbering for section six. ▪ Sue Priola pointed out that the disinfectant in the spill kit is different than the normal disinfectant used for procedures. Nancy Hoe stated that either disinfectant is effective for WNV. The committee agreed it may be best to

	include both disinfectants in the SOP (5% Microchem or 10% bleach). ▪ Sue Priola asked if the appropriate contact time should be specified in Section 6.3.1. The committee agreed that the section should be updated to clarify the contact time. ▪ The committee had no additional comments or concerns. Action: The committee unanimously approved **Standard Operating Procedures for Animal Biosafety Level 3 (ABSL-3): West Nile virus-Bosio (New SOP)** with the following minor modifications: 1. Remove references to (b)(6) as the facility direction and replace with (b)(6) 2. Fix the numbering for section six. 3. Include either 5% Microchem or 10% bleach in section 6.2 for spill kit contents. 4. Specify contact time in section 6.3.1.
Item 10:	**Standard Operating Procedure: ABSL-3 Operations and Safety Procedures (Update)** ▪ Nancy Hoe informed the committee that the OSP was updated because of an incident in the ABSL-3 (will be reviewed at the end of the meeting). This brought to our attention that eye protection should be added to the PPE requirements as well as more detailed cage changing procedures and a better description of entry/exit procedures. Finally, we decided to make sure the autoclave load parameters were clearer to the users. ▪ Clay Jarrett asked about the effectiveness of the autoclave testing. Becky Anderson described the process that was used for the testing. Becky Anderson confirmed that frozen mice and guinea pigs were used for the testing to simulate procedures in place for autoclaving carcasses. ▪ Sue Priola questioned why the wording on page 17 was deleted for women who are actively trying to conceive. Nancy Hoe stated that the wording may not be appropriate because women can become pregnant without actively trying to conceive. The committee agreed that Nancy Hoe should find the appropriate statement to use. ▪ The committee had no additional comments or concerns. Action: The committee unanimously approved **ABSL-3 Operations and Safety Procedures (Update)** with the following minor modification: 1. Determine the appropriate statement for women of child bearing age.

Item 11:	**Standard Operating Procedure: Standard Operating Procedures West Nile Virus (b)(6) (New SOP)** ▪ Becky Anderson informed the committee that this is a new SOP for (b)(6) (b)(6) for use of West Nile virus in (b)(6) ▪ Becky Anderson informed the committee that this SOP does include inactivation procedures, however these are procedures that were validated and reviewed by the IBC when the Feldmann lab presented their procedures. The Bosio lab will follow these specific procedures. ▪ The committee asked to have page numbers added to the document. ▪ The committee noticed that the bullet numbers in several places needed to be corrected. ▪ Sue Priola pointed out that section 4.4 is redundant with 4.3 and should be deleted. ▪ Sue Priola also noted that section 4.3 in SOP SP-WNV-1 did not include removal of outer gloves, this needs to be added. ▪ The committee had no additional comments or concerns. Action: The committee unanimously approved **Standard Operating Procedures West Nile Virus (b)(6) (New SOP)** with the following minor modifications: 1. The bullet numbers in several places need to be corrected. 2. Section 4.4 is redundant with 4.3 and should be deleted. 3. Section 4.3 in SOP SP-WNV-1 needs to have the removal of outer gloves added.
Item 12:	**Standard Operating Procedure: BSL3-C-8 Inactivation of Francisella spp. (New SOP for (b)(6) BSL-3 Lab)** ▪ Becky Anderson informed the committee that this SOP was updated to reflect the new and updated inactivation procedures that the working group reviewed April 4, 2016. Changes to the document were tracked. ▪ Nancy Hoe pointed out that on page 25 on the top of the page, the temperature for the fixation with glutaraldehyde and paraformaldehyde needs to be clarified. ▪ The committee had no additional comments or concerns. Action: The committee unanimously approved **BSL3-C-8 Inactivation of Francisella spp. (New SOP for (b)(6) BSL-3 Lab)** with the following minor modifications: 1. Clarify temperature for fixation with glutaraldehyde and paraformaldehyde at the top of page 25.

Item 13:	**Standard Operating Procedure: Standard Operating Procedures Inactivation and removal of Orthobunyavirus Samples by Hydrogen Peroxide (New SOP to be added to the Bunyavirus & Tickborne Orthomyxovirus SOP)** ▪ Becky Anderson informed the committee that this is a new SOP for the inactivation of Orthobunyaviruses with 1% hydrogen peroxide. ▪ The inactivation procedures were reviewed by the Working Group April 4, 2016. ▪ The committee had no additional comments or concerns. Action: The committee unanimously approved **Standard Operating Procedures Inactivation and removal of Orthobunyavirus Samples by Hydrogen Peroxide (New SOP to be added to the Bunyavirus & Tickborne Orthomyxovirus SOP)** approved as written.
Item 14:	**Standard Operating Procedure: SOP#BSL-4-28-28 Safety Procedures for Use of JLS Model 484 Irradiator (Update)** ▪ Becky Anderson informed the committee that Aaron Bestor has tested and implemented a new dosimetry system for the gamma irradiator and this SOP has been updated to reflect some of the minor changes. ▪ The committee had no additional comments or concerns. Action: The committee unanimously approved **SOP#BSL-4-28-28 Safety Procedures for Use of JLS Model 484 Irradiator (Update)** as written.
Item 15:	**Standard Operating Procedure: SOP#BSL-4-28-29 Using Dosimetry System for Gamma Irradiator (Update)** ▪ Becky Anderson informed the committee that the SOP has been updated to reflect the new dosimetry system. ▪ The committee had no additional comments or concerns. Action: The committee unanimously approved **SOP#BSL-4-28-29 Using Dosimetry System for Gamma Irradiator (Update)** as written.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Nancy Hoe presented the BSO report. ▪ Nancy Hoe reviewed the incident report for a splash to the eye that occurred on March 15 in the ABSL-3. ▪ Nancy Hoe informed the committee that RML had its BSL-4 CDC DSAT Inspection in March and that everything went well. We have not yet received the official inspection report. ▪ She also informed the committee that NIH OBA updated the NIH Guidelines to reflect changes in the requirements for non-human primate housing at BSL-4,

	requirements for certification of BSCs, and validation of effluent decon systems.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ The next drill with the St. Patrick Hospital will be June 20th. The drill is in the planning stages.
Report	**IRF Biosafety Manager Report/Megan Morgan** ▪ The annual shutdowns for the BSL-3 labs are complete. ▪ SEA will be at RML the first week of May to conduct fan failure testing. A schedule of the testing will be sent out to all of the users.
Report	**Associate Director Report/Marshall Bloom** ▪ Marshall Bloom pointed out that the OBA updates that Nancy Hoe mentioned were a herculean effort on everyone's part and they make a huge impact on our operations for the better. ▪ Marshall Bloom informed the committee that he is the new Chair of the High Containment Task Force and he will make sure that changes are not implemented without RML's input. The Logistics meeting (Operational Team) will be taken over by Megan Morgan.
Around the room	▪ Alida Merritt thanked Marshall Bloom for coming to the hospital to provide some education/information to hospital employees. ▪ The committee thanked George Risi for his contributions to the RML IBC, this was his last meeting before he moves on to BARDA in Washington D.C.

Other issues	▪ None.

Next Meeting:

- Date: 5/19/16
- Place: Bldg A Seminar Room
- Time: 1:00 PM

RML Biosafety Committee Meeting
April 21, 2016
Biosafety Officer/Responsible Official Report

1) ***Requests approved by BSO since last meeting:***
   a) ***None***
3) ***New requests approved by committee via electronic review:***
   a) *Feldmann HPRD-12-143: Characterization of a novel beta-coronavirus**:** Add bats as an animal model*
      i) *Approved 3-21-16*
4) ***New requests***
   a) *Human Pathogen Registration Documents*
      i) ***New***
         (a) *Bosio (LB)*
            (a) ***PRD-16-183:*** *West Nile Virus*
      ii) ***Amend***
         (a) *Feldmann (LV)*
            (a) ***HPRD 12-143****: Coronaviruses*
               (i) Add bat coronaviruses (e.g.WIV1, SHC014, HKU4)
   b) *Registration Documents for Recombinant DNA Experiments*
      i) ***New***
         (a) *Best (LV)*
            (a) ***RD 16-449:*** *Reverse genetics of Zika virus*
      ii) ***Amend***
         (a) *Hasenkrug (LPVD)*
            (a) ***RD 14-219****: Testing of HIV-1 vaccines in mice that have been reconstituted with human immune systems*
               (i) Add Ad5 vectors expressing human IL-6, IL-5, and IL-23
            (b) ***RD 15-223****: Adeno-associated virus*
               (i) Add defective AAV vector expressing human B cell activating factor (BAFF)
      iii) ***Renew***
         (a) *Feldmann (LV)*
            (a) ***RD 16-440****: Reverse genetics of coronaviruses (renew and add bat coronaviruses)*
   c) *Working Group Summaries*
      i) *Inactivation of Francisella tularensis with Earth Sense Neutral Disinfectant Detergent, fixation for electron microscopy, and isolation and analysis of nucleic acids and proteins*
      ii) *Inactivation of Orthobunyaviruses by hydrogen peroxide*
      iii) *Inactivation of Coxiella with Earth Sense Neutral Disinfectant Detergent*
      iv) *Inactivation of Yersinia pestis with Earth Sense Neutral Disinfectant Detergent*

d) *Standard Operating Procedures*

i) ***Updates***

(a) *SOP for ABSL-3: Yersinia pestis*

(a) *Add procedures for IVIAS*

(b) *ABSL-3 Operations and Safety Procedures*

(a) *Section on PPE: add specific facility entry and exit procedures*

(b) *SOP-3-25-1: added procedure for cage changing, clarified number of animals per autoclave bag, added procedure for when carcass freezer is unavailable*

(c) *BSL-3 SOP Inactivation of Francisella spp.*

(a) *Add new inactivation procedures*

(d) *SOP-BSL-4-28-28: Safety Procedures for Use of Irradiator*

(a) *Minor modifications related to new Gamma Dosimetry System*

(e) *SOP-BSL-4-28-29: Using Dosimetry System for Gamma Irradiator*

(a) *Replaced old procedures with new ones for new dosimetry system*

ii) ***New***

(a) *SOP for ABSL-3: West Nile virus – Bosio*

(b) *SOPs West Nile Virus (genus Flavivirus) BSL-3 Facility*

(c) *SP-BUNV-3: Inactivation and Removal of Orthobunyavirus Samples by Hydrogen Perodxide*

5) ***Animal Study Protocols Review***

Title	***Associated HPRD***	***Associated RD***	***Reviewer***
Pathogenicity and mortality of MA-ZEBOV in Balb/C rvb strain mice	*13-90 (Ebola virus)*	*14-407*	*B. Anderson*
Maintenance of experimental flea colonies using mice 2016-2019	*13-04 (Y. pestis) 13-07 (Y. pseudotb) 14-66 (Y. pestis-exempt)*	*15-320 15-321 15-303*	*M. Morgan*
Plethysmograph training program (NHP)	*NA*	*NA*	*M. Morgan*
Establishment of a mouse disease model for Zika virus infection	*16-182 (Zika virus)*	*NA*	*N. Hoe*
Establishment of a nonhuman primate disease model for Zika virus infection	*16-182 (Zika virus)*	*NA*	*M. Morgan*
Zika virus infection in mice	*16-182 (Zika virus)*	*NA*	*B. Anderson*
Antibody production in rabbits against Simbu serogroup Orthobunyaviruses inactivated with H2O2	*14-110 (Orthobunyaviruses)*	*NA*	*N. Hoe*
Treatment of La Crosse virus (LACV)-induced neurological disease in mice with FDA-approved drugs identified in neuronal apoptosis screen	*12-103 (LACV)*	*NA*	*N. Hoe*
Refining the rhesus macaque model for hantavirus cardiopulmonary syndrome using Sin Nombre virus	*12-81 (Hantavirus)*	*NA*	*N. Hoe*
Efficacy testing of intravenous GS-5734 in the rhesus macaque model of MERS-CoV infection	*12-143 (MERS)*	*NA*	*N. Hoe*

RML Biosafety Committee Meeting
April 21, 2016
Biosafety Officer/Responsible Official Report

Title	*Associated HPRD*	*Associated RD*	*Reviewer*
Immune responses to Zika virus infection in adult mice and the impact of pregnancy or Dengue infection on these responses	*16-182 (Zika virus) 12-140 (Dengue)*	*NA*	*N. Hoe*
Pathogenesis of K. pneumoniae ST258 in a murine bacteremia model	*16-180 (K. pneumoniae)*	*NA*	*B. Anderson*
Production and titration of rat-passaged prion stocks	*NA*	*NA*	*N. Hoe*
Transmission of MERS-CoV within immunocompromised hDPP4 transgenic mice	*12-143 (MERS)*	*NA*	*M. Morgan*
Prion infection in transgenic mice expressing human Apolipoprotein E	*NA*	*NA*	*B. Anderson*

6) ***Biosafety Training Performed – Megan Morgan, Becky Anderson***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
BSL2 Visitor Training	***1***	***12***
BSL3 Visitor Training	***3***	***7***
BSL-4 90-Day Refresher	***2***	***2***
Select Agent Initial	***1***	***1***
Biosafety Brief	***2***	***2 WIPS***
Zika Virus Hazard Awareness Training	***4***	***90***
RMVB Refresher Training	***3***	***21***

7) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
a) *Biological Incident Report:*
   i) *F. tularensis splash to eye*

8) ***Select Agent Issues***
a) *Results of DSAT BSL-4 inspection of March 8-17, 2016*

9) ***Other Issues***
a) *NIH Guidelines updated for housing of NHPs at BSL-4, recertification of BSCs, validation requirements for effluent decon systems, 4-15-16*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 05/19/16
Meeting Time: 1:02 PM **Adjourned:** 1:56 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Megan Morgan	☒	☐
Bob Heinzen, Vice Chair	☒	☐	Hideki Ebihara	☐	☒	Karin Peterson	☒	☐
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Dana Scott	☐	☒
Alan Applebury	☐	☒	Nancy Hoe	☒	☐	Alexandra Scranton	☐	☒
Chris Bosio	☐	☒	JR Iman	☐	☒			
Marshall Bloom (EO)	☒	☐	Clay Jarrett	☐	☒			
Teresa Borino	☒	☐	Josh Kellar (EO)	☐	☒			
Carol Calderwood	☐	☒	Scott Kobayashi	☒	☐			
Marcie Caldwell (EO)	☒	☐	Jamie Lovaglio	☒	☐			
Paul Carlson	☒	☐	Alida Merritt	☒	☐	Alternate for C. Calderwood: (b)(6)	☒	☐
Bruce Chesebro (EO)	☐	☒	Kevin Mora	☐	☒			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 4/21/16 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** Action: Meeting minutes for 4/21/16 were unanimously approved with the following minor modifications: 1. Minor typos from Sue Priola and Bob Heinzen.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment) ▪ Ebihara (LV)

	▪ **HPRD#14-110 Amend: Orthobunyaviruses** ▪ Becky Anderson presented the risk assessment. The amendment is to add rabbits to the HPRD, the ASP is attached to the registration. The ASP describes generating antibodies to specific Orthobunyaviruses that have been inactivated with peroxide. The primary lab hazards include scratching of personnel with hind legs and scratches with claws. To mitigate these hazards, the studies will be conducted in (b)(6) and all personnel must wear basic PPE: lab coat, gloves, and a surgical mask. Personnel must be trained on how to perform procedures on rabbits. ▪ BSL-2 is appropriate for the proposed experiments, all viruses will be inactivated with peroxide prior to inoculation of rabbits. ▪ Animal studies with rabbits were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **HPRD#14-110 Amend** as written.
Item 2:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment) ▪ Feldmann (LV) ▪ **HPRD#16-182 Amend: Zika virus** ▪ Becky Anderson presented the risk assessment. The amendment is to add three additional Flaviviruses: Spondweni virus, Kedougou virus, and Bagaza virus. The proposed studies are to elucidate the mechanisms of Zika virus pathogenesis and determine medical countermeasures. These additional viruses will be used for comparisons with Zika virus because these viruses are genetically related to Zika virus. Spondweni virus infection is characterized by fever, chills, headache, malaise, nausea, nose bleeds, and in one case rash. Kedougou-not much is known about human infections with Kedougou. There is one documented case in Africa, but no details available. It is classified as a member of the Dengue virus group. Bagaza virus (also called Israel Turkey meningoencephalomyelitis virus ITV)-serologic evidence suggests that the virus may infect humans, but its pathogenicity in humans is unclear. This virus is better known for causing high mortality in wild birds. There is no vaccine to prevent infection from the Flaviviruses listed and no specific medications for treatment of infections. The natural route of transmission for Spondweni, Kedougou, and Bagaza is through the bite of an infected mosquito. The primary lab hazards include generation of aerosols, accidental sharps injuries, parenteral inoculation or animal bites or scratches. ▪ Marshall Bloom asked if a USDA permit was required for Bagaza virus. Becky Anderson and Nancy Hoe were not sure, but will discuss with the Feldmann lab.

	▪ BSL-2/ABSL-2 is appropriate for work with the listed Flaviviruses: Spondweni virus, Kedougou virus, and Bagaza virus. These viruses will be handled with the same precautions set for Zika virus in the original HPRD. ▪ No new animal studies were proposed in the amendment. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **HPRD#16-182 Amend** with the following minor modifications: 1. Discuss with the Feldmann lab the requirement for a USDA permit for Bagaza virus.

Item 3:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New)
	▪ Peterson (LPVD)
	▪ **PRD#16-184: Zika virus**
	▪ Becky Anderson presented the risk assessment. She informed the committee that Karin Peterson and Kim Hasenkrug were originally covered under the Feldmann Zika virus HPRD in order to get approval quickly for these labs to start studying Zika virus. Now we have asked these labs to create their own PRDs to cover Zika virus separately, long term it makes documentation easier. The same precautions that were approved for the Feldmann lab will apply to both of the new PRDs. There are no new lab locations and there is only one additional staff member added to the Hasenkrug PRD.
	▪ BSL-2/ABSL-2 is appropriate for work with Zika virus with the following additional precautions:
	  ▪ Care should be taken to minimize worker exposure to aerosols, such as working in a certified Class II BSC at all times and using gasketed bucket covers when centrifuging infectious material. Gasketed bucket covers or sealed rotors must only be loaded/unloaded in a BSC. It is recommended if possible that work with Zika virus be performed in a small or dedicated lab away from the main lab areas. Women of child bearing years must be advised of the risks of working with this agent, please consult with OMS.
	  ▪ Animal studies with rodents will be performed in the Human Pathogen Wing of (b)(6) in (b)(6) or (b)(6). Both areas are restricted access. All manipulations must be performed in a BSC. A sign at the suite door will indicate when Zika procedures are in progress. PPE includes: Lab coat, gloves, surgical mask. Husbandry practices will include spraying used cages with disinfectant, autoclaving, and then dumping the used bedding or if disposable caging is used, cages will be bagged and then incinerated.

	▪ All personnel listed on the HPRD including animal caretakers, and staff working in shared lab or animal spaces must receive hazard awareness training. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Karin Peterson abstained) **PRD#16-184** as written.
Item 4:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New) ▪ Hasenkrug (LPVD) ▪ **PRD#16-186: Zika virus** ▪ Becky Anderson presented the risk assessment. She informed the committee that Karin Peterson and Kim Hasenkrug were originally covered under the Feldmann Zika virus HPRD in order to get approval quickly for these labs to start studying Zika virus. Now we have asked these labs to create their own PRDs to cover Zika virus separately, long term it makes documentation easier. The same precautions that were approved for the Feldmann lab will apply to both of the new PRDs. There are no new lab locations and there is only one additional staff member added to the Hasenkrug PRD. ▪ Nancy Hoe informed the committee that this PRD includes cell sorting procedures with Zika infected cells. These sorting experiments will be performed at BSL-2 according to the Sorting Infected Samples on the BDFacsAria SOP within a BSC. ▪ Sue Priola pointed out to the committee that Kim Hasenkrug's name was not associated with the attached ASP for work with mice. The committee discussed and agreed that an ASP needs to be associated with lab/PI in order for it to be attached to the PRD. The committee agreed that if Karin Peterson updated the ASP to include Kim Hasenkrug as an associated researcher, then the ASP could be attached to the PRD. ▪ BSL-2/ABSL-2 is appropriate for work with Zika virus with the following additional precautions: ▪ Care should be taken to minimize worker exposure to aerosols, such as working in a certified Class II BSC at all times and using gasketed bucket covers when centrifuging infectious material. Gasketed bucket covers or sealed rotors must only be loaded/unloaded in a BSC. It is recommended if possible that work with Zika virus be performed in a small or dedicated lab away from the main lab areas. Women of child bearing years must be advised of the risks of working with this agent, please consult with OMS.

	▪ Animal studies with rodents will be performed in the Human Pathogen Wing of (b)(6) in (b)(6) or (b)(6). Both areas are restricted access. All manipulations must be performed in a BSC. A sign at the suite door will indicate when Zika procedures are in progress. PPE includes: Lab coat, gloves, surgical mask. Husbandry practices will include spraying used cages with disinfectant, autoclaving, and then dumping the used bedding or if disposable caging is used, cages will be bagged and then incinerated. ▪ All personnel listed on the HPRD including animal caretakers, and staff working in shared lab or animal spaces must receive hazard awareness training. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **PRD#16-186** with the following minor modifications: 1. Karin Peterson must add Kim Hasenkrug as an associated researcher to the attached ASP.
Item 5:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New)</u> ▪ Hasenkrug (LPVD) ▪ **PRD#16-185: Lactate Dehydrogenase Elevating Virus (LDV)** ▪ Becky Anderson presented the risk assessment. The proposed registration is to study the immune response to LDV in mice. LDV does not infect humans. It infects mice with a low frequency in laboratory mice and is common in wild mice. The main clinical sign is the elevation of serum levels of an enzyme produced by the liver (and also by the heart and RBCs), lactate dehydrogenase. In some susceptible strains (AKR and C58), infected animals may present with a paralytic syndrome if immunosuppressed by age, chemicals, or immune system dysfunction. This syndrome is a result of the LDV interaction with ecotropic murine leukemia virus present in those strains of mice. There is no treatment, and the virus persists in infected mice, it is usually recommended to eliminate the infected colony. The virus is primarily transmitted in the lab through tumor stocks, cell lines, and mouse derived biological materials and can also be transmitted through re-use of contaminated needles. The primary lab hazards include accidental sharps injuries and production of aerosols. LDV can be safely worked with at BSL-1. The Hasenkrug lab is currently set up as a BSL-2 lab. Any aerosol generating procedures with LDV (i.e. cell sorting) should be conducted at BSL-2.

	▪ BSL-1/ABSL-1 is appropriate for work with LDV. Cell sorting procedures with LDV should be conducted at BSL-2. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#16-185** as written.
Item 6:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New) ▪ Hasenkrug (LPVD) ▪ **PRD#16-187: Murine Gammaretroviruses (Friend, Moloney, Rauscher, CasBrE, FMCF54, FMC98, Fr98)** ▪ Becky Anderson presented the risk assessment. The registration describes the study of virus virology, pathology, and immunology of murine leukemia viruses. The listed viruses are either polytropic viruses (that infect a variety of hosts including mice) or ecotropic and only infect mice. To date, no documented cases of human disease for any of the listed viruses. Infections with these viruses result in systemic hypergammaglobulanemia, splenomegaly, T and B cell dysfuntion and eventually neurological disorder. Several strains cause neurodegenerative disease in mice (Friend, CasBrE, Moloney temp sensitive mutants). There may be vertical transmission with the listed viruses, but minimal horizontal transmission. The primary lab hazards include accidental sharps injuries and production of aerosols. ▪ BSL-2/ABSL-2 is appropriate for work with the listed Murine Gammaretroviruses. Cell sorting procedures should be conducted at BSL-2 according to SOP. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#16-187** as written.
Item 7:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New) ▪ Feldmann (LV) ▪ **PRD#16-188: *Plasmodium berghei, Plasmodium yoelii***

	▪ Becky Anderson presented the risk assessment. The proposed studies are to study the effect of co-infection of rodent specific Plasmodium species with MA-EBOV. They will first prepare plasmodium stocks, then set up a malaria infection model in rodents, then move on to coinfection studies with MA-EBOV. *P. berghei* and *P. yoelii* are two species of malaria parasites that infect mammals other than humans. They are two of the four known species that have been described in murine rodents of West Africa (*Plasmodium berghei, P. yoelii, P. chabaudi* and *P. vinckei*). These rodent parasites do not infect humans, but provide an effective model for the study of human malaria in rodents. The natural route of transmission is through the bite of an infected mosquito. The primary lab hazards include accidental sharps injuries and production of aerosols. ▪ BSL-1/ABSL-1 is appropriate for work with *Plasmodium berghei, Plasmodium yoelii.* ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **PRD#16-188** as written.
Item 8:	<u>Registration Documents for Recombinant DNA Experiments (Amendment)</u> ▪ Ebihara (LV) ▪ **RD#14-431 Amend**: Molecular characterization of viral proteins of pathogenic RNA viruses ▪ Reviewers: Karin Peterson, Bob Heinzen ▪ **Summary:** The amendment is to add a new vector, two routes of inoculation for rabbits, and Spondweni virus, Kedougou virus, and Bagaza virus. ▪ Karin Peterson summarized the RD. The amendment is add a new vector, two routes of inoculation for rabbits (intradermal & subcutaneous), add Spondweni virus, Kedougou virus, and Bagaza virus. There are no dual use issues and the listed NIH Guidelines are appropriate. ▪ Karin Peterson had no concerns with the proposed work. ▪ Bob Heinzen questioned if the biosafety level listed is for the amendment only or if it pertains to the entire document. Becky Anderson informed the committee that that the biosafety level is only for the work described in the amendment. Once approved the amendment gets attached to the original RD. ▪ Additional routes of inoculation were proposed for rabbits. There were no new animal models proposed.

	▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#14-431 Amend** as written. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-2-a and III-E-1 of the NIH Guidelines.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Nancy Hoe presented the BSO report. ▪ Nancy Hoe reviewed the DSAT inspection report that was received for the BSL-4 DSAT inspection. ▪ The splash incident that was described last month has been closed out by DSAT and OBA. ▪ Bob Heinzen won the RML Safety Award for his outstanding effort to keep his lab safe.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ There was one injury since the last IBC meeting, an employee retrieving a hot pyrex dish from the microwave was burned. ▪ Paul Carson has performed many ergonomic evaluations throughout campus lately. ▪ Annual safety refresher training will be starting in the next few weeks.
Report	**IRF Biosafety Manager Report/Megan Morgan** ▪ Not present.
Report	**Associate Director Report/Marshall Bloom** ▪ Marshall Bloom informed the committee that he will be sending an email to remind everyone of the requirements for summer students working in labs.
Around the room	▪ None.

Other issues	▪ None.

Next Meeting:

- Date: 6/16/16
- Place: Bldg A Seminar Room
- Time: 1:00 PM

RML Biosafety Committee Meeting
May 19, 2016
Biosafety Officer/Responsible Official Report

1) Requests approved by BSO since last meeting:

a) Registration Documents for Recombinant DNA Experiments

i) Amend

(1) Feldmann (LV)

*(a) **RD-15-404**: VSV Replication competent*

(i) Add intranasal route of inoculation for hamsters – approved 5/12/16

b) Summer Student Projects

***i)** Steele-Mortimer*

(1) [(b)(6)] developing an animal model for Salmonella meningitis – approved 5/19/16

2) ***New requests approved by committee via electronic review:***

i) *None*

3) ***New requests***

a) *Human Pathogen Registration Documents*

i) ***New***

(a) *Peterson (LPVD)*

(a) ***PRD-16-184:** Zika virus infection in neurons and in mice*

(b) *Hasenkrug (LPVD)*

(a) ***PRD-16-186:** Zika virus infection of mice*

(b) ***PRD-16-185**: Lactate Dehydrogenase-elevating virus*

(c) ***PRD-16-187**: Murine Leukemia viruses*

(c) *Feldmann (LV)*

(a) ***PRD-16-188**: Plasmodium spp.*

ii) ***Amend***

(a) *Ebihara (LV)*

(a) ***HPRD 14-110**: Molecular biology, evolution and pathogenesis of Orthobunyaviruses*

(i) Add Rabbit as an animal model

(b) *Feldmann (LV)*

(a) ***HPRD 16-182**: Elucidate mechanisms of Zika Virus pathogenesis*

(i) Add Spondweni virus (SPOV), Kedougou virus (KEDV), and Bagaza virus (BAGV)

b) *Registration Documents for Recombinant DNA Experiments*

i) ***Amend***

(a) *Ebihara (LV)*

(a) ***RD 14-431**: Molecular characterization of viral proteins of pathogenic RNA viruses*

(i) Add additional cloning vectors

(ii) Add routes of inoculation in rabbits

(iii) Add Spondweni virus (SPOV), Kedougou virus (KEDV), and Bagaza virus (BAGV)

c) *Working Group Summaries*

d) *Standard Operating Procedures*

4) ***Animal Study Protocols Review***

Title	***Associated HPRD***	***Associated RD***	***Reviewer***
Production of polyclonal rabbit sera against Nipah virus in rabbit	*N/A (Nipah proteins)*	*14-431*	*B. Anderson*
Determining host responses in the Syrian hamster model upon immunization with recombinant vesicular stomatitis virus vectored vaccines	*13-82 (VSV exempt)*	*15-404*	*M. Morgan*
Stimulation of B cells by huBAFF, huIL6, and anti-CEACAM1 to improve antibody responses in HIV-infected humanized mice	*12-104 (HBBF) 12-55 (HIV)*	*14-219 15-223*	*N. Hoe*
Infectivity of olfactory mucosa tissue samples from CJD patients in human prion protein transgenic mice	*13-47 (CJD)*	*NA*	*B. Anderson*
Efficacy of Chimp Adenovirus (ChadCX1-MER-S) expressing MERS-CoV spike using transgenic hDPP4	*12-143 (MERS-CoV)*	*12-410*	*N. Hoe*

5) ***Biosafety Training Performed – Becky Anderson***

Type of Training	***Number of Sessions***	***Number of Employees Trained***
Select Agent Initial	***1***	***2***

6) ***Safety Audits and Inspections***

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

a) *Biological Incident Report:*
   i) *None*

7) ***Select Agent Issues***

a) *Results of DSAT BSL-4 inspection of March 8-17, 2016*

8) ***Other Issues***

a) *DSAT/OBA closeout of incident with splash to eye*
b) *BMBL update*
c) *Bob Heinzen safety award!*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 06/16/16
Meeting Time: 1:04 PM **Adjourned:** 1:44 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Megan Morgan	☒	☐
Bob Heinzen, Vice Chair	☒	☐	Hideki Ebihara	☐	☒	Karin Peterson	☒	☐
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Dana Scott	☐	☒
Alan Applebury	☐	☒	Nancy Hoe	☒	☐	Alexandra Scranton	☐	☒
Chris Bosio	☒	☐	JR Iman	☐	☒			
Marshall Bloom (EO)	☐	☒	Clay Jarrett	☒	☐			
Teresa Borino	☐	☒	Josh Kellar (EO)	☐	☒			
Carol Calderwood	☐	☒	Scott Kobayashi	☒	☐			
Marcie Caldwell (EO)	☐	☒	Jamie Lovaglio	☐	☒			
Paul Carlson	☐	☒	Alida Merritt	☒	☐	Alternate for C. Calderwood:		
Bruce Chesebro (EO)	☐	☒	Kevin Mora	☐	☒	(b)(6)	☒	☐

(P=present; A=absent)

Guests: (b)(6)

Minutes: Meeting minutes from 5/19/16 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** Action: Meeting minutes for 5/19/16 were unanimously approved.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New) ▪ Caughey (LPVD) ▪ **PRD#16-189: Transmissible spongiform encephalopathies (TSE) Agents, prions** (mouse adapted scrapie, hamster adapted scrapie, transmissible mink encephalopathy (TME), chronic wasting disease (CWD) from cervid species)

	▪ Becky Anderson presented the risk assessment. The proposed studies are to: understand the conversion process of normal host prion protein to its pathological isoform using cell biological, biochemical, and biophysical methods. To develop synthetic infectious prions *in vitro* and to test these preps in mouse and hamster models. Continue to develop a rapid, sensitive, and specific test for prion disease that affect human, bovine, cervid, and ovine species. TSE agents cause fatal neurodegenerative diseases that can affect both humans and animals. This registration is for the listed animal TSEs. TSE can be sporadic, familial, or acquired diseases. Signs and symptoms of scrapie vary widely among individual animals and develop very slowly. Due to damage to nerve cells, affected animals usually show behavioral changes, tremor (especially of head and neck), severe itching, and locomotor incoordination that progresses to recumbency and death. Signs of CWD in cervid species include excessive salivation, loss of appetite, progressive weight loss, excessive thirst and urination, listlessness, teeth grinding, holding the head in a lowered position and drooping ears. CWD is a slowly progressive disease. There are no treatments or vaccines for prevention of TSE caused disease. There is no known transmission of the listed agents to humans. The primary lab hazards include accidental sharps injuries and the production of aerosols. The TSE agents are more difficult to inactivate with common disinfectants and require 1-2% Environ LpH for 30 minutes, 1-2 N sodium hydroxide, 2.5% hypochlorite, or incineration. ▪ Sue Priola asked if the Organism/Toxin listed, "Scrapie Agent" was what PI Dashboard had listed or if the PI chose that option. Becky Anderson informed the committee that it was the best fit from the list, but could be deleted and leave what the PI had manually added. The committee agreed that either way it is listed in the registration is fine because the specific agents are clearly listed. ▪ BSL-2/ABSL-2 is appropriate for work with animal TSE agents. Human TSE agents are segregated in a separate lab suite from animal TSE agents. ▪ Animal studies with mice and hamsters were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **PRD#16-189** as written.
Item 2:	<u>Registration Documents for Recombinant DNA Experiments (Amendment)</u> ▪ Hinnebusch (LZP) ▪ **RD#15-320 Amend**: Site specific mutagenesis of CDC-exempt *Y. pestis* strains ▪ Reviewers: Bob Heinzen, Scott Kobayashi ▪ **Summary:** The amendment is to add a new bioluminescent reporter plasmid.

	▪ Bob Heinzen summarized the RD. The amendment is to add a new bioluminescent reporter plasmid to use with exempt strains of *Y. pestis*. This plasmid expresses luciferase which allows the Hinnebusch lab to perform *in vivo* imaging in mice and other small animals. The antibiotic resistance marker is ampicillin and is appropriate for this research. Bob Heinzen had no other comments or concerns. ▪ Scott Kobayashi had no additional comments or concerns. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#15-320 Amend** as written. Research using prokaryotic hosts is approved at BSL-2 under section III-D-1-a and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a of the NIH Guidelines.
Item 3:	**Full Length Clone Lab Report** ▪ Megan Morgan presented the annual Full Length Clone Lab report to the committee. ▪ There were no breaches in containment in 2015. ▪ There were no laboratory exposures in 2015. ▪ Sue Priola will submit the report to OBA.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Nancy Hoe presented the BSO report. ▪ Nancy Hoe provided Annual IBC Training to the committee. Training presentation is attached.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ Not present.
Report	**IRF Biosafety Manager Report/Megan Morgan** ▪ Completed validation testing of air handling systems in BSL-3 and BSL-4 in May. Facilities performed very well. The upgrades to the air controllers and monitors in the BSL-3 has improved performance. Have received most of the reports and all look great. We are only waiting for two more reports.

Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ None.

Other issues	▪ None.

Next Meeting:

- Date: 7/21/16
- Place: Bldg A Seminar Room
- Time: 1:00 PM

RML Biosafety Committee Meeting
June 16, 2016
Biosafety Officer/Responsible Official Report

1) ***Requests approved by BSO since last meeting:***
   a) *Pathogen Registration Documents*
      i) Amend
         (1) Peterson (LPVD)
            (a) ***PRD-16-184****: Zika virus*
               (i) Add subcutaneous route of inoculation for mice – approved 6/16/16
   b) *Summer Student Projects*
      i) *DeLeo*
         (1) (b)(6) *Study of Klebsiella pneumoniae– approved 6/9/16*
2) ***New requests approved by committee via electronic review:***
   i) *None*
3) ***New requests***
   a) *Pathogen Registration Documents*
      i) ***New***
         (a) *Caughey (LPVD)*
            (a) ***PRD-16-189:*** *Biology of transmissible spongiform encephalopathy (TSE, prion) diseases*
   b) *Registration Documents for Recombinant DNA Experiments*
      i) ***Amend***
         (a) *Hinnebusch (LZP)*
            (a) ***RD 15-320****: Site specific mutagenesis of CDC-exempt Y. pestis strains*
               (i) Add bioluminescent reporter plasmid (pGEN-luxCDABE)

4) ***Animal Study Protocols Review***

Title	***Associated HPRD***	***Associated RD***	***Reviewer***
Identification of immunogenic proteins in mice immune to virulent F. tularensis	*13-73 (LVS) 13-71 (F. tularensis)*	*NA*	*N. Hoe*
The production of Friend virus stocks in mice	*16-187 (Friend virus)*	*NA*	*B. Anderson*
Competence of B. burgdorferi variants in the mouse/tick infectious cycle	*12-24 (B. burgdorferi)*	*14-308*	*B. Anderson*
Cure of latent HIV infection in humanized mice using ART and Ixa20mib(MLN2238)	*12-55 (HIV)*	*NA*	*B. Anderson*
Evaluation of virulence and attenuation of various Salmonella mutants in mice	*12-44 (S. typhimurium)*	*NA*	*B. Anderson*

RML Biosafety Committee Meeting
June 16, 2016
Biosafety Officer/Responsible Official Report

5) ***Biosafety Training Performed – Becky Anderson***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
Select Agent Initial	***1***	***4***

6) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
   a) *Biological Incident Report:*
      i) *None*

7) ***Select Agent Issues***
   a) *None*

8) ***Other Issues***
   a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 07/21/16
Meeting Time: 1:03 PM **Adjourned:** 1:48 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Karin Peterson	☒	☐
Bob Heinzen, Vice Chair	☒	☐	Heinz Feldmann (EO)	☐	☒	Dana Scott	☒	☐
Becky Anderson (EO)	☒	☐	Nancy Hoe	☒	☐	Alexandra Scranton	☐	☒
Alan Applebury	☐	☒	JR Iman	☐	☒			
Chris Bosio	☒	☐	Clay Jarrett	☒	☐			
Marshall Bloom (EO)	☐	☒	Josh Kellar (EO)	☐	☒			
Teresa Borino	☐	☒	Scott Kobayashi	☐	☒			
Carol Calderwood	☐	☒	Jamie Lovaglio	☐	☒			
Marcie Caldwell (EO)	☐	☒	Alida Merritt	☒	☐			
Paul Carlson	☐	☒	Kevin Mora	☐	☒	Alternate for C. Calderwood:		
Bruce Chesebro (EO)	☐	☒	Megan Morgan	☒	☐	(b)(6)	☒	☐

(P=present; A=absent)

Guests: (b)(6)

Minutes: Meeting minutes from 6/16/16 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** Action: Meeting minutes for 6/16/16 were unanimously approved with the following minor modification: 1. Nancy Hoe informed the group that the wording on page 3 for Megan Morgan's report makes it sound like the current facility was not in good working condition. The wording for sentence two of bullet one should more accurately state, "The upgrades to the air controllers and monitors in the BSL-3 has improved performance."

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals

	(New) ▪ Chesebro (LPVD) ▪ **PRD#16-190: Transmissible spongiform encephalopathies (TSE) Agents, prions** (mouse adapted scrapie, hamster adapted scrapie, transmissible mink encephalopathy (TME), chronic wasting disease (CWD) from cervid species) ▪ Becky Anderson presented the risk assessment. The proposed studies are to: study the pathogenesis of prion disease with an overarching goal to define the mechanisms that lead to brain neurodegeneration and death. TSE agents cause fatal neurodegenerative diseases that can affect both humans and animals. This registration is for the listed animal TSEs. TSE can be sporadic, familial, or acquired diseases. Signs and symptoms of scrapie vary widely among individual animals and develop very slowly. Due to damage to nerve cells, affected animals usually show behavioral changes, tremor (especially of head and neck), severe itching, and locomotor incoordination that progresses to recumbency and death. Signs of CWD in cervid species include excessive salivation, loss of appetite, progressive weight loss, excessive thirst and urination, listlessness, teeth grinding, holding the head in a lowered position and drooping ears. CWD is a slowly progressive disease. There are no treatments or vaccines for prevention of TSE caused disease. There is no known transmission of the listed agents to humans. The primary lab hazards include accidental sharps injuries and the production of aerosols. The TSE agents are more difficult to inactivate with common disinfectants and require 1-2% Environ LpH for 30 minutes, 1-2 N sodium hydroxide, 2.5% hypochlorite, or incineration. ▪ BSL-2/ABSL-2 is appropriate for work with animal TSE agents. Human TSE agents are segregated in a separate lab suite from animal TSE agents. ▪ Animal studies with mice and rats were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#16-190** as written.
Item 2:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Heinzen (LB) ▪ **RD#14-106 Amend**: Genetic transformation of *Coxiella burnetii* ▪ Reviewers: Sue Priola, Chris Bosio ▪ **Summary:** The amendment is to introduce *lysA* and *birA* in virulent and avirulent *C. burnetii*. ▪ Sue Priola summarized the amendment to the RD. The previous amendment to the RD proposed to use Arginine as a selective marker for Coxiella. The Heinzen lab in this amendment proposes to use lysine as a selective marker

	instead of using antibiotics for selection. The second part of the amendment includes using a biotin ligase to identify protein-protein interactions. They will use this system to identify host cell binding partners of *Coxiella* type IV secretion system effector proteins. The vector maps are included and appropriate for the proposed work. The NIH Guidelines listed are also appropriate. The biosafety levels are BSL-2 and BSL-3 depending on the strain of *C. burnetii* used for the experiments and this is clearly stated in the RD amendment. ▪ Chris Bosio had no additional comments or concerns. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#14-106 Amend** as written. Research using prokaryotic hosts is approved at BSL-2 or BSL-3 under section III-D-1-a, III-D-1-b, and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 or BSL-3 under III-D-1-a and Appendix G-II-C of the NIH Guidelines.
Item 3:	**Standard Operating Procedure: Standard Operating Procedures for Animal Biosafety Level 3 (ABSL-3) Powassan virus (Updated)** ▪ Becky Anderson informed the committee that the update to the Bloom lab SOP is to include procedures for the formalin fixation of mouse tissues in the ABSL-3 lab for animals infected with Powassan virus. Section 5.3 has been updated to include those procedures. The validation data for these procedures is the same as what was presented by Elaine Haddock for the BSL-4 lab. All procedures are the same for BSL-3 and BSL-4. ▪ Becky Anderson pointed out that the first sentence should state that the 10% formalin is provided by RML Histopathology. ▪ Dana Scott informed the committee that the paragraph on formalin fixation should be updated to include information on the size restrictions for tissues. This information could be copied from the BSL-4 SOP to ensure the procedures are consistent. ▪ There were no additional comments or concerns. Action: The committee unanimously approved **Standard Operating Procedures for Animal Biosafety Level 3 (ABSL-3) Powassan virus (Updated)** with the following minor modifications: 1. Indicate in the first sentence that 10% formalin is provided by RML Histopathology. 2. Add a sentence to the formalin fixation paragraph (5.3.2) from the BSL-4 SOP

	that gives size restrictions based on the tissue cassette size.
Item 4:	**Operations and Safety Procedures: BSL-3 Operations and Safety Procedures (OSP) IRF (b)(6) Updated)** ▪ Becky Anderson informed the committee that the OSP for (b)(6) was updated to consolidate several SOPs that were redundant into one document. The procedure specific SOPs were added to Appendix A, the Agent Summaries were added to Appendix B, and there were minor edits throughout. Finally, the inactivation SOPs were updated to match the BSL-4 inactivation SOPs. Previously the inactivation SOPs were present, but lacked detail, they are now consistent with the BSL-4 SOPs. ▪ Bob Heinzen pointed out that there are some formatting issues in the document. Becky Anderson stated that those issues would be fixed. ▪ The committee had extensive discussion about the length of the document. It was agreed that although the document is long, the content was necessary so it could be read annually by the users, no alternatives to making the document shorter were presented. ▪ There were no additional comments or concerns. Action: The committee unanimously approved **BSL-3 OSP IRF (b)(6) (Updated)** with minor modifications: 1. Fix formatting in the document.
Item 5:	**Exposure Control Plan (Annual Review)** ▪ Sue Priola informed the committee that the Exposure Control Plan has been updated for the annual review and changes are tracked. ▪ Alida Merritt stated that she was not sure everyone would know what the symptoms of a fever are. She proposed including the following symptoms to the document on page 7 and 17: sweating, shivering, headache, muscle aches, loss of appetite, dehydration, general weakness. The group agreed that information would be helpful. Nancy Hoe stated that Biosafety would make sure the change is approved by Dr. Jim Schmitt at NIH. ▪ In the same section the committee pointed out that the work "unexplained" febrile illness was confusing and perhaps it should be removed. The committee agreed that it was not necessary. ▪ Alida Merritt also pointed out that "Universal Precautions" should be updated with "Standard Precautions". The committee agreed this would be appropriate. ▪ Becky Anderson summarized to the committee the results of the annual review of safer sharps devices by members of RMVB. The summary is attached to this document.

	Action: The committee unanimously approved the **Exposure Control Plan (Annual Review)** with minor modifications: 1. Delete "unexplained" from page 7 in the Workers section, second bullet. 2. Include symptoms of a fever as stated above to pages 7 and 17. 3. Change "Universal Precautions" to "Standard Precautions" on pages 18, 39, and 49.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Nancy Hoe presented the BSO report.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ Not present.
Report	**IRF Biosafety Manager Report/Megan Morgan** ▪ Nothing to report.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ None.

Other issues	▪ Sue Priola reminded the committee that Hideki Ebihara left RML in July. Heinz Feldmann has requested to become PI for all PRD and RD registrations for Hideki Ebihara. The locations of the work and personnel lists will all stay the same, Heinz Feldmann will be the supervisor for those employees and their work. The committee unanimously approved the PI change on all Ebihara PI Dashboard documents.

Next Meeting:

- Date: 8/18/16
- Place: Bldg A Seminar Room
- Time: 1:00 PM

RML Biosafety Committee Meeting
July 21, 2016
Biosafety Officer/Responsible Official Report

1) Requests approved by BSO since last meeting:

a) Pathogen Registration Documents

i) Amend

(1) Peterson (LPVD)

*(a) **PRD-16-184**: Zika virus*

(i) Add intranasal route of inoculation for mice – approved 7/15/16

b) Summer Student Projects

***i)** Hinnebusch*

(1) (b)(6) Yersinia pestis (exempt) - Enumeration of bacteria from the flea, biofilm assay, dissection of fleas– approved 7/18/16

2) ***New requests approved by committee via electronic review:***

i) *None*

3) ***New requests***

a) *Pathogen Registration Documents*

i) ***New***

(a) *Chesebro (Race) (LPVD)*

(a) ***PRD-16-190:** Pathogenesis and biology of transmissible spongiform encephalopathy (TSE, prion) diseases*

b) *Registration Documents for Recombinant DNA Experiments*

i) ***Amend***

(a) *Heinzen (LB)*

(a) ***RD 14-106**: Genetic transformation of Coxiella burnetii*

(i) Introduction of lysA from Legionella pneumophila and birA from Aquifex aeolicus into virulent and avirulent Coxiella

ii) *Standard Operating Procedures*

(a) ***Amend***

(a) *SOP for Animal Biosafety Level 3 (ABSL-3): Powassan virus (including lineage II of POWV know as deer tick virus)*

(i) Add procedure for tissue fixation

(b) *BSL-3 Operations and Safety Procedures, (b)(6)*

(i) Consolidate information from specific agent SOPs so these can be inactivated

(ii) Add individual SOPs for agent inactivation

c) *RML Exposure Control Plan – Annual Review*

4) ***Animal Study Protocols Review***

Title	*Associated PRD*	*Associated RD*	*Reviewer*
Evaluation of the antiviral compound griffithsin against the newly emerging coronavirus MERS-CoV in rhesus macaques	*12-143 (MERS-CoV)*	*NA*	*N. Hoe*
Mapping a susceptibility allele for Ebola hemorrhagic fever pathogenesis and resistance in mice	*13-90 (Ebola)*	*NA*	*M. Morgan*
Tissues from TSE infected mice and hamsters for use in biochemical and biophysical analyses	*13-47 (human TSE) 16-189 (rodent TSE)*	*NA*	*B. Anderson*
Innate immune responses and Zika virus pathogenesis in the CNS of mice	*16-184 (Zika)*	*NA*	*N. Hoe*
Effect of NK/T cell depletion on Andes virus pathogenesis in hamsters	*12-81 (Andes virus)*	*NA*	*M. Morgan*

5) ***Biosafety Training Performed – Becky Anderson, Megan Morgan***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
Annual Employee Refresher	***4***	***All***
BSL-3 Laboratory Safety	***2***	***4***
BSL-4 Laboratory Safety	***7***	***2***
BSL-3/4 for Support Personnel	***1***	***1***
Biosafety Briefs	***2***	***WIPs***

6) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
a) *Biological Incident Report:*
i) *None*

7) ***Select Agent Issues***
a) *None*

8) ***Other Issues***
a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 08/18/16
Meeting Time: 1:05 PM **Adjourned:** 1:57 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Karin Peterson	☒	☐
Bob Heinzen, Vice Chair	☐	☒	Heinz Feldmann (EO)	☒	☐	Dana Scott	☒	☐
Becky Anderson (EO)	☒	☐	Nancy Hoe	☒	☐	Alexandra Scranton	☐	☒
Alan Applebury	☐	☒	JR Iman	☐	☒			
Chris Bosio	☒	☐	Clay Jarrett	☒	☐			
Marshall Bloom (EO)	☒	☐	Josh Kellar (EO)	☐	☒			
Teresa Borino	☒	☐	Scott Kobayashi	☒	☐			
Carol Calderwood	☒	☐	Jamie Lovaglio	☐	☒			
Marcie Caldwell (EO)	☐	☒	Alida Merritt	☒	☐			
Paul Carlson	☐	☒	Kevin Mora	☐	☒	Alternate for C. Calderwood:		
Bruce Chesebro (EO)	☐	☒	Megan Morgan	☐	☒	(b)(6)	☐	☒

(P=present; A=absent)

Guests: (b)(6)

Minutes: Meeting minutes from 7/21/16 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** Action: Meeting minutes for 7/21/16 were unanimously approved as written.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment) ▪ de Leo (LB) ▪ **PRD#16-180 Amend: Klebsiella pneumoniae** ▪ Becky Anderson presented the risk assessment. The amendment is to add recombinant strains to the PRD that will be used to assess the contribution of *K.*

	pneuomoniae capsule to resistance of killing by human polymorphonuclear cells, whole blood, and serum. No recombinant work will be performed at RML, the strains will be obtained from a collaborator. The collaborator is listed on the PRD and they have IBC approval for these strains at their institution. *Klebsiella* is a type of bacteria that can cause different types of healthcare-associated infections, including pneumonia, bloodstream infections, wound or surgical site infections, and meningitis. Increasingly, *Klebsiella* bacteria have developed antimicrobial resistance, most recently to the class of antibiotics known as carbapenems. The recombinant strains in this amendment include deletion mutants of capsular polysaccharide export protein and capsular polysaccharide polymerase and the corresponding complement strains. The deletion mutants in this addendum were selected by expression of the GFP reporter and verified by PCR. The final strains contain no additional antibiotic resistance selectable markers. ▪ BSL-2/ABSL-2 is appropriate for work with strains of Klebsiella pneumoniae. ▪ No new animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved (Scott Kobayashi abstained) **PRD#16-180 Amend** as written.
Item 2:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment)</u> ▪ Feldmann (LV) ▪ **PRD#13-190 Amend: Ebola, Marburg, & LLoviu viruses** ▪ Becky Anderson presented the risk assessment. The purpose of the amendment is to add Lloviu virus. Ultimately the Feldmann lab wants to develop a reverse genetics system so that they can characterize the virus and compare pathogensis to other Filoviruses, test antivirals and therapeutics. Lloviu virus (LLOV) genetic material was identified in the tissues of Schreiber's bat carcasses in Spain. Lloviu virus is the proposed etiologic agent of die-offs of Schreiber's long fingered bats. A nearly complete genome of Lloviu virus was determined from a tissue sample through a combination of deep sequencing and PCR-based approaches. Based on these sequences, Lloviu virus has been assigned to a new genus, *Cuevavirus*, in the family *Filoviridae*. The filovirus family also includes the Ebola viruses and Marburg viruses. Lloviu virus has a genomic organization similar to those of Ebola viruses and Marburg viruses with a single stranded negative-sense RNA genome, 19 kb in length that contains 7 open reading frames (ORF). Because infectious Lloviu virus has not been isolated, the capacity of Lloviu virus to infect cells of different species and its potential to cause disease in humans is unclear. However, the Lloviu virus GP

	protein was recently shown to enter human cells utilizing a mechanism comparable to other filoviral glycoproteins, which suggests the potential for human infection. To date there has been no known human disease from Lloviu virus, therefore there are no treatments. Because of the similarity of Lloviu virus to Ebola and Marburg, it will be handled at BSL-4/ABSL-4. ▪ The RD to describe the reverse genetics system to generate the virus will be described in RD 16-450 and will be reviewed in this meeting. ▪ Alex Scranton submitted questions by email to Sue Priola. Alex Scranton stated that on page 1 under the strain section it lists, "unknown" and this sounds unnecessarily scary. Would "N/A" be more appropriate? The committee agreed that "N/A" would be better. ▪ Alex Scranton also asked if the personnel list should be shortened to people directly working with Lloviu virus. The committee agreed that for the Feldmann lab, it is standard to include the full list. The committee did agree that the list needs updating to remove a few personnel that have left RML. ▪ Alex Scranton also asked if the Full length clone lab should be added to the PRD. Becky Anderson stated that it should only be on the RD and not the PRD. The reason is that Lloviu virus as a live virus will only be worked with in the BSL-4 and not in the full length clone lab. ▪ BSL-4 is appropriate for work with LLoviu virus. ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **PRD#13-190 Amend** with minor modifications: 1. On page 1 under the strain section, remove "unknown" and replace with "N/A". 2. Update the attached personnel list.
Item 2:	<u>Registration Documents for Recombinant DNA Experiments (New)</u> ▪ Feldmann (LV) ▪ **RD#16-450**: Reverse genetics system for Lloviu virus ▪ Reviewers: Sue Priola, Karin Peterson ▪ **Summary:** The RD describes developing a reverse genetics system for Lloviu virus. ▪ Sue Priola summarized the RD. The RD is for the development of a reverse genetics system for Lloviu virus, an Ebola-like virus. The Feldmann lab will have the nucleic acids synthesized into three fragments commercially, then they will combine in the full length clone lab to make the full length genome, and then make live virus in the BSL-4. The sequence for Lloviu virus is already published so the concern that the Feldmann lab is going to publish new information that

	could be misused is moot. They will follow the same procedures that they use for Ebola by using the full length clone lab and then the BSL-4 lab for live virus experiments. They will do standard experiments to study the virus in vitro. The dual use questionnaire had one question filled out yes, question 7B. They marked it yes because they will be generating a virus that has never been isolated or cultured, however, the virus does already exist and the sequence is published. Sue Priola asked the committee if they had any additional concerns about this virus because it needs to be reverse engineered to make it. No one on the committee had concerns with the proposed work. ▪ Sue Priola pointed out that in the Prokaryote Host section, III-D-2-b should be removed as it is not appropriate. ▪ Karin Peterson asked if the Feldmann lab would be using bat cells for *in vitro* studies. Heinz Feldmann stated that initially they would not because they do not have those systems up and working yet, but maybe later on they would like to use bat cells. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **RD#16-450** with minor modifications: 1. Remove III-D-2-b from the Prokaryote Host section. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a III-D-1-c, and III-D-3-c of the NIH Guidelines.
Item 3:	<u>Registration Documents for Recombinant DNA Experiments (Amendment)</u> ▪ Feldmann (LV) ▪ **RD#16-440 Amend**: Reverse genetics system for Coronaviruses ▪ Reviewers: Scott Kobayashi, Clay Jarrett ▪ **Summary:** The amendment is add a new system for preparing full-length recombinant coronavirus using bacterial artificial chromosomes (BAC). ▪ Scott Kobayashi summarized the amendment to the RD. The amendment is to add a new system to clone and express Coronaviruses. Basically, the changes will be to use a new set of plasmids. They attached a schematic that describes what they will do. They will put 4 fragments into the BAC and then will get the full length clone out of it. The BAC will be transfected into mammalian cells and the virus will be isolated from the supernatant. The biosafety level will be determined by the virus that they are using in the BAC system. There were no dual use questions marked yes and Scott Kobayashi had no dual use concerns.

	▪ Clay Jarrett had no additional comments or concerns. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#16-440 Amend** as written. Research using prokaryotic hosts is approved at BSL-2 to BSL-4 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 to BSL-4 under III-D-3-a, III-D-3-b, and III-D-1-a of the NIH Guidelines.
Item 4:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Rosa (LZP) ▪ **RD#14-308 Amend**: Molecular genetic approaches to elucidate the mechanisms of adaptation and variation used by *B. burgdorferi*. ▪ Reviewers: Chris Bosio, Sue Priola ▪ **Summary:** The amendment is to exchange the OspC allele from one strain of *B. burgdorferi* with the OspC allele of a different strain. ▪ Chris Bosio summarized the amendment to the RD. The amendment is to exchange the OspC allele from one spirochete to another. OspC is an abundant outer membrane protein. OspC is upregulated when an infection is established, but is downregulated to become a persistent infection. The Rosa lab wants to test the effect of switching the OspC to see if *B. burgdorferi* can infect a new animal and circumvent the immune system. There are two dual use questions marked yes with a comprehensive description by the Rosa lab. Ultimately, this exchange of OspC already occurs naturally and does not affect the immunogenicity of the bacteria. The same NIH Guidelines and biosafety levels in the original RD still apply with this amendment. ▪ Sue Priola stated that there are two dual use questions marked yes on the questionnaire, but it does not indicate that this is dual use of concern, this is because *B. burgdorferi* are natural exchangers and they are testing the effect of this natural exchange. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#14-308 Amend** as written. Research using prokaryotic hosts is approved at BSL-2 under section III-D-1-a and III-D-2-a of the NIH Guidelines.
Item 5:	**Working Group Summaries**

	▪ Sue Priola reviewed the Working Group summaries with the committee. ▪ The first Working Group met to review inactivation of *Francisella tularensis* infected mouse tissues with 10% formalin for the Bosio lab. ▪ The second Working Group met to review the inactivation of *Coxiella burnetii* in infected cells with 4% paraformaldehyde, 100% methanol, 50% methanol/50% acetone, and by solubilization using TRIzol LS for the Heinzen lab. ▪ See both summaries attached. Action: The committee approved (Chris Bosio abstained) ***Francisella* formalin fixation validation studies** as written. Action: The committee unanimously approved ***Coxiella* fixation and solubilization validation studies** as written.
Item 6:	**Standard Operating Procedures: BSL-3-Cb-5 Inactivation of *Coxiella burnetii* and subcomponents for removal from the BSL-3 laboratory (Updated)** ▪ Sue Priola informed the committee that the updates to the SOP reflect the procedures for the inactivation of *C. burnetii*. The working group reviewed the SOP to ensure they matched the validation procedures. ▪ There were no comments or concerns. Action: The committee unanimously approved **BSL-3-Cb-5 Inactivation of *Coxiella burnetii* and subcomponents for removal from the BSL-3 laboratory (Updated)** as written.
Item :	**Standard Operating Procedures for Animal Biosafety Level 3 (ABSL-3): *Francisella tularensis* (Updated)** ▪ Sue Priola informed the committee that the updates to the SOP reflect the procedures for the inactivation of *F. tularensis*. The working group reviewed the SOP to ensure they matched the validation procedures. ▪ There were no comments or concerns. Action: The committee approved (Chris Bosio abstained) **Standard Operating Procedures for Animal Biosafety Level 3 (ABSL-3): *Francisella tularensis* (Updated)** as written.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Nancy Hoe presented the BSO report.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ Not present.

Report	**IRF Biosafety Manager Report/Megan Morgan** ▪ Not present.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ None.

Other issues	▪ None.

Next Meeting:

- Date: 9/15/16
- Place: Bldg A Seminar Room
- Time: 1:00 PM

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1) ***Requests approved by BSO since last meeting:***
   i) *None*
2) ***New requests approved by committee via electronic review:***
   i) *None*
3) ***New requests***
   a) *Pathogen Registration Documents*
      i) ***Amend***
         (a) *Feldmann (LV)*
            (a) ***PRD-13-90:*** *Filoviridae, Ebolavirus and Marburgvirus*
               (i) Add Lloviu cuevavirus
         (b) *DeLeo (LB)*
            (a) ***PRD 16-180:*** *Pathogenesis of Klebsiella pneumoniae*
               (i) Addition of 10 recombinant, Amp-resistant, K. pneumoniae ST258 strains
   b) *Registration Documents for Recombinant DNA Experiments*
      i) ***New***
         (a) *Feldmann (LV)*
            (a) ***RD-16-450****: Development of a reverse genetics system for Lloviu virus (LLOV)*
      ii) ***Amend***
         (a) *Feldmann (LV)*
            (a) ***RD-16-440****: Development of a reverse genetics system for Coronaviruses*
               (i) Addition of a bacterial artificial chromosome (BAC)-based system for producing viruses
         (b) *Rosa (LZP)*
            (a) ***RD-14-308****: Molecular genetic approaches to elucidate the mechanisms of adaptation and variation used by B. burgdorferi*
               (i) Addition of experiments to replace the OspC allele of one strain of B. burgdorferi with OspC alleles from other strains of B. b.
      iii) *Standard Operating Procedures*
         (a) ***New***
            (a) ***Bosio/BSL3-3:*** *Inactivation of F. tularensis in lung and spleen tissue using 10% formalin*
         (b) ***Amend***
            (a) ***Heinzen/BSL-3-Cb-5****: Inactivation of Coxiella burnetii and subcomponents for removal from the BSL-3 laboratory*
               (i) Add procedures for fixation of Coxiella-infected monolayers and RNA isolation using TRizol LS

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4) ***Animal Study Protocols Review***

Title	*Associated PRD*	*Associated RD*	*Reviewer*
Localization of T cells during Tularemia in mice	*13-73 (LVS) 13-71 (Schu4) 14-156 (LCMV)*	*13-125*	*B. Anderson*
Defining the effect of unique host genetic backgrounds and sex in Ebola virus pathogenicity in mice and linking genetic loci to phenotype	*13-90 (Ebola)*	*NA*	*M. Morgan*
Model of microcephaly following vaginal inoculation of pregnant mice with Zika virus	*16-182 (Zika, Spondweni virus) 16-184 (Zika virus)*	*NA*	*N. Hoe*
Establishment of an "Old World" NHP disease model for Zika virus infection	*16-182 (Zika)*	*NA*	*B. Anderson*
Protective efficacy of humanized monoclonal antibody therapy against Ebola virus in hamsters	*13-90 (Ebola virus)*	*NA*	*B. Anderson*

5) ***Biosafety Training Performed – Becky Anderson, Nancy Hoe***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
Select Agent Initial	***1***	***3***
BSL-4 Annual Refresher	***1***	***19***
BSL-3/4 for Support Personnel	***1***	***1***
Biosafety Briefs	***1***	***RMVB***

6) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
a) *Biological Incident Report:*
i) *None*

7) ***Select Agent Issues***
a) *None*

8) ***Other Issues***
a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 09/15/16
Meeting Time: 1:05 PM **Adjourned:** 2:18 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Karin Peterson	☒	☐
Bob Heinzen, Vice Chair	☒	☐	Heinz Feldmann (EO)	☐	☒	Dana Scott	☒	☐
Becky Anderson (EO)	☒	☐	Nancy Hoe	☒	☐	Alexandra Scranton	☐	☒
Alan Applebury	☐	☒	JR Iman	☐	☒			
Chris Bosio	☒	☐	Clay Jarrett	☒	☐			
Marshall Bloom (EO)	☒	☐	Josh Kellar (EO)	☐	☒			
Teresa Borino	☐	☒	Scott Kobayashi	☐	☒			
Carol Calderwood	☐	☒	Jamie Lovaglio	☒	☐			
Marcie Caldwell (EO)	☒	☐	Alida Merritt	☐	☒			
Paul Carlson	☒	☐	Kevin Mora	☐	☒	Alternate for C. Calderwood:		
Bruce Chesebro (EO)	☐	☒	Megan Morgan	☒	☐	(b)(6)	☐	☒

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 8/18/16 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** ▪ Sue Priola recommended changing the first sentence on page 4, from "not a concern" to "moot". Action: Meeting minutes for 8/18/16 were unanimously approved with the following modification: 1. On page 4, first sentence, replace, "not a concern" with "moot".

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New)

	▪ Priola (LPVD) ▪ **PRD#16-191: Rodent transmissible spongiform encephalopathy (TSE)** ▪ Becky Anderson presented the risk assessment. The PRD is for rodent TSE agents. The proposed studies are to understand how transmissible spongiform encephalopathy agents replicate and cause disease. TSE agents are a group of fatal neurodegenerative diseases that can affect both humans and animals. This registration is for the listed rodent TSEs. TSEs can be sporadic, familial, or acquired diseases. Signs of scrapie vary widely among individual animals and develop very slowly. Due to damage to nerve cells, affected animals usually show behavioral changes, tremor (especially of head and neck), severe itching, and locomotor incoordination that progresses to recumbency and death. There are no treatments for any of the listed rodent TSEs and there is no known transmission from the rodent TSE agents to humans. Disinfectants that are effective include: 1-2% Environ LpH for 30 min, incineration, 1-2 N sodium hydroxide, or 2.5% hypochlorite. ▪ BSL-2/ABSL-2 is appropriate for work with rodent TSEs. Work with human pathogenic TSE agents is segregated from other TSE lab work and kept in the human TSE lab suite. ▪ Animal studies with mice and hamsters were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved (Sue Priola abstained) **PRD#16-191** as written.
Item 2:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New)</u> ▪ Fischer (RTB) ▪ **PRD#16-192: Zika virus** ▪ Becky Anderson presented the risk assessment. The PRD is for studies with Zika virus. The Fischer lab proposes to study Zika virus structure and epitope display. The most common symptoms of Zika virus infection are fever, rash, joint pain, or conjunctivitis. Other common symptoms include muscle pain and headache. The incubation period for Zika virus disease is likely to be a few days to a week. The illness is usually mild with symptoms lasting for several days to a week. People usually are not hospitalized, and they very rarely die from Zika virus infections. Zika virus usually remains in the blood of an infected person for about a week but it can be found longer in some people. There is now strong evidence that Zika infection during pregnancy can cause a birth defect of the brain called microcephaly and other severe fetal brain defects. Other problems have been detected among fetuses and infants infected with Zika virus before birth, such as defects of the eye, hearing deficits, and impaired growth. There have also been increased reports of Guillain-Barré syndrome, an

uncommon sickness of the nervous system, in areas affected by Zika. The primary lab hazards include accidental sharps injuries, and parenteral inoculation. Zika is not known to be transmitted by aerosols, however generation of aerosols should still be avoided. There is no vaccine or treatment for Zika virus infections. The natural route of infection is by the bite of an infected mosquito, sexual transmission, vertical transmission to newborns, and through blood transfusions.

- BSL-2 is appropriate for work with Zika virus with the following additional precautions:
    a. Care should be taken to minimize worker exposure to aerosols, such as working in a certified Class II BSC at all times and using gasketed bucket covers when centrifuging infectious material. It is recommended if possible that work with Zika virus be performed in a small or dedicated lab away from the main lab areas. Women of child bearing years must be advised of the risks of working with this agent, please consult with OMS.
    b. A sign at the lab door will indicate when Zika procedures are in progress. PPE includes: Lab coat, gloves.
    c. Hazard awareness training must be provided to all individuals listed on the PRD,
- Becky Anderson stated that the precaution for "Women of child bearing years" should be updated to include men as well. The group discussed and agreed the best wording should be, "all laboratorians must be advised of the risks of working with this agent, please consult with OMS".
- The group also agreed that the PPE should include eye protection. This should be added to the recommendation section.
- Marshall Bloom asked what procedures they would perform with Zika virus. (b)(6) stated that they will mostly pipette virus onto the grids for microscopy. Marshall Bloom asked if they will incubate Zika with antibodies or if the preps would come pre-incubated. (b)(6) stated that they will take small microfuge tubes and incubate virus with antibodies, then pipette that small amount onto their grids. The committee discussed that those procedures need to be performed in a BSC. They also asked for more information to be added to the Description section in the Synopsis section. (b)(6) informed the committee that she will need to add a room to the PRD that contains their BSC. Becky Anderson indicated that she can add the room and the description once provided by (b)(6)
- Sue Priola pointed out that Appendix B-11-D Group II should be deleted from the Eukaryote Cell section, no NIH Guidelines need to be listed on the PRD.
- Sue Priola stated that the attached SOP was a little confusing on when to wear gloves. The committee agreed that in the "Before Use" section, the reference to bare hands or clean gloves should be removed. Then in the "During Use"

	section, add a statement to indicate the remainder of the procedures require gloves. ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **PRD#16-192** with minor modifications: 1. Clarify in recommendations section, "all laboratorians must be advised of the risks of working with this agent, please consult with OMS". 2. Add eye protection to the Recommendations section, PPE list. 3. Add detail to the description section about what they will do with Zika virus. 4. Add a room number for the BSC. 5. Delete Appendix B-11-D Group II from the Eukaryote Cells section, NIH Guidelines. 6. Update the SOP, remove reference in "Before Use" section to bare hands or clean gloves. Add statement before the "During Use" section to indicate the remainder of the procedures require gloves.
Item 3:	<u>Registration Documents for Recombinant DNA Experiments (Amend)</u> ▪ Feldmann (LV) ▪ **RD#15-404 Amend**: VSV Replication Competent ▪ Reviewers: Sue Priola, Bob Heinzen ▪ **Summary:** The RD amendment describes adding the intranasal route of inoculation to mice as well as adding work with orthomyxoviruses to list of viruses being studied. ▪ Sue Priola summarized the RD. The amendment is to add the intranasal route of inoculation for mice, which is an already approved animal species. They also want to add orthomyxoviruses to the list of viruses that are being studied. The current RD uses VSV as a platform for studying the function of genes or for use as vaccines. The Feldmann lab inserts viral genes from other viruses like glycoproteins and structural proteins. They want to add orthomyxoviruses to the list for cloning individual genes. For this RD amendment they will take HA from H5N1, which is an irreversibly defective fraction and insert it into VSV. They do not expect any increase in virulence of VSV, because typically inserting genes into VSV lowers it virulence. Sue Priola stated that the NIH Guidelines are correct and there are no dual use concerns. ▪ Becky Anderson explained the vaccine construct that is listed in the attached animal study proposal to the committee. She stated that the construct is on the VSV platform and is expressing Ebola virus glycoprotein in place of the VSV glycoprotein and HA from influenza virus H5N1. The expression of Ebola virus

	glycoprotein targets the VSV to antigen presenting cells like macrophages and dendritic cells. This targeted expression enables the cells to generate an immune response to HA from H5N1. The committee discussed and had no concerns with the proposed vaccine. ▪ Bob Heinzen had no additional comments or concerns. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#15-404 Amend** as written. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a and III-D-1-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a and III-D-3-a of the NIH Guidelines.
Item 4:	**Standard Operating Procedures: BSL-3-Yp-4 Use of the Pump 11 Elite apparatus for accurate injection of small volumes of *Y. pestis* inocula (New)** ▪ Sue Priola informed the committee that this is a new SOP for the use of the Pump 11 Elite apparatus in the ABSL-3 for Joe Hinnebusch's lab. This SOP is part of the ABSL-3 SOP for *Y. pestis*. ▪ Sue Priola asked if the power cord was inside the BSC. Chris Bosio stated that there is an outlet in the BSC so the power cord stays inside the BSC with the Pump 11 Elite. ▪ Sue Priola also asked how the syringe and butterfly needle attachment will work. It was not clear if a new needle will be used for every animal and if not, how will the needle be safely kept in between animals. A lab representative was not available to answer this question, Becky Anderson will follow up with Jeff Shannon to outline how the needle will be used and/or kept safe while moving between animals. ▪ Bob Heinzen stated that the SOP proposes to advance fluid out of the needle until a little comes out. Where is this fluid (inoculum) going to go? Dana Scott stated that typically people put it back into a tube of inoculum. Becky Anderson stated if it is a small volume, they can use a disinfectant soaked gauze pad. The committee agreed that this needs to be clarified in the SOP. ▪ Alex Scranton submitted questions by email to Sue Priola. She asked if there were concerns about using equipment that cannot be adequately decontaminated and questioned if this would adversely affect future experiments. The committee discussed that it is normal that some equipment by design is not able to be sufficiently decontaminated. They discussed the Pump 11 design and stated that the reason it is unable to be thoroughly decontaminated is because soaking it in disinfectant would ruin the electrical components of the pump, all they can do is wipe it down gently. The

	committee agreed there was no risk of cross contamination to other experiments because the inoculum is placed in a disposable syringe and disposable butterfly needle for each experiment. ▪ Alex Scranton also questioned if the order of the SOP is correct for the most efficient process. For example, the SOP states that the pump would be set up then the inoculum is prepared in the BSL-3 lab, then a researcher would come back and use the Pump 11 Elite. Becky Anderson stated that the inoculum would be prepared in the BSL-3 lab, then brought to the ABSL-3 animal suite, and then the user would set up the equipment to infect animals. The committee discussed the best way organize the SOP and decided that the SOP should refer to SOP Yp-1 for preparation of the inoculum, then describe the set up for the Pump 11 Elite. The first sentence in section 1.3 should be deleted where it describes preparing the inoculum because the reference to SOP Yp-1 covers that step. ▪ Jamie Lovaglio questioned what the intended route of inoculation was, the SOP was not clear. She stated that if it is for intradermal injections, the needle will quickly dull if repeatedly used and they may have trouble getting an accurate injection. The route should be stated in the SOP and the frequency that the needle will be changed should also be considered. ▪ Sue Priola stated that it will be useful to include a picture of the equipment as well as a statement about why it cannot be sufficiently decontaminated. ▪ There were no additional comments or concerns. Action: The committee unanimously approved **BSL-3-Yp-4 Use of the Pump 11 Elite apparatus for accurate injection of small volumes of *Y. pestis* inocula (New)** with minor modifications: 1. Clarify how the butterfly needle will be used and kept safe in between animals. Also state the route of inoculation. 2. Specify how the inoculum will be handled when it is advanced out of the needle. 3. Add a picture and specify why the equipment cannot be decontaminated. 4. Add a reference to YP-1 to indicate how to prepare the inoculum at the beginning of the SOP. Then delete the reference in 1.3 on preparing the inoculum.
Item 5:	**Standard Operating Procedures: BSL-3-Operations and Safety Procedures (Annual Review)** ▪ Sue Priola informed the committee that the document was updated for annual review and all the changes were tracked. ▪ Alex Scranton submitted questions by email to Sue Priola. Alex Scranton noted

	that the statement on page 29, Section 2.d. sounds like there needs to be an escort for an escort. Nancy Hoe stated that the first sentence in 2.d could be deleted entirely to make it more clear. ▪ Alex Scranton noted that page 64 contains a new instruction to include the experiment number in the purpose of use column of inventory records and asked if it would be helpful to include experiment number in the purpose of use column in the template of the activity Log. Nancy Hoe agreed that it would be helpful. ▪ There were no additional comments or concerns. Action: The committee unanimously approved **BSL-3-Operations and Safety Procedures (Annual Review)** with the following minor modifications: 1. Delete the first sentence in 2.d. on page 29. 2. Add Experiment Number to the Purpose of use column heading on the template for the activity log.
Item 6:	**Standard Operating Procedures: ABSL-3-Operations and Safety Procedures (Annual Review)** ▪ Sue Priola informed the committee that the document was updated for annual review and all the changes were tracked. ▪ Alex Scranton submitted questions by email to Sue Priola. Alex Scranton point out that on page 19, Section 2.d. sounds like there needs to be an escort for an escort. Nancy Hoe stated that the first sentence in 2.d could be deleted entirely similar to the BSL-3 OSP. ▪ Alex Scranton also pointed out that the "a." below section 2.d. should be changed to a "c.)". ▪ Alex Scranton noted that page 38 now instructs users to include the experiment number in the number infected column. Should this also be added to the column heading to in the Animal Census Log? Nancy Hoe agreed that this should also be included. ▪ There were no additional comments or concerns. Action: The committee unanimously approved **ABSL-3-Operations and Safety Procedures (Annual Review)** with the following minor modifications: 1. Delete the first sentence in 2.d. on page 19. 2. Change the "a." below section 2.d. to a "c.)". 3. Add experiment number to the column heading number Infected on the Animal Census log.
Item 7:	**Standard Operating Procedures: SOP#4-28-22 Immobilization and Anesthesia of**

	Nonhuman Primate in Level 4 Biocontainment (Updated) ▪ Sue Priola informed the committee that there was only one change to the SOP and that change was tracked. ▪ Jamie Lovaglio stated that the drug doses need to be updated and was concerned that they are a little binding for the veterinary staff. Megan Morgan stated 5.3 and 5.4 could be replaced with a reference to an ACUC approved animal study proposal. The committee agreed that the change was appropriate for drug dosing information. ▪ Jamie Lovaglio also noted that the first sentence in the Use of Biobubble section should be deleted. Nancy Hoe agreed there is no longer a requirement for Biobubbles when housing non-human primates. ▪ Alex Scranton questioned by email the statement in section 5.6, " if the squeeze mechanism is not equipped with a functioning locking system", why wouldn't the equipment be taken out of service until fixed, or is the language just misleading. Dana Scott agreed that the language is misleading. In the BSL-4, there are always two people to perform sedation, that one person squeezes and holds the NHP in place until the second person can administer the drug intramuscularly. For accuracy, it may be best to delete the first sentence of 5.6. ▪ Jamie Lovaglio stated that any specific drug name should be change to "drug" so it can be flexible to accommodate what is approved in the ASP. ▪ There were no comments or concerns. Action: The committee unanimously approved **B SOP#4-28-22 Immobilization and Anesthesia of Nonhuman Primate in Level 4 Biocontainment (Updated)** with the following minor modifications: 1. Replace 5.3 and 5.4 with a reference to an ACUC approved animal study proposal. 2. Delete the first sentence of 5.6. 3. Change specific drug names to "drug".
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Nancy Hoe presented the BSO report.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ December 9 is the next drill with the regional referral hospital, if anyone has ideas of specific scenarios they want to drill, contact Paul. ▪ The annual shutdown for BSL-4 (b)(6) and (b)(6) are complete for this year. ▪ There have been more animal bites this year in BSL-2 labs than normal. Please

	be sure to train people properly.
Report	**IRF Biosafety Manager Report/Megan Morgan** ▪ There will be some minor maintenance to the ABSL-3 cage wash in (b)(6) during the week of September 26.
Report	**Associate Director Report/Marshall Bloom** ▪ None.
Around the room	▪ None.

Other issues	▪ None.

Next Meeting:

- Date: 10/20/16
- Place: Bldg A Seminar Room
- Time: 1:00 PM

RML Biosafety Committee Meeting
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1) ***Requests approved by BSO since last meeting:***
   i) *None*
2) ***New requests approved by committee via electronic review:***
   i) *None*
3) ***New requests***
   a) *Pathogen Registration Documents*
      i) ***New***
         (a) *Priola (LPVD)*
            (a) ***PRD-16-191:*** *Prion pathogenesis (Transmissible spongiform encephalopathies)*
         (b) *Fischer (RTB)*
            (a) ***PRD 16-192:*** *Ultrastructural analysis of Zika Virus in collaboration with Dr. Audray Harris (HPRD #6762)*
   b) *Registration Documents for Recombinant DNA Experiments*
      i) ***Amend***
         (a) *Feldmann (LV)*
            (a) ***RD-15-404****: VSV Replication competent*
               (i) Addition of orthomyxoviruses to the list of viruses being studied
               (ii) Addition of the intranasal route of infection for mice
      ii) *Standard Operating Procedures*
         (a) ***New***
            (a) ***Hinnebusch/ABSL- YP-4:*** *Use of the Pump 11 Elite apparatus for accurate injection of small volumes of Y. pestis inocula*
         (b) ***Annual Review***
            (a) ***BSL-3 Operations and Safety Procedures***
            (b) ***ABSL-3 Operations and Safety Procedures***
            (c) ***SOP#: BSL-4-28-22:*** *Immobilization and Anesthesia of Nonhuman Primates in Level 4 Biocontainment*

4) ***Animal Study Protocols Review***

Title	***Associated PRD***	***Associated RD***	***Reviewer***
Localization of T cells during Tularemia in mice	*13-73 (LVS)* *13-71 (Schu4)* *14-156 (LCMV)*	*13-125*	*B. Anderson*
ZIKV infection and immunity in TKO-BLT mice	*16-186*	*NA*	*M. Morgan*
Model of microcephaly following vaginal inoculation of pregnant mice with Zika virus	*16-186 (Zika)*	*NA*	*N. Hoe*

RML Biosafety Committee Meeting
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Title	Associated PRD	Associated RD	Reviewer
Nature of the protective CD8 T cell response during tularemia in mice	*13-73 (LVS)* *13-71 (F. tularensis)* *14-156 (LCMV)* *15-179 (Pichinde virus)* *14-157 (Listeria monocytogenes)*	*13-125*	*N. Hoe*
Determining the efficacy of GMP VSV-Lassa GPC vaccine in the Hartley guinea pig model of Lassa fever	*13-94 (Lassa virus)* *13-82 (VSV)*	*15-404*	*N. Hoe*
Determining the efficacy of a GMP VSV-Lassa GPC vaccine in the cynomolgus macaque model of Lassa fever	*13-94 (Lassa virus)* *13-82 (VSV)*	*15-404*	*N. Hoe*
Production of antibodies in rabbits	*N/A*	*14-431*	*R. Anderson*
Analysis of disease progression of CCHF in NHPs	*13-92 (CCHF)*	*NA*	*R. Anderson*
Pre- and post-exposure treatment with the VSV-MARV vaccine against Marburg hemorrhagic fever in macaques	*13-90 (Marburg virus)* *13-82 (VSV)*	*15-404*	*N. Hoe*
Protective efficacy of the novel VSV-Makona vaccine against lethal EBOV infection in macaques	*13-90 (Ebola virus)* *13-82 (VSV)*	*15-404*	*N. Hoe*

5) ***Biosafety Training Performed – Becky Anderson, Nancy Hoe, Megan Morgan***

Type of Training	Number of Sessions	Number of Employees Trained
Select Agent Refresher	***2***	***60***
Select Agent Initial	***1***	***3***
Visitor	***1***	***2***
BSL-4 Annual Refresher	***1***	***20***
BSL-4 Laboratory Biosafety	***7***	***2***
BSL-3 Laboratory Biosafety	***5***	***6***

6) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
a) *Biological Incident Report:*
   i) *None*

7) ***Select Agent Issues***
a) *Appointment of* (b)(6); (b)(3):42 U.S.C. 262a(h) (Public Heatlh Security and Bioterrorism Preparedness and Response Act)
b) *DSAT is requesting comments on updates to Form 3 (Report of Theft, Loss, or Release)*

8) ***Other Issues***
a) *NIH Office of Science Policy announced that October will be National Biosafety Month*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 10/20/16
Meeting Time: 1:05 PM **Adjourned:** 2:18 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Megan Morgan	☒	☐
Bob Heinzen, Vice Chair	☒	☐	Heinz Feldmann (EO)	☐	☒	Karin Peterson	☐	☒
Becky Anderson (EO)	☐	☒	Nancy Hoe	☒	☐	Dana Scott	☒	☐
Alan Applebury	☐	☒	JR Iman	☐	☒	Alexandra Scranton	☐	☒
Chris Bosio	☒	☐	Clay Jarrett	☒	☐			
Marshall Bloom (EO)	☒	☐	Josh Kellar (EO)	☐	☒			
Teresa Borino	☒	☐	Scott Kobayashi	☐	☒			
Carol Calderwood	☐	☒	Jamie Lovaglio	☒	☐			
Marcie Caldwell (EO)	☐	☒	Andrea Marzi	☒	☐			
Paul Carlson	☒	☐	Alida Merritt	☐	☒	Alternate for C. Calderwood:		
Bruce Chesebro (EO)	☐	☒	Kevin Mora	☐	☒	(b)(6)	☐	☒

(P=present; A=absent)

Guests: K(b)(6)

Minutes: Meeting minutes from 9/15/16 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** ▪ Sue Priola noted that Bob Heinzen and Marcie Caldwell were marked both as present and absent for the meeting, change both to present. Action: Meeting minutes for 9/15/16 were unanimously approved with the following modification: 1. On page 1, change attendance for Bob Heinzen and Marcie Caldwell to present.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration Documents for Recombinant DNA Experiments (Amend)

	▪ Bosio (LB) ▪ **RD#13-125 Amend**: Molecular genetics of *F. tularensis* ▪ Reviewers: Clay Jarrett, Bob Heinzen ▪ **Summary:** The RD amendment describes addition of genes and a new vector. ▪ Clay Jarrett summarized the RD. The amendment is to add plasmids expressing CD8 and CD4 epitopes of LCMV, OVA, and *Listeria monocytogenes*. These plasmids will be transformed into *F. tularensis* SchuS4 and *F. tularensis* Live Vaccine Strain resulting in expression of the epitopes by SchuS4 or LVS. Kanamycin will be used as the selectable marker for SchuS4 and spectinomycin will be used as the selectable marker for LVS. The vector, pBB103 is being added to the RD and encodes for the selectable marker spectinomycin. ▪ (b)(6) clarified for the committee that spectinomycin is only going to be used for LVS and not SchuS4. Bob Heinzen suggested that they add a sentence clarifying that spectinomycin will only be used for LVS and not SchuS4. ▪ Sue Priola pointed out that Section B on the form should be checked "Yes" on the form. ▪ Nancy Hoe noted that the personnel listed in Section D had not initialed the document, this needs to be completed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#13-125 Amend** with the following minor modifications: 1. Add a sentence in section A to clarify that spectinomycin will only be used for LVS and not SchuS4. 2. Section B on the form should be checked "Yes" on the form. 3. In Section D, obtain initials from all personnel listed. Research using prokaryotic hosts is approved at BSL-2 or BSL-3 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 and BSL-3 under III-D-1-a and III-D-1-b of the NIH Guidelines.
Item 2:	**Working Group Summaries** ▪ Sue Priola reviewed the Working Group summaries with the committee. ▪ The first Working Group met to review inactivation of *R. ricketsii* using 2% Earth Sense Neutral disinfectant for Ted Hackstadt's lab. This meeting was held to follow up on requests made by the working group that reviewed the data earlier this year. The working group asked for triplicate samples and to test a longer inactivation time as well. The Working Group met to review the

	additional data provided. ▪ The second Working Group met to review reducing the dunk tank time in the BSL-4 from 15 minutes to 10 minutes with 5% MicroChem Plus disinfectant. ▪ See both summaries attached. Action: The committee unanimously approved ***Earth Sense Neutral disinfectant*** validation studies as written. Action: The committee unanimously approved ***Microchem Plus inactivation for 10 minutes*** as written.
Item 3:	**Standard Operating Procedures: BSL-3-C-3 Equipment Operation (Updated)** ▪ (b)(6) described for the committee how the Seahorse equipment works. She stated that this equipment allows the lab to measure metabolic changes in prokaryotic and eukaryotic cells in real time. This is a gold standard for measuring metabolic changes in a high-throughput manner. (b)(6) from the (b)(6) lab brought one of the 2-part plates used with the Seahorse and explained to the group how it is used. The plate has a membrane on the end of a probe sleeve to prevent the probe from contacting the media in the well and the cells. The drugs get injected into the plate pneumatically and the equipment takes instantaneous measurements as soon as the drugs are added to the cells. ▪ (b)(6) informed the group that they will not use the wash feature of the equipment in the BSL-3 lab, but it is still attached so the Prep Station so that part will be placed in a BSC. The Analyzer will be on the open bench. ▪ Bob Heinzen questioned how contained the sample is in the analyzer as the ports are essentially open. Nancy Hoe informed the committee that the BMBL states that you cannot manipulate infectious materials outside of primary containment at BSL-3, although Bob Heinzen stated that they do similar procedures when reading plates on a microscope. ▪ The committee agreed that the highest risk in the procedure is when someone removes the plate from the transport box and places it on the arm of the Seahorse. Nancy Hoe suggested taping the lid onto the plate until the plate is placed on the Seahorse arm, however, the committee thought this introduced another risk when you need to remove the tape. ▪ The committee discussed the features of the equipment that mitigate cross-contamination of samples and contamination of internal parts of the equipment. It was explained that the probe sleeves on the plate that contact the media are disposable. (b)(6) explained that the internal membrane within the Analyzer does not get changed between experiments however (b)(6) stated they have not seen any cross contamination as long as they have had the machine in use at BSL-2. The controls in the same plate would also be a good indicator of cross contamination and they have not seen

any instances of that. (b)(6) stated that they could run a blank plate of media on a regular basis to demonstrate no contamination has occurred. The committee agreed that was a good idea.

- The committee discussed the appropriateness for whether the Analyzer should also be placed within the biosafety cabinet. (b)(6) stated that even if both the Prep Station and Analyzer were to fit inside the BSC, there would likely be no room left within the work surface for the users to work. It is also not clear that the airflow within the BSC would not be compromised and affect its ability to sufficiently contain any infectious aerosols. The committee agreed that since the samples within the wells are not pressurized or aspirated within the machine in any way, as described above, there is a very minimal risk for aerosols or splashes being generated outside the BSC. Therefore, the act of placing the plate on the arm, sliding it into the Analyzer, and the probes taking readings within the wells are not considered aerosol-producing procedures.
- In addition, (b)(6) explained that the plates contain a lid that is kept on top of the 2-part plate at all times while it is outside of the BSC being transported to the Analyzer until after it is placed securely on the Analyzer arm. The plate gently snaps securely into place without causing any splashes and cannot be easily knocked off of the arm.
- For all of these reasons described above, the committee agreed that it is appropriate for the Analyzer to remain outside of the BSC for the procedures described in the SOP.
- Alex Scranton was not in attendance but submitted several questions by email to Sue Priola:

    a. Alex Scranton stated that the most risky procedure is when the plate is "carefully" moved by hand between the secondary container and the Prep Station (and vice versa). If the prep station is outside of the BSC, are we okay with the potential risks of transferring the plate simply recommending it is done carefully. The committee stated that this risk is mitigated as the Prep Station will be inside the BSC.

    b. Alex Scranton asked about including spill procedures if the plate is dropped. The committee stated that this is one section of the entire BSL-3 Suite SOP and that general spill procedures are included in another part of the SOP.

    c. Referring to section 4.1 Alex Scranton asked if eye protection is the only protection necessary. The committee stated that the Suite SOP in its entirety includes the PPE requirements already, but suggested that 4.1 could be updated to state, "in addition to standard PPE" . . . wear eye protection".

    d. Alex Scranton asked if there needed to be a procedure for cleaning or

decon of the equipment if a spill or contamination occurs. As discussed already, the inside of the machine should not become contaminated, so standard surface decontamination should be sufficient. If any spills or incidents occur that cause gross contamination, a decon procedure (autoclaving, formaldehyde gas, etc.) can be determined at that time. If service was needed, the (b)(6) lab would rather have the service technician talk a (b)(6) lab member through the procedure rather than try to have the technician work on it while the lab was shut down. Thus, any individual performing service work would be adequately protected by the PPE prescribed in the Suite SOP.

e. (b)(6) asked if the filter replacement date can be written on the outside of the machine as well as on the filter. The committee agreed this would be useful.

f. Referring to the section describing removal of the flash drive from the lab, (b)(6) asked how it could possibly get contaminated. The committee discussed that the sentence should be updated to state "with clean gloves, thoroughly wipe off the USB drive and transfer to the clean area". This clarifies that the flash drive is properly decontaminated and protected from becoming re-contaminated during the removal process.

- (b)(6) nformed the committee that the lab could put the door back on the small room so that in case of a spill the plate contamination would be contained away from the main lab area. Megan Morgan stated that they could check with Kevin Mora to make sure that the room pressure for the small room could be made more negative to the rest of the lab. The (b)(6) lab will also post a sign on the small room door when the Seahorse is in use.
- The committee discussed that the quotation marks around "clean area" are confusing and agreed to remove them.
- There were no additional comments or concerns.

Action: The committee unanimously approved **BSL-3-C-3 Equipment Operation (Updated)** with minor modifications:

1. In section 4.1 include, "in addition to standard PPE" . . . wear eye protection.
2. Add the statement that the filter replacement date should be written on the outside of the machine as well.
3. In section 4.9, the sentence should be clarified to state the "with clean gloves, thoroughly wipe off the USB drive and transfer to the clean area".
4. Remove quotation marks from clean area in section 4.9.
5. Add to SOP that a sign will be posted on the small room door when the Seahorse is in use.

Item 4:	**Standard Operating Procedures: SOP#4-28-27 Removal of Specimens for Irradiator (Update)** ▪ Sue Priola informed the committee that the changes to the four BSL-4 SOPs are to reduce the dunk tank time from 15 minutes to 10 minutes. In addition, for this SOP, they removed the table that identified the type of samples receiving the different doses of irradiation and updated the text to include similar information. ▪ Alex Scranton submitted questions by email to Sue Priola. She noted that the formatting is off and needs to be fixed. ▪ The committee discussed that the beginning of number 16 should state "the required minimum" instead of "a minimum". ▪ The committee agreed to change "Ebola infected" to "Ebolavirus-infected samples". ▪ There were no additional comments or concerns. Action: The committee unanimously approved **SOP#4-28-27 Removal of Specimens for Irradiator (Update)** with the following minor modifications: 1. On item 16, change the beginning of the sentence to, "The required minimum". 2. Fix formatting. 3. Change "Ebola infected" to "Ebolavirus-infected samples".
Item 5:	**Standard Operating Procedures: SOP#4-28-31 Removal of Specimens for Protein Analysis (Update)** ▪ Sue Priola informed the committee that the change to this SOP is to reduce the dunk tank time from 15 minutes to 10 minutes. ▪ There were no additional comments or concerns. Action: The committee unanimously approved **SOP#4-28-31 Removal of Specimens for Protein Analysis (Update)** as written.
Item 6:	**Standard Operating Procedures: SOP#4-28-32 Removal of Specimens for Nucleic Acid Extraction (Update)** ▪ Sue Priola informed the committee that the change to this SOP is to reduce the dunk tank time from 15 minutes to 10 minutes. ▪ There were no additional comments or concerns. Action: The committee unanimously approved **SOP#4-28-32 Removal of Specimens for Nucleic Acid Extraction (Update)** as written.
Item 7:	▪ **Standard Operating Procedures: SOP#4-28-33 Removal of Specimens for Fluroescence, Immunofluorescence, Histopathology, Immunohistopathology,**

	and Flow Cytometry (Update) ▪ Sue Priola informed the committee that the change to this SOP is to reduce the dunk tank time from 15 minutes to 10 minutes. ▪ There were no additional comments or concerns. ▪ Action: The committee unanimously approved **SOP#4-28-33 Removal of Specimens for Fluroescence, Immunofluorescence, Histopathology, Immunohistopathology, and Flow Cytometry (Update)** as written.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Nancy Hoe presented the BSO report. ▪ Nancy Hoe briefed the committee on the recently released GAO report, High-Containment Laboratories: Improved Oversight of Dangerous Pathogens Needed to Mitigate Risk.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ Employee reported potential exposure to isoflurane during their handling of animals and it was determined that isoflurane use in the area was extensive. The individual is now wearing a PAPR and Paul is working with RMVB to ensure proper evacuation of isoflurane in those areas. ▪ There was an injury where an employee moving compressed gas tanks was going through a door and they crushed their hand. The individual then passed out. An ambulance was called, but the person recovered and was not transported. ▪ An employee received an injury while opening a Conex box on campus for storage. It was an older one and was harder than normal to open and caused shoulder/lower back strain or sprain to the individual who went to the hospital for treatment. ▪ There will be construction in the quad next week. They will be welding and will do their best to reduce odors during that time.
Report	**IRF Biosafety Manager Report/Megan Morgan** ▪ A drill was conducted yesterday for a medical emergency in the ABSL-3. The drill tested calling both 9-911 and 0, as well as entry of RML EMT's and First Responders and extraction of a patient. Overall it went very well and a few areas were identified where we can improve, mostly with communication between RML and Ravalli County Dispatch center with getting RML emergency personnel dispatched properly.

Report	**Associate Director Report/Marshall Bloom** ▪ Marshall Bloom announced that there is a new lighting system in the seminar room.
Around the room	▪ None.

Other issues	▪ None.

Next Meeting:

- Date: 10/20/16
- Place: Bldg A Seminar Room
- Time: 1:00 PM

RML Biosafety Committee Meeting
October 20, 2016
Biosafety Officer/Responsible Official Report

1) Requests approved by BSO since last meeting:

i) None

2) ***New requests approved by committee via electronic review:***

i) *None*

3) ***New requests***

a) *Pathogen Registration Documents*

i) *None*

b) *Registration Documents for Recombinant DNA Experiments*

i) ***Amend***

(a) *Bosio (LB)*

(a) ***RD-13-125****: survival and replication of F. tularensis*

(i) Addition of work with mice

(ii) Addition of plasmids expressing LCMB, OVA, and Listeria monocytogenes CD8 and CD4 epitopes (KanR, SpcR)

ii) *Validation Studies Reports from Working Groups*

(a) ***R. rickettsia****: inactivation by Earth Sense Neutral Detergent*

(b) ***Ebola****: 10 mins with 5% Microchem Plus*

iii) *Standard Operating Procedures*

(a) ***Update***

(a) ***Bosio/BSL3-C-3:*** *Equipment Operation*

(i) add procedures for Seahorse XFe96 Analyzer and PrepStation

(b) ***SOP-4-28-27*** *Removal of Specimens for Irradiator*

(i) Update dunk tank incubation time

(ii) Update section on irradiation doses and specimens

(c) ***SOP-4-28-31*** *Removal of Specimens for Protein Analysis*
SOP-4-28-32 *Removal of Specimens for Nucleic Acid Extraction*
SOP-4-28-33 *Removal of Specimens for Fluorescence, Immunofluorescence, Histopathology, Immunohistopathology, and Flow Cytometry*

(i) Update dunk tank incubation time

4) ***Animal Study Protocols Review***

Title	***Associated PRD***	***Associated RD***	***Reviewer***
Localization of T cells during Tularemia in mice	*13-73 (LVS)* *13-71 (Schu4)* *14-156 (LCMV)*	*13-125*	*B. Anderson*
ZIKV infection and immunity in TKO-BLT mice	*16-186*	*NA*	*M. Morgan*

RML Biosafety Committee Meeting
October 20, 2016
Biosafety Officer/Responsible Official Report

Title	***Associated PRD***	***Associated RD***	***Reviewer***
Efficacy of a new VSV-NiV vaccine against Nipah virus Bangladesh in Syrian hamsters	*13-82 (VSV) 13-91 (Nipah virus)*	*15-404*	*B. Anderson*
Comparison of age-dependent pathogenesis and neurological disease induced by La Crosse (LAC), Tahyna (TAH), Jamestown Canyon (JC), Snowshoe Hare (SSH), and Inkoo (INK) Viruses.	*12-103 (LaCross and Orthobunyaviruses)*	*N/A*	*M. Brose*
Normal Blood and Tissue Donors to Support Ongoing Research 2016	*N/A*	*N/A*	*N. Hoe*

5) ***Biosafety Training Performed – Becky Anderson, Nancy Hoe, Megan Morgan***

Type of Training	***Number of Sessions***	***Number of Employees Trained***
Select Agent Refresher	***4***	***119***
Select Agent Initial	***1***	***2***
Visitor	***1***	***3***
BSL-4 Annual Refresher	***1***	***2***
BSL-4 Laboratory Biosafety	***2***	***1***
BSL-3 Laboratory Biosafety	***3***	***5***
BSL-3 Visitor	***1***	***1***
Biosafety Brief	***1***	***LV***

6) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
a) *Biological Incident Report:*
i) *None*

7) ***Select Agent Issues***
a) *None*

8) ***Other Issues***
a) *GAO report "High-Containment Laboratories: Improved Oversight of Dangerous Pathogens Needed to Mitigate Risk"*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 11/17/16
Meeting Time: 1:04 PM **Adjourned:** 2:30 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Karin Peterson	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Dana Scott	☒	☐
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Alexandra Scranton	☐	☒
Alan Applebury	☐	☒	Nancy Hoe	☒	☐			
Chris Bosio	☒	☐	JR Iman	☐	☒			
Marshall Bloom (EO)	☐	☒	Clay Jarrett	☒	☐			
Teresa Borino	☒	☐	Josh Kellar (EO)	☐	☒			
Megan Brose	☒	☐	Scott Kobayashi	☐	☒			
Carol Calderwood	☒	☐	Jamie Lovaglio	☐	☒			
Marcie Caldwell (EO)	☐	☒	Alida Merritt	☐	☒	Alternate for C. Calderwood:		
Paul Carlson	☐	☒	Kevin Mora	☐	☒	(b)(6)	☐	☒

(P=present; A=absent)

Guests: (b)(6)

Minutes: Meeting minutes from 10/20/16 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** Action: Meeting minutes for 10/20/16 were unanimously approved as written.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment) ▪ Steele-Mortimer (LB) ▪ **PRD#12-44 Amend: Salmonella typhimurium** ▪ Becky Anderson presented the risk assessment. The amendment is to add rabbits and guinea pigs to the PRD, the ASP is attached to the amendment.

	Their goal is to establish new animal models that they hope will become a model for Salmonella gastroenteritis/localized intestinal infection. The primary lab hazards include: scratching of personnel with hind legs and scratches with claws. To mitigate the hazards, studies will be conducted in (b)(6) all personnel must wear basic PPE of lab coat, gloves, and mask. Finally, all personnel must be trained on how to perform procedures on rabbits and guinea pigs. ▪ BSL-2/ABSL-2 is appropriate for work with Salmonella typhimurium. ▪ Nancy Hoe and Sue Priola questioned whether disposable gowns should be used since these animals may develop diarrhea. The disposable PPE should be used to help eliminate contamination from being removed from the room. The committee discussed and agreed that disposable clothing should be required until the Steele-Mortimer lab determines if the new animal models develop gastroenteritis symptoms. This should be added to the recommendations section. ▪ Animal studies with guinea pigs and rabbits were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **PRD#12-44 Amend** with the following modifications: <u>1.</u> Add disposable PPE to the recommendations section.
Item 2:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New)</u> ▪ Feldmann (LV) ▪ **PRD#16-193: Porcine Reproductive and Respiratory Syndrome virus (PRRSV)** ▪ Becky Anderson presented the risk assessment. The proposed studies are to understand the mechanism through which the arterivirus co-infection enables Reston Ebolavirus replication or enhances Reston Ebolavirus pathogenicity. PRRSV is the number one disease problem in major swine producing areas around the world. As the name suggests there are two syndromes associated with PRRSV; reproductive failure in sows, and respiratory disease in young pigs. The reproductive failure is characterized by infertility, abortions, stillbirths, or the birth of weak piglets that often die soon after birth from respiratory disease and secondary infections. The stage of gestation, the immune status of the sow, and the virulence of the virus determine the effects of infection. There is no evidence of transmission to humans. There are no treatments since there is no human disease. Farms depopulate, clean, and disinfect to eliminate infection. For pigs, there is a vaccine available. The primary lab hazards include parenteral inoculation, sharps injuries, and generation of aerosols.

	▪ BSL-2 is appropriate for work with PRRSV. The Feldmann lab does have an isolate that was co-infected with Reston Ebolavirus, this strain will be kept in BSL-4. ▪ Alex Scranton submitted questions by email to Sue Priola. She questioned why the Eukaryote Cell section biosafety level was BSL-2 when the comments section talked about BSL-4. The committee discussed that there were two different strains, one that was obtained from ATCC that can be worked with at BSL-2, while the other is an isolate from a pig that was co-infected with PRRSV and Reston Ebola virus. The strain that was co-infected (SPB200809289) will be worked with at BSL-4. The committee agreed that to clarify, the recommendations section should list the biosafety levels for each strain. ▪ Alex Scranton also asked about the differences in PI on the PRD versus the animal study proposal and why they are different. The committee discussed that the IBC only has PI's registered, while the NIAID animal program allows other personnel to be listed as the "PI" on an animal study proposal. The committee also discussed that the personnel list will be updated after approval by the IBC. Becky Anderson informed the committee that when a lab submits a registration through PI Dashboard, all employees listed have to electronically sign before it gets submitted to Biosafety. This often takes too long to get all the signatures before the IBC deadline so the Feldmann lab commonly adds all personnel after IBC approval to make sure they do not miss the submission deadline. ▪ Nancy Hoe also noted that the appropriate permits were included in the registration. ▪ Animal studies with pigs were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **PRD#16-193** with minor modifications: 1. State which strains of PRRSV will be worked with at BSL-2 and which one must be worked with at BSL-4.
Item 3:	<u>Registration Documents for Recombinant DNA Experiments (New)</u> ▪ Bloom (LV) ▪ **RD#16-451**: CRISPR gene knock-out and plasmid based over-expression for studying vector-borne Flavivirus biology ▪ Reviewers: Sue Priola, Chris Bosio ▪ **Summary:** The RD is for work with CRISPR gene knock-out and over-expression of mammalian genes.

	▪ Sue Priola summarized the RD. The Bloom lab studies Flavivirus infections and they have found that some proteins in mammalian and tick cell lines may influence replication in those cells. They want to use new DNA editing technology to knock out genes that they think are important to viral replication in the mammalian and tick cell lines. They will also over-express those genes to see the effect on viral infection. The Bloom lab did not provide suggested NIH Guidelines. The committee discussed the appropriate NIH Guidelines for each section, Appendix C-II should be added to the Prokaryote Host section and III-D-1-a should be added to the Eukaryote Cell Section. ▪ There were no dual use questions marked yes, but the Bloom lab did describe that a knock-out of SP100 is expected to increase viral replication in the cells. The committee discussed that this is not a change to the virus, but rather the cells being infected and, therefore it does not meet the criteria for dual use research. ▪ The cells will be infected with Langat virus or Powassan virus after knock out or transfection has occurred, the registration lists the appropriate biosafety level for when those viruses are used. ▪ Chris Bosio had no additional comments or concerns. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **RD#16-451** with the following minor modifications: 1. Add NIH Guidelines Appendix C-II to the Prokaryote Host Section. 2. Add NIH Guidelines III-D-1-a to the Eukaryote Cells Section. Research using prokaryotic hosts is approved at BSL-2 under section Appendix C-II of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a of the NIH Guidelines.
Item 4:	<u>Registration Documents for Recombinant DNA Experiments (Amend)</u> ▪ Steele-Mortimer (LB) ▪ **RD#15-108 Amend**: Salmonella Host Cell Interactions ▪ Reviewers: Bob Heinzen, Clay Jarrett ▪ **Summary:** The RD amendment is to develop "suicide vectors" that cause Salmonella to die under specific intracellular conditions. ▪ Bob Heinzen summarized the RD. The Steele-Mortimer lab wants to determine whether Salmonella can escape the vacuole where they reside inside the cell. They want to know what the significance is for this disease pathway. They

	would like to eliminate those bacteria that escape into the cytosol so they will create a strain that does not escape. They will transform strains with a plasmid containing a reporter that is activated in the cytosol which results in bacterial death, this vector is called a "suicide vector". Suicide genes include vibrio toxin and the two others are from lytic phages. There are no concerns with these genes being expressed in Salmonella. The listed antibiotics are fine to use as well. ▪ Clay Jarrett noted that there were no suicide vector maps in the original RD, the committee pointed out that this is being added as part of the amendment. Clay Jarrett had no additional comments or concerns. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#15-108 Amend** as written. Research using prokaryotic hosts is approved at BSL-2 under sections III-D-2-a and III-D-1-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a of the NIH Guidelines.
Item 5:	**Standard Operating Procedures: West Nile Virus BSL-3 Facility (b)(6) (Updated)** ▪ Becky Anderson informed the committee that the document was updated to include inactivation procedures for WNV with 2% glutaraldehyde, 2% paraformaldehyde, and 10% formalin. These procedures were previously validated by the BSL-4 and IBC reviewed and approved. The (b)(6) BSL-3 also follows these procedures and the SOP was copied from the approved versions. ▪ The committee noted that it appeared as if the Bosio lab would fix everything twice, is that necessary? Dana Scott informed the committee that the idea for the container change and fresh fixative originated with the BSL-4 lab for tissues because they worry that the threads on the container might remain contaminated. The committee discussed clarifying that bullet to make the procedures more clear in Section 5.f. to better describe fixative and container changes. ▪ Sue Priola questioned how the cells are spun onto the slides. Is it with a cytospin? How is that done to ensure containment? Could this be performed after the cells are fixed? (b)(6) and (b)(6) stated that the cytospin has a removable rotor that has an aerosol tight lid. The rotor is loaded/unloaded in the BSC. (b)(6) described to the committee how the slides fit into the rotor with a funnel that is secured onto the slide to contain the sample. The committee discussed that the last three sentences in 5.a.2 should include more detail about how to use the cytospin. ▪ Clay Jarrett questioned how the inner parts of tissue culture plates get

	decontaminated for removal when you have cells in them. (b)(6) stated that she completely fills the plate, including center parts of the plate and fills the lid to ensure that all surfaces are inactivated before removal. The committee discussed that more detail for this procedure should be added to 5.a.1. ▪ There were no additional comments or concerns. Action: The committee unanimously approved **West Nile Virus BSL-3 Facility** (b)(6) (b)(6) **(Updated)** with the following minor modifications: 1. In Section 5.a.1 state that the fixative will be added to completely fill the wells. 2. In Section 5.a.2., include more detail about the cytospin and how to use with the removable rotor safely. 3. For Section 5.f. add a statement that cells in multi-well plates will have fresh fixative added before removing samples from the lab.
Item 6:	▪ **Standard Operating Procedures: SOP#4-28-56 Husbandry Procedures for Bats in Level 4 Biocontainment (Updated)** ▪ Becky Anderson informed the committee that the document was updated to include bat handling procedures now that bats have been onsite and training has been completed with RMVB. The SOP was previously approved for training and it has been finalized. ▪ Alex Scranton submitted questions by email to Sue Priola. She questioned in Section D.2., if the grate in the cage should be soaked then scrubbed, or scrubbed then soaked. The committee discussed that the disinfectant needs to soak prior to scrubbing because scrubbing the grate can create aerosols with a contaminated surface. ▪ Alex Scranton also questioned what kind of tool is used and how is it decontaminated? Dana Scott informed the committee that it is a scrub brush and it is cleaned/decontaminated with Microchem after use and stays inside the room until the study is complete. Once the study is complete, the scrub brush is autoclaved and discarded. The committee did not see a need to include this detail in the SOP as it is part of RMVB's normal husbandry procedures. ▪ There were no additional comments or concerns. Action: The committee unanimously approved **SOP#4-28-56 Husbandry Procedures for Bats in Level 4 Biocontainment (Updated)** as written.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Nancy Hoe presented the BSO report. ▪ Nancy Hoe informed the committee about a needle stick with Salmonella. An

	employee was euthanizing and bleeding a mouse in the human pathogen wing of (b)(6) After withdrawing blood from the mouse, the employee transferred the syringe to their other hand, then handed it off to the person next to them in a 4 foot BSC to express the blood into a tube. The employee stuck themselves in the finger of the right hand during hand off. They followed proper response procedures for a needle stick. One strain that the mouse was infected with was a recombinant Salmonella strain and the incident was immediately reported to OBA. ▪ Two issues were identified with this incident, first, the person was handing off a syringe with the needle attached to another person, and secondly, there were two people working together in a 4 foot BSC. For the syringe hand off, Nancy Hoe recommended that they use safer sharps devices to keep both employees safe from the sharp. For the use of a 4 foot BSC, the IBC committee discussed that two people in a 4 foot BSC is not good practice, it may affect airflow, and there is minimal room for two people to work effectively. Dana Scott stated that there is a lot of work with animals that required two people to process samples and handle necropsy. The committee discussed that a 6 foot BSC is more appropriate for this type of work. The committee agreed that work with two people in a 4 foot BSC should not be allowed and discussed making this an RML policy. Megan Morgan read wording from University of Nebraska that the committee liked, it stated, "Restrict use of the cabinet to one person at a time. Exceptions to this would be for certain procedures requiring two people or limited to experienced and highly trained personnel and only when working in 6' or 8' biosafety cabinets." The committee agreed that Sue Priola would look into how to make this a policy or recommendation for the RML campus. The committee also discussed that is was imperative to obtain 6 foot BSCs for the procedure rooms in (b)(6) so employees had room if a procedure called for two people in a BSC.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ Not present.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ Megan Brose stated that we are in the process of planning BSL-3 annual shutdown for this year. o We usually do the shutdowns the 3rd week of March every year, however last year they had to spread it out to make HVAC repairs and upgrades. This year each suite is due for its annual recertification of BSCs in a different month, starting in January. We would like to keep them spread out so it minimizes the down time for each suite and also plan to replace one B1 BSC in each suite with a new model (older one is outdated and can't get replacement

	parts if things start to break). ○ We would like to replace these during the shutdowns, but the problem is they were just ordered today and have a 3 month turnaround time. So they will not be here in time for at least 2 of the suites. ○ We will likely go ahead and do the annual shutdowns when they are due (January for (b)(6) February for (b)(6) and put an Out of Use sticker on that BSC until the new ones come in. Then schedule a few days with the lab to take out old one, install new one and certify. ○ We should have the BSCs by mid-February, so we would probably plan (b)(6) (b)(6) for end of February so we can do annual shutdown and BSC replacement at once and not have to take suite down twice (as that's our busiest suite)
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ None.

Other issues	▪ None.

Next Meeting:

- Date: 12/15/16
- Place: Bldg A Seminar Room
- Time: 1:00 PM

RML Biosafety Committee Meeting
October 20, 2016
Biosafety Officer/Responsible Official Report

1) Requests approved by BSO since last meeting:

a) *Pathogen Registration Documents*

i) *Feldmann (LV)*

(a) ***HPRD-12-143****: Coronaviruses*

(a) *Add subcutaneous and intramuscular routes of inoculation in rabbits*

ii) *Peterson (LPVD)*

(a) ***PRD-16-184****: Zika virus*

(a) *Add intravaginal route of inoculation in mice.*

3) ***New requests approved by committee via electronic review:***

i) *None*

4) ***New requests***

a) *Pathogen Registration Documents*

i) ***New***

(a) *Feldmann (LV)*

(a) ***PRD-16-193:*** *Porcine Respiratory and Reproductive Syndrome Virus (PPRSV)*

ii) ***Amend***

(a) *Steele-Mortimer (LB)*

(a) *HPRD-12-44: Salmonella typhimurium infection of primary human macrophages*

(i) Add two animal species

b) *Registration Documents for Recombinant DNA Experiments*

i) ***New***

(a) *Bloom (LV)*

(a) ***RD-16-451:*** *CRIPSR gene knock-out and plasmid-based over-expression for studying vector-borne flavivirus biology*

ii) ***Amend***

(a) *Steele-Mortimer (LB)*

(a) ***RD-15-108****: Salmonella Host Cell Interactions*

(i) Addition of suicide vectors for Salmonella

iii) *Standard Operating Procedures*

(a) ***Update***

(a) ***Bosio/Standard Operating Procedures for West Nile virus***

(i) add SP-WNV-3: Removal of Specimens for Fluorescence, Immunofluorescence, Histopathology, Immunohistopathology, and Flow cytrometry

(b) *BSL-4-28-56: Husbandry Procedures for Bats in Level 4 Biocontainment*

RML Biosafety Committee Meeting
October 20, 2016
Biosafety Officer/Responsible Official Report

(i) General updates

5) ***Animal Study Protocols Review***

Title	***Associated PRD***	***Associated RD***	***Reviewer***
Evaluation of viral variants of La Crosse virus (LACV) and Zika virus (ZIKV) that mediate neuroinvasion (LACV) and placental crossing (ZIKV)	*12-103 (La Crosse virus) 16-184 (Zika virus)*	*NA*	*B. Anderson*
Role of macrophages/monocytes in Ebola virus pathogenesis in mice	*NA*	*NA*	*N. Hoe*
Comparison of two different Nipah viruses in African green monkeys	*13-91 (Nipah virus)*	*N/A*	*M. Brose*
Establishment of a mouse model for Lassa virus infection	*13-94 (Lassa virus)*	*N/A*	*N. Hoe*
Production of Antibodies in Rabbits	*12-143 (Coronavirus)*	*N/A*	*B. Anderson*
Production of rabbit antibody against K. pneumoniae capsule	*NA*	*NA*	*N. Hoe*
Using intravital microscopy to examine the dissemination of Salmonella Typhimurium in a mouse model of infection.	*12-44 (Salmonella typhimurium)*	*15-106*	*B. Anderson*

6) ***Biosafety Training Performed – Becky Anderson, Megan Morgan***

Type of Training	***Number of Sessions***	***Number of Employees Trained***
Select Agent Initial	***1***	***1***
BSL-3 Visitor	***1***	***1***
BSL-3/4 for Support Personnel	***1***	***1***
BSL-4 Annual Refresher	***1***	***1***
BSL-4 Laboratory Biosafety	***6***	***1***
BSL-3 Laboratory Biosafety	***2***	***2***
Biosafety Brief	***1***	***LV/LZP***

7) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
a) *Biological Incident Report:*
   i) *Needlestick with exposure to Salmonella enterica serovar Typhimurium*

8) ***Select Agent Issues***
a) *Receive close-out letter for January, 2014 DSAT inspection*

9) ***Other Issues***
a) *Evaluation of 2-person work in 4-ft. BSCs*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 01/19/17
Meeting Time: 1:04 PM **Adjourned:** 1:55 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Kevin Mora	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Karin Peterson	☐	☒
Becky Anderson (EO)	☐	☒	Heinz Feldmann (EO)	☐	☒	Dana Scott	☐	☒
Alan Applebury	☐	☒	Nancy Hoe	☒	☐	Alexandra Scranton	☐	☒
Chris Bosio	☐	☒	JR Iman	☐	☒			
Marshall Bloom (EO)	☒	☐	Clay Jarrett	☒	☐			
Teresa Borino	☐	☒	Josh Kellar (EO)	☐	☒			
Megan Brose	☒	☐	Scott Kobayashi	☒	☐			
Carol Calderwood	☐	☒	Jamie Lovaglio	☒	☐			
Marcie Caldwell (EO)	☐	☒	Andrea Marzi	☒	☐	Alternate for C. Calderwood:		
Paul Carlson	☒	☐	Alida Merritt	☐	☒	(b)(6)	☐	☒

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 11/17/16 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** ▪ Nancy Hoe pointed out that on page 5, item 4 on the top of the page, 4th line states that suicide genes include vibrio toxins, this should be changed to clarify that it is not cholera toxin. Change the wording to, "HigB1, the toxin component of the vibrio cholera toxin/anti-toxin system". ▪ Sue Priola recommended changing on page 6, item 6, the 3rd bullet, in the last sentence it states "disinfectant needs to be soaked prior . . ." , should change "disinfectant" to "grate." Action: Meeting minutes for 11/17/16 were unanimously approved with the above modifications.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment) ▪ Hasenkrug (LPVD) ▪ **PRD#12-104 Amend: Human Blood and Body Fluids (HBBF)** ▪ Nancy Hoe presented the risk assessment. The PRD amendment is for the addition of blood and tissues from non-human primates (NHPs). The proposed studies are to stimulate NHP cells with different interferon subtypes to determine how NHP cells respond in terms of their induction of interferon stimulating genes. Following stimulation, the RNA from the cells will be subjected to PCR analysis. The lab hazards include accidental needle sticks or splashes because NHP fluids can transmit Herpes B virus. NHPs can be infected and have no or only mild symptoms, herpes B virus in humans can cause severe, fatal disease. Disease onset in humans typically occurs within a month of exposure, although the actual incubation period can be a little as 3 to 7 days. Symptoms of B virus include skin lesions and aches and pains, flu-like symptoms. Treatment is with antiviral therapy. The infectious dose in unknown. The typical route of transmission is through a bite or scratch from an infected NHP. ▪ Nancy Hoe pointed out that the precautions that we normally add to blood borne pathogen registrations need to be added to the recommendation section. The recommendations section should also include the following statement, "Eye protection must be worn for procedures with the potential for splashes." ▪ Nancy Hoe also added that a bite/scratch kit must be in place in the lab prior to starting work with NHP material. This statement should also be added to the recommendations section. ▪ BSL-2 is appropriate for work with NHP blood and tissues. ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#12-104 Amend** with minor modifications: 1. Add to the recommendations section: a. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Blood borne Pathogens, must have access to and be familiar with the RML exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at X59755. b. Eye protection must be worn for procedures with the potential for

	splashes. c. Bite/scratch kit must be in place in the lab prior to starting work with NHP material.
Item 2:	**Working Group Summary** ▪ Sue Priola reviewed the Working Group summary with the committee. Bob Heinzen, Clay Jarrett, and Karin Peterson were the working group members that reviewed the inactivation method from Catharine Bosio's lab. ▪ The Bosio lab tested the ability of 100% methanol to inactivate West Nile virus infected cells. They used a very high titer of virus in a cell based assay. They showed in two different experiments that all the virus was inactivated. ▪ The only request the Working Group made was to have the Bosio lab make sure the protocol matched the wording in the validation study. ▪ See summary attached. Action: The committee unanimously approved *100% methanol fixation of West Nile virus infected cells* validation studies as written.
Item 3:	**Standard Operating Procedures: (b)(6) West Nile Virus, SP-WNV-1 General Laboratory Practices (Update)** ▪ Sue Priola informed the committee that the WNV SOP was updated to include the methanol fixation procedures that were reviewed by the IBC Working Group. ▪ The only change to the SOP was in Section 3.1 on page 6, the Working Group had the Bosio lab add that they flood the entire plate and spaces between the wells with fixative as well as in the wells. ▪ There were no additional comments or concerns. Action: The committee unanimously approved (b)(6) **West Nile Virus, SP-WNV-1 General Laboratory Practices (Update)** as written.
Item 4:	**Standard Operating Procedures: (b)(6) *F. tularensis*, BSL3-C-3 Equipment Operation (Update)** ▪ Nancy Hoe informed the committee that the SOP was updated for the use of the Seahorse Analyzer for mitochondrial respiration in (b)(6) They were going to use the Prep Station as a non-CO2 incubator, but they found that they had one in their lab so they no longer want to use the Prep Station. ▪ Nancy Hoe pointed out in Section 4.7 at the end of the sentence it should state, "transfer to (b)(6) instead of "transfer to SeaHorse XFe96 analyzer" because it is repetitive with the following bullet.

	▪ There were no additional comments or concerns. Action: The committee unanimously approved (b)(6) **BSL-3 *F. tularensis*, BSL3-C-3 Equipment Operation (Update)** with minor modifications: 1. Change Section 4.7 to state, "transfer to (b)(6) instead of "transfer to SeaHorse XFe96 analyzer".
Item 5:	**Standard Operating Procedures: SOP# 2/3-28-01 Handling Field Collected Fluid Blood and Tissue Samples (Update)** ▪ Nancy Hoe informed the committee that this SOP is associated with the field sample processing room. In order to receive these samples, they need to get an import permit from CDC to import the samples. The CDC Permit Office will be inspecting this room as they have the right to do at any time. There are minor updates throughout. They updated the donning and doffing PPE section to accurately reflect what they do in which room. On page 6 they clarified that they will use a homogenizer within the BSC. ▪ They also explained that waste will be taken back into the (b)(6) which is directly adjacent to it. Alex Scranton submitted questions to Sue Priola by email. She stated that 6.6.A. might be missing some words that make this section a little ambiguous. Nancy Hoe informed the committee that it should read, ". . . work should be suspended through the shutdown unless determined that it is appropriate to continue work by the Lab Chief of the MCL, the Containment Suite Manager, the IRF Biosafety Manager, and the Responsible Official". ▪ Nancy Hoe pointed out that on D.4. it should state "cracks or leaks" instead of inspected for "good condition". ▪ Nancy Hoe noted on page 7 that they wanted to remove "Biological Spill" from the do not enter sign. They should leave the "Biological Spill" part unless they have good reason to delete it. ▪ On page 9, Section 6.9.D. the last sentence should have "any dedicated" added before Tyvek gowns. ▪ Sue Priola noted that there were some minor typos that will be submitted for changes. ▪ There were no additional comments or concerns. Action: The committee unanimously approved **SOP# 2/3-28-01 Handling Field Collected Fluid Blood and Tissue Samples (Update)** with minor modifications: 1. Change 6.6.A. to state, "" ". . . work should be suspended through the shutdown unless determined that it is appropriate to continue work by the Lab Chief of the MCL, the Containment Suite Manager, the IRF Biosafety Manager, and the Responsible Official".

	2. Update 6.5.D.4. to state "cracks or leaks" instead of inspected for "good condition". 3. On page 7, do not delete Biological Spill from the do not enter sign. 4. On page 9, Section 6.8.D. the last sentence should have "any dedicated" added before Tyvek gowns. 5. Fix minor typos.
Item 6:	**Standard Operating Procedures: SOP# 4-28-38 Husbandry Procedures for ferrets in Level 4 biocontainment (Update)** ▪ Nancy Hoe informed the committee that the SOP was updated to include mink. They also changed general language sections to make them more consistent with other SOPs. They also added sections to combine into one SOP for ferret/mink so we reduce the total number of documents. SOPs 4-28-39 and 4-28-40 can be inactivated after this information is added to this SOP. ▪ Sue Priola noted that there were minor typos and she submitted them so they can be updated. ▪ There were no additional comments or concerns. Action: The committee unanimously approved **SOP# 4-28-38 Husbandry Procedures for ferrets in Level 4 biocontainment (Update)** as written.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Nancy Hoe presented the BSO report. ▪ Nancy Hoe also informed the committee that she attended the CDC Responsible Official Workshop in December. ▪ The close-out letter from OBA on the needle stick with exposure to *Salmonella enterica* serovar typhimurium was received. ▪ The recent GAO engagement for High Containment Laboratories: Comparative Oversight Models regarding the Federal Select Agent Program. Nancy Hoe summarized the questions they asked and the answers provided. ▪ Megan Brose presented the biological incident report on Salmonella typhimurium. The report was submitted to OBA. The IBC had no additional recommendations or changes. ▪ Nancy Hoe informed the committee that the FDA banned the use of powdered gloves.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ Regarding the needle stick incident that was discussed at the November 17, 2016 IBC meeting, one result was to switch BSC's from 4ft to 6ft, we now have

	the funding approved and should be getting them from LabConoco. ▪ There will be a crane in back of (b)(6) tomorrow so please stay away from that area. ▪ There was a thumb laceration in an autoclave room this week. Megan Brose will be investigating the incident. ▪ The regional referral hospital drill with St. Patrick Hospital in December went well. ▪ Influenza cases in Ravalli County are above normal, so please remind employees to stay home if they are sick. ▪ DOL annual report was received last week, Paul Carlson will get that submitted soon. ▪ Bureau of Labor statistics focused on guard employees, so they will be under the microscope as to what happens to them safety-wise throughout the year. ▪ The stock room is going to start carrying goggles, Paul Carlson will send out an email to RML campus.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ BSL-3 annual shutdowns are spread out between now and April and will begin next week with (b)(6) Megan Brose will update and send out the entire schedule this week. ▪ The (b)(6) (b)(6) annual shutdown is finishing up this week, everything went very well. ▪ (b)(6) (b)(6) lab shutdown is scheduled to start at the end of the month.
Report	**Associate Director Report/Marshall Bloom** ▪ (b)(6) ▪ (b)(6) ▪ Every 2 years we have to send out list of all level 4 agents along with signs and symptoms of disease to all doctors, naturopaths, osteopaths in Ravalli County. Marshall Bloom updated the list and sent it out.

Around the room	▪ Sue Priola informed the committee that JR Iman is no longer a commissioner so we will need to find another replacement, Sue Priola will email Marshall Bloom to follow up. ▪ Paul Carlson said the BMBL is going to be reviewed for 6th edition, Nancy Hoe is reviewing the Biosafety sections, (b) (6) nd LPVD will review the prion section.

Other issues	▪ None.

Next Meeting:

- Date: 2/16/17
- Place: Bldg A Seminar Room
- Time: 1:00 PM

RML Biosafety Committee Meeting
January 19, 2017
Biosafety Officer/Responsible Official Report

1) ***Requests approved by BSO since last meeting:***
   a) *Pathogen Registration Documents*
   b) *Standard Operating Procedures*
      i) ***Update***
         (a) ***SOP#4-28-54:*** *Husbandry and manipulation for rabbits in level 4 biocontainment*
            (a) *add anesthesia procedures from SOP#4-28-39 and recapture procedure from SOP#4-28-40*
         (b) ***SOP#4-28-55****: Husbandry and manipulation of sheep and goats in level 4 biocontainment*
            (a) *General changes to make this SOP consistent with the other MCL husbandry SOPs. No procedural changes.*
      ii) ***Inactivate***
         (a) ***SOP#4-28-39 and 4-28-40***
            (a) *procedures now included in 4-28-54*
3) ***New requests approved by committee via electronic review:***
      i) *None*
4) ***New requests***
   a) *Pathogen Registration Documents*
      i) ***Amend***
         (a) *Hasenkrug (LPVD)*
            (a) *PRD-12-104: Production of humanized mice*
               (i) Add NHP blood and tissue
   b) *Working Group Summaries*
      i) *Inactivation of West Nile Virus in tissue culture using fixation in 100% methanol*
   c) *Standard Operating Procedures*
         (a) ***Update***
            (a) ***Bosio/Standard Operating Procedures for Francisella tularensis***
               (i) BSL-3-C-3: Equipment Operation
                  1. Update procedures for Seahorse XFe96 analyzer
            (b) ***Bosio/Stand Operating Procedures for West Nile Virus***
               (i) SP-WNV-1: General Laboratory Practices
                  1. Add methanol fixation of cell monolayer
            (c) ***LV/SOP 2/3-28-01: Processing of Field Samples***
               (i) General updates
            (d) ***LV/SOP#4-28-38: Husbandry and manipulation of Ferrets in level 4 biocontainment***
               (i) Add mink

RML Biosafety Committee Meeting
January 19, 2017
Biosafety Officer/Responsible Official Report

5) ***Animal Study Protocols Review***

Title	*Associated PRD*	*Associated RD*	*Reviewer*
Selection of virulent mutants of Rickettsia rickettsii in guinea pigs	*14-38 (R. ricketsii)*	*NA*	*M. Brose*
A Conditional System for Inexpensive Manufacture of Attenuated Vaccines in Mice	*13-90 (Ebola virus) 13-82 (VSV)*	*15-442 15-406*	*B. Anderson*
Prion infection in transgenic mice expressing human tau	*16-190 (Mouse-adapted scrapie)*	*N/A*	*N. Hoe*
Modulation of host metabolism for protection against tularemia in mice	*13-71 (F. tularensis)*	*N/A*	*B. Anderson*
Inactivation of rodent prions in mice by reactive oxygen species	*16-190 (Mouse-adapted scrapie)*	*N/A*	*M. Brose*
Genomic Content and Virulence of Coxiella burnetii in Guinea Pigs	*13-43 (Coxiella burnetii) 13-70 (C. burnetii(exempt))*	*NA*	*B. Anderson*

6) ***Biosafety Training Performed –Megan Morgan***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
BSL-4 Visitor Training	***1***	***5***
BSL-4 Laboratory Biosafety	***1***	***1***

7) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
a) *Biological Incident Report:*
   i) *Salmonella splash to face from waste container*

8) ***Select Agent Issues***
a) *RO workshop December 6-8, 2016*

9) ***Other Issues***
a) *Closeout letter received from OBA re: Needlestick with exposure to Salmonella enterica serovar Typhimurium*
b) *GAO Engagement – "High-Containment Laboratories: Comparative Oversight Models"*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 02/16/17
Meeting Time: 1:02 PM **Adjourned:** 1:58 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Kevin Mora	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Karin Peterson	☒	☐
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Dana Scott	☒	☐
Alan Applebury	☐	☒	Nancy Hoe	☒	☐	Alexandra Scranton	☐	☒
Chris Bosio	☒	☐	JR Iman	☐	☒			
Marshall Bloom (EO)	☐	☒	Clay Jarrett	☒	☐			
Teresa Borino	☒	☐	Josh Kellar (EO)	☐	☒			
Megan Brose	☒	☐	Scott Kobayashi	☒	☐			
Carol Calderwood	☐	☒	Jamie Lovaglio	☒	☐			
Marcie Caldwell (EO)	☐	☒	Andrea Marzi	☐	☒			
Paul Carlson	☒	☐	Alida Merritt	☐	☒			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 1/19/17 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** ▪ Sue Priola pointed out a couple of minor typos. ▪ Alex Scranton submitted comments to Sue Priola by email. She pointed out in the BSO report section that "powered" gloves should be "powdered". Action: Meeting minutes for 1/19/17 were unanimously approved with the above modifications.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment)

- Steele-Mortimer (LB)
- **PRD#12-44 Amend: *Salmonella typhimurium***
- Becky Anderson presented the risk assessment. The PRD amendment is for the addition of African clinical isolates. The Steele-Mortimer lab is interested in comparing these clinical isolates with their lab strains. The two strains being added to this PRD are both members of the multi locus sequence type ST313 of *Salmonella typhimurium*. These strains are associated with invasive disease in immunocompromised people. In developed countries these infections are infrequent, however in developing countries strains frequently cause severe illness, invasive infections, and possibly even death. These strains in particular are currently circulating in Sub-Saharan Africa. Symptoms can include diarrhea, fever, and abdominal cramps 12 to 72 hours after infection. Some of these strains may be multi-drug resistant. Once the Steele-Mortimer lab can begin working with these strains, they will perform antibiotic resistance profiling and add that information to the PRD. Treatment can include antibiotic therapy depending on what the isolates are resistant to. The normal route of transmission for humans is through consuming contaminated food and water. The primary lab hazards include ingestion, parenteral inoculation, aerosol generation, and accidental needle sticks.
- BSL-2+ is appropriate for work with Salmonella typhimurium ST313 clinical isolates. Employees must be trained on the SOP. The current SOP has been updated to include additional information on the clinical isolates described in the PRD amendment. Additionally, immunocompromised persons must be warned of the risks of working with these strains.
- Nancy Hoe stated that the boiler plate language about reporting illnesses should be updated in the SOP to make it consistent with all our other SOPs.
- Nancy Hoe also pointed out that in the Biological Agents and Disease Section, it should state that these strains do not typically present with diarrhea, so it should be made clear that you may have illness without diarrhea so employees are more ready to recognize illness.
- Sue Priola noted that the USDA permit was not attached even though the PRD states that it is. It should be added.
- No animal studies were submitted, proposed, or reviewed.
- The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.

Action: The committee unanimously approved **PRD#12-44 Amend** with minor modifications:

1. Attach the USDA permit.
2. Update the SOP to include the most recent language on reporting illnesses.
3. Update the SOP to state that diarrhea may not be a symptom of these

	infections.
Item 2:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment) ▪ de Leo (LB) ▪ **PRD#13-1 Amend: *Staphylococcus aureus*** ▪ Becky Anderson presented the risk assessment. The purpose of the proposed studies are to develop a rabbit model of *S. aureus* infection. They would like to test recombinant strains that they will receive from a collaborator to determine if they can recapitulate the course of human infection and avoid the use of a high inoculum. The PRD amendment is for the addition of recombinant *S. aureus* strains. The recombinant strains the de Leo lab will use are the *S. aureus* USA 300 and Newman strains that have mutations that are expected to increase rabbit tropism of human strains. The mutations have been found in several naturally occurring *S. aureus* strains with rabbit tropism. It is believed that these mutations enabled the evolution of human strains to adapt to rabbits. The mutations that were engineered into the human strains include a nonsense mutation in the *rot* gene and a point mutation in the *dltB* genes- the rot gene (repressor of toxins) and the *dltB* gene (D-alanine lipoteichoic acid and wall teichoic acid esterification protein). *Rot* is not only a repressor, but a global regulator with both positive and negative effects on the expression of *S. aureus* genes. Treatment of abscesses usually does not need antibiotic therapy; appropriate drainage is usually sufficient. However, proper antibiotic therapy is required for more serious infections. Primary hazards are ingestion, parenteral inoculation, aerosol generation, accidental needle stick. ▪ Becky Anderson informed the committee that two dual use questions are marked yes, question A1 and 5 because they are altering the tropism of a human strain to rabbits and they are decreasing the infective dose for rabbits. The overall dual use of concern was marked no by the de Leo lab. Sue Priola questioned the committee if they had any concerns with how the questionnaire was filled out or overall dual use concerns, no one on the committee had any comments or concerns. ▪ BSL-2 is appropriate for work with recombinant strains of *S. aureus*. ▪ No animal studies were submitted, proposed, or reviewed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee (Scott Kobayashi abstained) approved **PRD#13-1 Amend** as written.
Item 3:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Feldmann (LV)

	▪ **RD#17-431**: Molecular Characterization of viral proteins of pathogenic RNA viruses ▪ Reviewers: Sue Priola, Clay Jarrett ▪ **Summary:** The RD renewal describes a system to express viral proteins from several RNA viruses the Feldmann lab studies. ▪ Sue Priola summarized the RD. This is a renewal of Hideki Ebihara's RD 14-431. When Hideki Ebihara left RML last summer, Heinz Feldmann became the PI of the registration and this is a renewal of that work. This RD renewal combines all of the previous amendments into one document and moves it from paper to PI Dashboard. The RD describes expressing individual proteins in eukaryotic and prokaryotic cells. All of the genes are less than 2/3 of the genome with the exception of one, but that is only one segment of a three segmented genome, so it is considered totally and irreversibly defective. There are no dual use concerns marked and Sue Priola had no concerns with the proposed work. No infectious viruses are used in this RD so BSL-2 is appropriate. ▪ Clay Jarrett had no additional comments or concerns. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **RD#17-431** as written. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 and BSL-3 under III-D-2-a and III-E-1 of the NIH Guidelines.
Item 4:	<u>Registration Documents for Recombinant DNA Experiments (Amendment)</u> ▪ Feldmann (LV) ▪ **RD#14-402 Amend**: Lentiviral vectors ▪ Reviewers: Karin Peterson, Dana Scott ▪ **Summary:** The RD amendment describes a new system for CRISPR. ▪ Karin Peterson summarized the RD. The amendment is to add a new system that uses lentiviral vectors to deliver guide RNAs using CRISPR. The goal of the project is to make a cell line knock out library. This cell line knock out library will subsequently be infected with various viruses listed in the RD to determine the host gene's role in the viral life cycle. ▪ Dana Scott had no additional comments or concerns. ▪ Alex Scranton questioned by email if BSL-2 was still appropriate for this amendment. She stated that the cell library will be infected with filo-, bunya-, arena-, paramyxo-, orthomyxo-, corna-, and Flaviviruses. Karin Peterson stated

	that the work described in the amendment is still BSL-2, however, when they do infect the cells with the listed viruses, the biosafety level described in the PRD should be followed. This detail is also included in the original RD. Sue Priola stated that the biosafety level of the lentiviral work and the infections should be reiterated in the recommendations section so it appears on the same page as the amendment. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#14-402 Amend** with the following minor modifications: 1. Add a statement to the Recommendations section that indicates the biosafety level for the lentiviral work and the viruses used when infecting the cell library. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-2-a of the NIH Guidelines.
	Working Group Summary ▪ Sue Priola reviewed the Working Group summary with the committee. Scott Kobayashi and Chris Bosio were the working group members that reviewed the inactivation method from Heinz Feldmann's lab. ▪ The Feldmann lab tested the ability of 100% methanol to inactivate Ebola virus infected blood smears on microscopy slides. They showed in two different experiments that all the virus was inactivated. ▪ The requests the Working Group made were to have the Feldmann lab list the specific strain of Ebola used, add a conclusions section to the validation data, and clearly state the conditions that will be used in the SOP. ▪ See summary attached. Action: The committee unanimously approved *100% methanol fixation of Ebola virus blood smears* validation studies as written.
Item 3:	**Standard Operating Procedures: SOP#4-28-58 Removal of Ebola-Infected Blood Smears fixed with Methanol (Update)** ▪ Sue Priola informed the committee that the new SOP for methanol fixation follows what the Feldmann lab validated and the working group reviewed the SOP. ▪ Alex Scranton questioned by email the order in which the steps are performed for placing samples in the Nalgene tank, logging into the dunk tank log, and adding samples to the dunk tank for removal from the lab. The committee

	discussed the steps followed and had no concerns with the current steps as written. ▪ Alex Scranton pointed out in an email that there is a typo on page 3, Section 7, bullet 2. Delete the "a" before 'select agents'. ▪ There were no additional comments or concerns. Action: The committee unanimously approved **SOP#4-28-58 Removal of Ebola-Infected Blood Smears fixed with Methanol (Update) with minor modifications:** 1. On page 3, Section 7, bullet 2, delete the "a" before 'select agents'.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Nancy Hoe presented the BSO report. ▪ Nancy Hoe informed the IBC committee of the changes to the Select Agent regulations that will be effective on March 21, 2017. The original date was February 21, 2017, but a notice just came out that gives an extra 30 days.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ With all of the ice around campus this winter, the number of slips, trips, and falls has increased. ▪ An employee that was tattooing a mouse accidentally tattooed their finger. ▪ One employee fell out of their chair while leaning over and hit the floor and received a shoulder contusion. ▪ The pop up barrier north of (b)(6) leaked hydraulic fluid into the pit. ▪ An O-ring failed on a fuel filter for the diesel tank and leaked 100 gallons into (b)(6) It was all contained within the pit. ▪ A lab employee misread 100% bleach as 10% bleach and mixed with another chemical causing a hazardous chemical release inside a vacuum system so there was no damage.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ Annual shutdowns are complete for the (b)(6) and (b)(6) ▪ The annual shutdown is currently underway for the (b)(6) ▪ We are planning the annual shutdown for the (b)(6) in March.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.

Around the room	▪ None.

Other issues	▪ None.

Next Meeting:

- Date: 3/16/17
- Place: Bldg A Seminar Room
- Time: 1:00 PM

RML Biosafety Committee Meeting
February 16, 2017
Biosafety Officer/Responsible Official Report

1) Requests approved by BSO since last meeting:

a) *Registration Documents for Recombinant Nucleic Acid Experiments*

i) *Gherardini (LZP)*

(a) ***RD-14-319***

(a) *Add intradermal and subcutaneous routes of inoculation*

3) ***New requests approved by committee via electronic review:***

i) *None*

4) ***New requests***

a) *Pathogen Registration Documents*

i) ***Amend***

(a) *Steele-Mortimer (LB)*

(a) ***PRD-12-44****: Salmonella typhimurium infection of primary human macrophages*

(i) Add 2 clinical strains of multi-locus sequence type ST313

(b) *DeLeo (LB)*

(a) ***PRD-13-1****: Evasion of innate immunity by human bacterial pathogens (S. aureus)*

(i) Addition of rabbit-tropic strains of S. aureus

b) *Registration Documents for Recombinant Nucleic Acid Experiments*

i) ***Renewal***

(a) *Feldmann (LV)*

(a) ***RD-17-431****: Molecular characterization of viral proteins of pathogenic RNA viruses*

(i) Converting RD from paper to electronic format

ii) ***Amend***

(a) *Feldmann (LV)*

(a) ***RD-14-402****: Lentiviral vectors*

(i) Add vectors to prepare genome-wide knockout cell libraries by CRISPR/Cas9 mutagenesis

c) *Working Group Summaries*

i) *Inactivation of Ebola via methanol fixation*

d) *Standard Operating Procedures*

(a) ***New***

(a) ***LV/SOP#4-28-58:*** *Removal of Ebola-Infected Blood Smears Fixed with Methanol*

RML Biosafety Committee Meeting
February 16, 2017
Biosafety Officer/Responsible Official Report

5) ***Animal Study Protocols Review***

Title	*Associated PRD*	*Associated RD*	*Reviewer*
Assessment of the role of cellular proteins during Ebola virus infection in mice	*13-90 (Ebola virus)*	*NA*	*M. Brose*
Natural host immunity and the infectious cycle of Borrelia burgdorferi	*12-24 (Borrelia burgdorferi)*	*14-308*	*N. Hoe*
The effect of maintenance bloodfeeding and time after infection on the efficiency of early phase transmission of Yersinia pestis by Oropsylla montana	*13-04 (Y. pestis)*	*15-303*	*N. Hoe*
Investigating the effect of pregnancy on acute and chronic immune responses and viral load in a model of murine retrovirus infection.	*16-187 (Friend virus)*	*N/A*	*N. Hoe*

6) ***Biosafety Training Performed –Megan Morgan, Rebecca Anderson***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
Select Agent Initial	***1***	***2***
BSL-3 Visitor	***2***	***3***
BSL-3 Laboratory Biosafety	***2***	***4***
BSL-4 Laboratory Biosafety	***7***	***3***
BSL-4 Annual Refresher	***2***	***2***

7) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
a) *Biological Incident Report:*
   i) *None*

8) ***Select Agent Issues***
a) *Updated Select Agent Regulations*

9) ***Other Issues***
a) *Closeout letter received from OBA re: Salmonella splash to face from waste container*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 03/16/17
Meeting Time: 1:02 PM **Adjourned:** 1:58 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Kevin Mora	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Karin Peterson	☒	☐
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Dana Scott	☒	☐
Alan Applebury	☐	☒	Nancy Hoe	☒	☐	Alexandra Scranton	☐	☒
Chris Bosio	☐	☒	JR Iman	☐	☒			
Marshall Bloom (EO)	☐	☒	Clay Jarrett	☒	☐			
Teresa Borino	☐	☒	Josh Kellar (EO)	☐	☒			
Megan Brose	☒	☐	Scott Kobayashi	☐	☒			
Carol Calderwood	☐	☒	Jamie Lovaglio	☒	☐			
Marcie Caldwell (EO)	☐	☒	Andrea Marzi	☒	☐			
Paul Carlson	☒	☐	Alida Merritt	☒	☐			

(P=present; A=absent)

Guests: (b)(6)

Minutes: Meeting minutes from 2/16/17 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** ▪ Sue Priola pointed out a couple of minor typos. Action: Meeting minutes for 2/16/17 were unanimously approved with the above modifications.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Feldmann (LV) ▪ **RD#14-402Amend**: Lentiviral vectors ▪ Reviewers: Bob Heinzen, Sue Priola

	▪ **Summary:** The RD amendment describes adding a method of generating both a genome-wide knockout cell library and a genome-wide cell line of activated cellular genes. It also adds new cloning vectors to the RD. ▪ Bob Heinzen summarized the RD. This amendment is an extension of last month's amendment. They will use retroviruses containing gene-traps that randomly integrate throughout the replicon. These lentiviral systems are commercially available and are not replication competent. Once the cell libraries are generated, they will do a selection with virus to see what cells escape infection and then identify the genes in those cells that were knocked out. They will use a similar approach with the CRISPR/Cas9 system to randomly activate cellular genes and then infect the cells with virus to see which cells escape death by viral infection. They will then identify the protective genes that were activated. The special Cas9 they use is engineered to alter transcription. Bob Heinzen had no concerns or dual use issues. ▪ Sue Priola agreed that there were no dual use issues with the RD and the NIH Guidelines listed are ok. Sue Priola noted that two vector maps were missing in the amendment. The Feldmann lab needs to add pCMV-Gag-Pol and pGT-Puro. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#14-402Amend** with minor modifications: 1. Add the two missing vector maps, pCMV-Gag-Pol and pGT-Puro. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a and III-D-3-a of the NIH Guidelines.
Item 2:	**Working Group Summary** ▪ Sue Priola reviewed the Working Group summary with the committee. Andrea Marzi, Dana Scott, and Karin Peterson were the working group members that reviewed the inactivation methods from Catharine Bosio's lab. ▪ The Bosio lab tested the ability of 3% paraformaldehyde (PFA) to inactivate *Francisella tularensis* (*F. tularensis*) bacterial pellets. They showed in two different experiments that all the bacteria was inactivated. The Bosio lab also tested the ability of 3% PFA to inactivate *F. tularensis* infected animal tissue homogenates that are subsequently used in cytometric bead arrays. They showed in two different experiments that all the bacteria was inactivated. ▪ The requests the Working Group made were to have the Bosio lab: a. specify in the validation experiments and the SOP that the 3% PFA was

	made in PBS 7.4. b. In the validation procedure methods section point #7, specify that the plates were washed 2x to ensure removal of residual PFA in order to reduce the chances of PFA carryover to the MMH agar plate used to measure bacterial growth. c. In the validation procedure results section point #1, insert a table summarizing the results on fixed samples. d. In 6.5.1., reference the Homogenization procedure section of the SOP, i.e. "Tissues were prepared according to SOP BSL3-C4, Section 2.7." e. Fix the numbering in 6.5.5. ▪ These changes were made to the SOP and the validation protocol. ▪ See summary attached. Action: The committee unanimously approved the Working Group recommendation that treatment with 3% PFA of bacterial cell pellets and *F. tularensis* infected animal tissue homogenate completely inactivated *F. tularensis* and approved the validation studies as written.
Item 3:	**Standard Operating Procedures: BSL-3 (b)(6) SOP, BSL-3-C-8 Inactivation of Francisella spp. (Update)** ▪ Sue Priola informed the committee that the new SOP for PFA fixation follows the procedures that the Bosio lab validated and the working group reviewed the SOP. ▪ There were no additional comments or concerns. Action: The committee unanimously approved **BSL-3 (b)(6) SOP, BSL-3-C-8 Inactivation of Francisella spp. (Update)** as written.
Item 4:	**Standard Operating Procedures: SOP#4-28-59 Use of the BD BACTEC FX40 Blood Culturing System (New)** ▪ Becky Anderson informed the committee that this is a new SOP for culturing blood in the BD BACTEC blood culture system. ▪ Sue Priola was concerned that the media bottles would tip easily and questioned if a rack could be used. (b)(6) stated that they do have racks and could easily use them. Sue Priola stated that the SOP should be updated to include using the rack. ▪ Nancy Hoe stated that after 6.g., add the following step, "Detach vacutainer adapter/syringe from the bottle." ▪ Nancy Hoe pointed out that in 6.j., add "remove from BSC" after "Disinfect the inoculated media bottles with 70% EtOH. . . ".

	▪ Nancy Hoe also noted that after 7.v., add the following step, "Wipe down plates with 70% EtOH and remove from BSC." She also stated stated that 7.v. should be reworded to the following, "Transfer the inoculated agar plates in a secondary container to appropriate incubators for sub-culturing". ▪ Bob Heinzen questioned what the Feldmann lab was looking for in these samples. (b)(6) stated that they will be screening blood from human patient samples from Liberia, they expect that during Ebola infection there is gut translocation of bacteria so they expect to find skin or gut bacteria. Nancy Hoe stated that if they want to take any of the bacterial samples out of the BSL-4, they will need to validate the inactivation procedures on Gram positive and Gram negative bacteria. ▪ The group discussed the need to vent the bottles additionally to relieve built up pressure or to be able to add more Microchem at the end of the experiment. The committee agreed that there is no concern with the way the SOP is written and the current proposed procedures. ▪ There were no additional comments or concerns. Action: The committee unanimously approved **SOP#4-28-59 Use of the BD BACTEC FX40 Blood Culturing System (New)** with minor modifications**:** 1. Add to Section 6.b., "place the blood culture media bottles in a rack". 2. After Section 6.g., add the following step, "Detach vacutainer adapter/syringe from the bottle." 3. In 6.j., add "remove from BSC" after "Disinfect the inoculated media bottles with 70% EtOH. . . ". 4. After 7.v., add the following step, "Wipe down plates with 70% EtOH and remove from BSC." 5. Section 7.v. should be reworded to the following, "Transfer the inoculated agar plates in a secondary container to appropriate incubators for sub-culturing".
Item 5:	**Irradiator Turntable Issues:** ▪ Nancy Hoe informed the committee that the irradiator has recently had problems with the turntable not functioning properly. JL Shepherd no longer makes the replacement parts so the Biomed Technician had to do some modification to the turntable motor. This was outside the chamber so no NRC approval was necessary. Nancy Hoe informed Heinz Feldmann that no irradiation for inactivation could occur while the turntable was not working. Heinz Feldmann questioned if it was necessary to stop irradiating samples until the turntable was fixed. Nancy Hoe wanted the IBC to discuss this issue and determine how to proceed if/when the turntable is out of service. Nancy Hoe read from the CDC DSAT Guidance document on inactivation that, "If there is any deviation or modification to an inactivation or select agent removal

	procedure that was previously validated on-site, the entity should revalidate the procedure under the new conditions to ensure the procedure still achieves the appropriate result". Nancy Hoe also read excerpts from the Office of Inspector General's "Evaluation of DoD Biological Safety and Security implementation" as well as from the "Executive Summary: AR 15-6 Investigation Report- Individual and Institutional Accountability for the Shipment of Viable *Bacilllus Anthracis* from Dugway Proving Ground". In the incidents that involved Dugway Proving Ground, the facility sent spores to outside labs that were irradiated, but still contained live bacteria in them. CDC DSAT shut Dugway Proving Grounds down and many people were put on prophylaxis antibiotics. From the reports, it was noted that many people knew of the various problems with the irradiator but did nothing about the issues and continued sending samples out. One of the relevant issues to RML is that the turntable at Dugway did not work. Nancy Hoe stated that sample inactivation using an irradiator without a working turntable was similar to the sample inactivation issues that Dugway Proving Grounds had and that, if we want to irradiate samples without a working turntable at RML, then the change in procedure needs to be revalidated. ▪ Bob Heinzen asked if they could use dosimeters to check the dose. (b)(6) (b)(6) stated that yes, they can put dosimeters all over the chamber with the turntable on and off to make sure the samples are receiving a consistent dose. ▪ Sue Priola asked how the samples are prepared. Andrea Marzi stated that they are prepared in 2 mL Starstedt tubes, 8 to 12 samples per pack and 6-8 packs per run which are then placed on dry ice on the turntable. Sue Priola asked where the dosimeters were placed during a run and if they were placed with the samples in the container. (b)(6) stated that they can't put the dosimeters in the container because the dry ice inhibits the dosimeters from working. They have used sugar instead of dry ice as a surrogate because it has the same density. ▪ Alida Merritt stated that as a community member she feels you must validate inactivation of the samples without a turntable. She stated that it is the process that matters, not just the dosage that the samples receive. Dana Scott agreed with Alida Merritt, the process is what you validate, not just the outcome. ▪ Andrea Marzi asked if the Feldmann lab could validate only one virus instead of all of them. Sue Priola stated that they could use one virus if it is the one that is most resistant to inactivation and if they state why it is representative and appropriate as a sample to validate the inactivation protocol. The IBC agreed with this approach. (b)(6) could also use the dosimetry system to test the difference between having the turntable on versus off. The committee agreed that this work must be performed, IBC reviewed and approved before the Feldmann lab can use the irradiator when the turntable is out of service.

Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Nancy Hoe presented the BSO report.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ Annual Safety Refresher training will be conducted in May, let Paul know if you want additional topics covered. ▪ Slips, trips, and falls have been increased over the winter months with the number one incident being slips on ice. Please be careful on campus. ▪ An incident occurred with an employee that fell in a manhole because they opened the cover, walked away, and came back and fell in. They received laceration their hands, but had no other injuries. ▪ One employee received a splash to the eye while not wearing safety glasses. They were mixing disinfectant into a pump sprayer and a little bit of disinfectant splashed into their eye. Employees are reminded to wear safety glasses whenever working with chemicals and there is a potential for splashes.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ The BSL-4 annual shutdown is almost complete. ▪ The next BSL-3 shutdown will be next week in the (b)(6) .
Report	**Associate Director Report/Marshall Bloom** ▪ Nothing to report.
Around the room	▪ None.

Other issues	▪ None.

Next Meeting:

- Date: 4/20/17
- Place: Bldg A Seminar Room
- Time: 1:00 PM

RML Biosafety Committee Meeting
March 16, 2017
Biosafety Officer/Responsible Official Report

1) Requests approved by BSO since last meeting:

a) *Registration Documents for Recombinant Nucleic Acid Experiments*

i) *Gherardini (LZP)*

3) ***New requests approved by committee via electronic review:***

i) *None*

4) ***New requests***

a) *Registration Documents for Recombinant Nucleic Acid Experiments*

i) ***Amend***

(a) *Feldmann (LV)*

(a) ***RD-14-402****: Lentiviral vectors*

(i) Add additional method to generate genome-wide knockout cell library: retroviral gene-trap

(ii) Modification of the previously-approved CAS 9 system

(iii) KBM7 and haploid cells to the list of cells

(iv) Vectors and guide RNA library plasmid

b) *Working Group Summaries*

i) *Francisella tularensis: Fixation of bacterial pellets and infected tissue homogenates with 3% paraformaldehyde*

c) *Standard Operating Procedures*

(a) ***Updated***

(a) ***Francisella tularensis BSL-3 SOP***

(i) BSL3-C-8: Inactivation of Francisella spp.

(b) ***New***

(a) ***LV/SOP#4-28-59:*** *Use of BD BACTEC FX40 Blood Culturing System*

5) ***Animal Study Protocols Review***

Title	***Associated PRD***	***Associated RD***	***Reviewer***
Temporal and dose-dependent transcriptional, proteomic, metabolic and virological profile in a MERS-CoV mouse model	*12-143 (MERS-CoV)*	*NA*	*M. Brose*
Evaluating the therapeutic potential of GS-5734 against Nipah virus infection in the African green monkey model	*13-91 (Nipah virus)*	*NA*	*M. Brose*
Adaptation of human derived, genetic prion diseases (Y226X, Q227X, and G131V) to transgenic mice	*14-166 (human prion agents)*	*NA*	*B. Anderson*
Tracking bats with GPS to elucidate their role in the zoonotic ecology of EBOV	*NA*	*N/A*	*N. Hoe*

RML Biosafety Committee Meeting
March 16, 2017
Biosafety Officer/Responsible Official Report

Title	***Associated PRD***	***Associated RD***	***Reviewer***
Comparative analysis of virulence and pathogenicity of Salmonella Typhimurium clinical isolates in various mouse strains.	*12-44 (Salmonella enterica serova Typhimurium)*	*NA*	*B. Anderson*
Generation of monoclonal antibodies against Crimean Congo Hemorrhagic Fever Virus	*13-82 (VSV)*	*15-404 17-431*	*B. Anderson*
The role of Arterivirus co-infection in the pathogenesis of Reston Ebola Virus in swine	*13-90 Ebola virus) 16-193 (PRRSV)*	*NA*	*N. Hoe*

6) ***Biosafety Training Performed –Megan Morgan, Rebecca Anderson***

Type of Training	***Number of Sessions***	***Number of Employees Trained***
Select Agent Initial	***1***	***1***
BSL-3 Visitor	***2***	***3***
BSL-3 Laboratory Biosafety	***1***	***1***
BSL-4 Laboratory Biosafety	***6***	***2***
BSL-4 Annual Refresher	***2***	***2***

7) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
a) *Biological Incident Report:*
i) *None*

8) ***Select Agent Issues***
a) *MCL Annual DSAT inspection: April 4-13th*

9) ***Other Issues***
a) *none*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 04/20/17
Meeting Time: 1:02 PM **Adjourned:** 2:20 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Kevin Mora	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Karin Peterson	☒	☐
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Dana Scott	☒	☐
Alan Applebury	☐	☒	Nancy Hoe	☒	☐	Alexandra Scranton	☐	☒
Chris Bosio	☒	☐	Chris Hoffman	☐	☒			
Marshall Bloom (EO)	☐	☒	Clay Jarrett	☒	☐			
Teresa Borino	☒	☐	Josh Kellar (EO)	☐	☒			
Megan Brose	☒	☐	Scott Kobayashi	☒	☐			
Carol Calderwood	☐	☒	Jamie Lovaglio	☒	☐			
Marcie Caldwell (EO)	☐	☒	Andrea Marzi	☐	☒			
Paul Carlson	☐	☒	Alida Merritt	☐	☒			

(P=present; A=absent)

Guests: (b)(6)

Minutes: Meeting minutes from 3/16/17 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** ▪ Sue Priola pointed out a couple of minor typos. ▪ Bob Heinzen noted in Item 2, *F. tularensis* was referred to as a virus instead of a bacteria, this should be corrected. Action: Meeting minutes for 3/16/17 were unanimously approved with the above modifications.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New)

- Bosio (LB)
- **PRD#17-194: *Mycobacterium tuberculosis, Mycobacterium bovis* strain BCG**

- Becky Anderson presented the risk assessment. The goal of the Bosio lab is to understand the features of innate and adaptive immunity to *M. tuberculosis* that result in control of disease and pathology. They will study various parameters of the immune response *in vitro* as well as perform *in vivo* studies with vaccinated or naïve mice challenged with virulent *M. tuberculosis*. Symptoms of *M. tuberculosis* infection depend on where in the body the bacteria are growing. *M. tuberculosis* usually grow in the lungs (pulmonary TB), tuberculosis in the lungs may cause symptoms such as:
    - a bad cough that lasts 3 weeks or longer
    - pain in the chest
    - coughing up blood or sputum (phlegm from deep inside the lungs)
  - Other symptoms of TB disease include
    - weakness or fatigue
    - weight loss
    - no appetite
    - chills
    - fever
    - sweating at night
- BCG, or bacille Calmette-Guerin, is a vaccine for tuberculosis. Many foreign-born persons have been BCG-vaccinated. BCG is used in many countries with a high prevalence of tuberculosis to prevent childhood tuberculous meningitis and miliary disease. However, BCG is not generally recommended for use in the United States because of the low risk of infection with *Mycobacterium tuberculosis*, the variable effectiveness of the vaccine against adult pulmonary TB, and the vaccine's potential interference with tuberculin skin test reactivity. Common side effects can include: soreness at the injection site and a raised blister. Less common side effects can include: headache and a high temperature, a small ulcer which develops from the blister at the injection site two to six weeks after injection, or an enlarged lymph node near the injection site.
- The most serious complication of BCG vaccination is disseminated BCG infection. BCG osteitis affecting the epiphyses of the long bones, particularly the epiphyses of the leg, can occur from 4 months to 2 years after vaccination. Fatal disseminated BCG disease has occurred at a rate of 0.06–1.56 cases per million doses of vaccine administered; these deaths occurred primarily among immunocompromised persons.
- Transmission of *M. tuberculosis* can be nosocomial or airborne (inhalation of droplet nuclei carrying *M. tuberculosis*, which are generated when patients with tuberculosis cough). Other modes occur through percutaneous injury, bites, fomites, and aerosols from infected lab animal bedding. The exposure to

	laboratory generated aerosols is the most important hazard to avoid. *M. tuberculosis* infections can be treated by taking several drugs for 6 to 9 months. There are 10 drugs currently approved by the FDA for treating TB. Of the approved drugs, the first-line anti-TB agents that form the core of treatment regimens are: isoniazid (INH), rifampin (RIF), ethambutol (EMB), pyrazinamide (PZA). *M. bovis* BCG can be worked with at BSL-2. *M. tuberculosis* strains can be worked with at BSL-3. All personnel listed on the PRD must be enrolled in the *M. tuberculosis* surveillance program. Immunocompromised persons must be advised of the risks of working with this agent. Becky Anderson stated that the precaution for immunocompromised persons needs to be added to the recommendations section. ▪ Nancy Hoe pointed out that the Bosio lab's BSL-2 lab space is not included on the registration and it should be. She also noted that in the Recommendations section, "BSL-2" should be removed from the following sentence, "*Mycobacterium bovis* strain BCG will be used in (b)(6) at BSL-2/ABSL-2." ▪ Bob Heinzen asked if the Bosio lab personnel will receive the TB skin test prior to the start of work. (b)(6) said they will, many have employees already had theirs completed. This is all part of enrollment in the *M. tuberculosis* surveillance program. ▪ Sue Priola questioned if any of the strains will be drug resistant. Becky Anderson will follow-up with Catharine Bosio to determine if there are drug resistant strains. ▪ Sue Priola informed the committee that the IBC will only approve the PRD for work with *M. bovis* strain BCG today. This will allow the Bosio lab to obtain BCG and begin performing validation testing of disinfectants using BCG as a surrogate for *M. tuberculosis*. Once the Bosio lab completes their validation testing they will submit the data for IBC review and update the BSL-3 Suite C SOP to include specific *M. tuberculosis* procedures and disinfectants. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved (Chris Bosio abstained) **PRD#17-194** with minor modifications: 1. Add precautions for immunocompromised persons to the Recommendations section. 2. Delete "BSL-2" from the recommendations section that lists (b)(6) 3. Add Bosio BSL-2 lab room numbers to Associated Laboratories section. 4. Determine if there are any drug resistant *Mycobacterium tuberculosis* strains.
Item 2:	<u>Registration Documents for Recombinant DNA Experiments (Renewal)</u>

	▪ Feldmann (LV) ▪ **RD#17-410**: Adenovirus vaccine vector ▪ Reviewers: Chris Bosio, Clay Jarrett ▪ **Summary:** The RD renewal describes an adenoviral system to express viral proteins from several RNA viruses the Feldmann lab studies. ▪ Chris Bosio summarized the RD. This is a renewal of previously approved work with adenoviral vectors. Everything in the renewal is the same except for the addition of chimp adenovirus (ChAd), they will use it to compare to the other approved adenoviral vectors to determine efficacy. The ChAd looks promising for use in humans because it alleviates the problems with pre-existing immunity to human Adenovirus. Chris Bosio stated that all the NIH Guidelines look good. There were no dual use concerns. ▪ Clay Jarrett had no additional comments or concerns. ▪ Sue Priola questioned if Section III-D-3-a of the NIH Guidelines should be added to the Eukaryote Cells section. The committee agreed that it should be added. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **RD#17-410** with minor modifications: 1. Add Section III-D-3-a to the Eukaryote Cells section. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a and III-E-1 of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a and III-D-3-a of the NIH Guidelines.
Item 3:	<u>Registration Documents for Recombinant DNA Experiments (Amendment)</u> ▪ Feldmann (LV) ▪ **RD#15-404 Amend**: VSV Replication competent ▪ Reviewers: Dana Scott, Sue Priola ▪ **Summary:** The RD amendment describes adding Zika virus to the list of viruses being studied. ▪ Dana Scott summarized the RD. The RD amendment by the Feldmann lab is to add Zika virus to the list of viruses being studied in the original RD. There are already several amendments to the RD, all of which are included in the submission. There were no dual use concerns with the addition of this work. ▪ Sue Priola stated that the addition of Zika virus is fine because they will still be working with less than two-thirds of the viral genome.

	▪ Nancy Hoe questioned if the Feldmann lab needs to update the list of ORFs. The committee agreed that was not necessary. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#15-404 Amend** as written. Research using prokaryotic hosts is approved at BSL-2 under section III-D-1-a and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-3-a and III-D-1-a of the NIH Guidelines.
Item 4:	**Standard Operating Procedures: SOP#4-28-43 Aerosol Exposure System Operation (Update)** ▪ Sue Priola informed the committee that the Feldmann lab had updated the aerosol exposure SOP to include new procedures. ▪ Megan Brose described the changes to the committee, SOP updates now include transmission caging. The general setup includes two non-human primate containment cages set up adjacent to each other with a tube containing baffles connecting them. The aerosols would be generated with the AeroMP aerosol generation system with the intent to see if non-human primates can be infected. These studies would be carried out in an animal holding room and not in a BSC like all the other aerosol exposure experiments. Megan Brose expressed the concerns that biosafety had with the current version of the SOP. The transmission caging setup was put together by (b)(6) (b)(6), it is important that the modified caging be tested with fluorescein to ensure there are no major leaks in the caging system. Biosafety also agreed that the transmission caging would need to be put in a bioBUBBLE to capture any aerosols that escape the caging unit, either during aerosol generation or when opening the cages afterwards, for non-human primate transport, cage cleaning, etc. The committee agreed that testing of the transmission caging should be conducted to ensure there are no leaks. Additionally, the committee agreed that if aerosols were being generated outside a BSC, alternative containment like bioBUBBLEs should be used. ▪ (b)(6) informed the committee that they have three experiments that plan to perform: initially, they will test particle size and viability in the transmission caging in the absence of animals, next they will test with an NHP on the right (end of the caging unit) and aerosolize virus on the left to see if they can infect the NHP on the right side, the third experiment will be to have an already infected NHP on the left and see if it infects the NHP on the right side of the caging system. The first two experiments are to prove that their caging system works and can test natural aerosol transmission. The final experiment will test natural aerosol transmission.

	▪ Nancy Hoe questioned how they were deconning the cages. (b)(6) stated that the cages will be deconned by nebulizing 70% ethanol followed by water. This is the same procedure that IRF Frederick uses on their aerosol equipment. Nancy Hoe questioned if it was effective. Becky Anderson stated that the SOP does not clearly spell out the decon step for the transmission caging. ▪ Dana Scott also questioned if the ethanol spray was effective. Dana Scott stated that he was also concerned about jumping NHPs between cages because this is the highest risk procedure RMVB does. He wants to work with (b)(6) (b)(6) o come up with a safe and effective plan to transport the NHPs, perhaps using transport boxes if LV wants to keep the NHPs awake after the aerosol procedure. (b)(6) nformed the committee that they would like to have the ability to transfer the NHPs out of the cage both awake and sedated. ▪ Nancy Hoe stated that there is so much content in the SOP that it is hard to differentiate the procedures for transmission caging from the current procedures that are performed in the biosafety cabinet. The procedures for transmission caging should be put into a new, separate SOP. ▪ There was extensive discussion with the committee on the details of how to perform the procedures safely with NHP, how to best mitigate the risks of working with aerosols in an animal room, and decon of aerosol transmission caging. The committee agreed that the SOP could not be approved the way it was written and required more refinement before it came back to the committee. Action: The committee unanimously Tabled **SOP#4-28-43 Aerosol Exposure System Operation (Update)** and requested the following: 1. Separate the transmission caging into a new SOP to make it more easy to read. The committee had a hard time distinguishing between the procedures in a BSC and the procedures for transmission caging. 2. Work with RMVB to determine NHP handling and movement between cages after aerosol challenge. 3. Fluorescein testing should be performed to ensure the there are no major leaks in the transmission caging system. 4. bioBUBBLE usage must be described in the SOP.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Nancy Hoe presented the BSO report.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ Not present.

Report	**IRF Biosafety Manager Report/Megan Brose** ▪ The (b)(6) s shutdown currently and will be complete on Monday. ▪ SEA will be onsite May 15-17 to perform annual validation testing.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ Sue Priola informed the committee that the next IBC meeting will be in the new conference room in the library. If the committee likes the new location, we will continue to meet there.

Other issues	▪ None.

Next Meeting:

- Date: 4/18/17
- Place: Library conference room
- Time: 1:00 PM

RML Biosafety Committee Meeting
April 20, 2017
Biosafety Officer/Responsible Official Report

1) Requests approved by BSO since last meeting:

i) *None*

3) ***New requests approved by committee via electronic review:***

i) *None*

4) ***New requests***

a) *Pathogen Registration Documents*

i) *New*

(a) *Bosio (LB)*

(a) ***PRD 17-194****: Mycobacterium tuberculosis (virulent strains, M. bovis BCG)*

b) *Registration Documents for Recombinant Nucleic Acid Experiments*

i) ***Renewal***

(a) *Feldmann (LV)*

(a) ***RD-17-410****: Adenoviral vectors for protein expression*

(i) Renewal includes addition of vector based on chimp adenovirus Y25 (ChAdOX1)

ii) *Amend*

(a) *Feldmann (LV)*

(a) ***RD-15-404****: Replication competent VSV*

(i) Add Zika virus

c) *Standard Operating Procedures*

(a) ***Updated***

(a) ***SOP#4-28-43: Aerosol Exposure System***

(i) Add new procedures for whole-body aerosol and transmission

5) ***Animal Study Protocols Review***

Title	***Associated PRD***	***Associated RD***	***Reviewer***
Laboratory Animal Care and Use Training Program (Small Lab Animals)	*NA*	*NA*	*N. Hoe*
MERS-CoV strain comparison in a MERS-CoV susceptible mouse model	*12-143 (MERS-CoV)*	*13-440*	*R. Anderson*
Protective efficacy of an equine antiserum treatment against Ebola virus infection in Guinea pigs	*13-90 (Ebola virus)*	*NA*	*M. Brose*
Laboratory Animal Care and Use Training Program - Rabbit	*NA*	*N/A*	*N. Hoe*
Comparative efficacy of ribavirin and favipiravir against two strains of Crimean Congo Hemorrhagic Fever Virus in mice	*13-92 (Crimean Congo Hemorrhagic Fever virus)*	*NA*	*R. Anderson*
Assessing LHF-535 as a post-exposure countermeasure to Lassa virus infection in Cynomolgus macaque	*13-94 (Lassa virus)*	*NA*	*M. Brose*

RML Biosafety Committee Meeting
April 20, 2017
Biosafety Officer/Responsible Official Report

Title	***Associated PRD***	***Associated RD***	***Reviewer***
Laboratory Animal Holding	*NA*	*NA*	*R. Anderson*
Sentinel Animal Surveillance Program	*NA*	*NA*	*R. Anderson*
Guinea pig antibodies against Coxiella burnetii and purified proteins	*13-70 (Coxiella burnetiid – exempt)*	*14-106*	*M. Brose*

6) ***Biosafety Training Performed –Megan Morgan, Rebecca Anderson***

Type of Training	***Number of Sessions***	***Number of Employees Trained***
BSL-3 Visitor	***2***	***2***
BSL-3 Laboratory Biosafety	***2***	***3***
BSL-4 Laboratory Biosafety	***1***	***1***
BSL-4 Refresher	***1***	***5***
BSL-4 Visitor Training	***1***	***3***
BSL-4 Emergency Extraction	***1***	***8***
Biosafety for Maintenance/Support Personnel	***1***	***3***

7) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
a) *Biological Incident Report:*
   i) *None*

8) ***Select Agent Issues***
a) *Preliminary results of MCL Annual DSAT inspection: April 4-13th*

9) ***Other Issues***
a) *none*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 06/15/17
Meeting Time: 1:04 PM **Adjourned:** 2:11 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☐	☒	Bruce Chesebro (EO)	☐	☒	Kevin Mora	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Karin Peterson	☒	☐
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Dana Scott	☒	☐
Alan Applebury	☐	☒	Nancy Hoe	☒	☐	Alexandra Scranton	☐	☒
Chris Bosio	☒	☐	Chris Hoffman	☐	☒			
Marshall Bloom (EO)	☒	☐	Clay Jarrett	☐	☒			
Teresa Borino	☒	☐	Josh Kellar (EO)	☐	☒			
Megan Brose	☒	☐	Scott Kobayashi	☒	☐			
Carol Calderwood	☐	☒	Jamie Lovaglio	☐	☒			
Marcie Caldwell (EO)	☐	☒	Andrea Marzi	☒	☐			
Paul Carlson	☐	☒	Alida Merritt	☒	☐			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 5/18/17 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** ▪ Nancy Hoe pointed out that JR Iman on the roster should be switched to Chris Hoffman. Action: Meeting minutes for 5/18/17 were unanimously approved with the above modifications.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New) ▪ Bosio (LB)

- **PRD#13-195: *Bordetella pertussis***
- Becky Anderson presented the risk assessment. The goal of the proposed study from the Bosio lab is to define the role of circulating versus resident CD4+ T cells in the lung for combating pulmonary infections. *Bordetella pertussis* is the causative agent of Whooping cough, which is a highly contagious acute respiratory infection. The acute respiratory disease has 3 stages: a catarrhal stage that starts with a cough and lasts about 1 to 2 weeks; a paroxysmal stage which is known for the violent coughs followed by a high pitched inspiratory whoop, lasts 2 to 6 weeks; and finally a convalescent stage in which the cough slowly decreases-this can last several weeks. The mortality rate for infants is 75%. *Bordetella pertussis* is primarily a toxin-mediated disease (pertussis toxin). The bacteria attach to the cilia of the respiratory epithelial cells, produce toxins that paralyze the cilia, and cause inflammation of the respiratory tract, which interferes with the clearing of pulmonary secretions.
- The natural route of transmission is primarily by direct contact with discharges from respiratory mucous membranes of infected persons or by inhalation of bacteria bearing droplets expelled in cough spray. The primary lab hazards include direct contact of mucous membranes and inhalation of infectious aerosols and droplets. Infections can be treated with erythromycin or TMP-SMX (Trimothoprim/sulfamethoxazole).
- Becky Anderson stated that the biosafety level for work with *B. pertussis* is BSL-2 with some additional precautions.
    - Care should be taken to minimize worker exposure to aerosols, such as working in a certified Class II BSC and using gasketed bucket covers when centrifuging infectious material.
    - Intranasal inoculation of mice must be conducted in a BSC.
    - OMS will offer a Tdap vaccination to anyone in the lab who has not received it in the last 3 years; so anyone working with *B. pertussis* or working in the same space while others are doing the work with it that cannot produce documentation or clearly remembers getting Tdap (i.e., birth of child, last 3 years).
- Becky Anderson informed the committee that the intranasal inoculation and the vaccine requirement should be added to the recommendations section.
- Alida Merritt questioned if they are required to wear any respiratory protection. Becky Anderson stated that there is no requirement to wear respiratory protection, but they are required to work with material in a BSC and used sealed centrifuge cups/rotors.
- Marshall Bloom asked if the Tdap vaccination was also for animal caretakers? Becky Anderson stated that it covers both laboratorians and animal caretakers. The recommendation should be updated to make it clear that it is for both lab and animal staff.
- Marshall Bloom also questioned if the inocula that is transported between the lab and animal facility requires any special procedures. Nancy Hoe explained

	that transporting with a sealed leak-proof container is standard for all BSL-2 labs, but that could be added to the recommendations section as a reminder. ▪ Alida Merritt questioned why the vaccination is only a recommendation and not a requirement. The committee discussed that OMS made the determination and that we cannot mandate anyone to receive the vaccine. Nancy asked if there should be any additional precautions for personnel that are not vaccinated? The committee discussed that unvaccinated individuals should be required to wear an N95 respirator as an added layer of protection. ▪ Alida Merritt asked if mice sneeze. Dana Scott said that they don't really sneeze, but as an added precaution all the inoculations are performed in a BSC and the mice are housed in microisolator cages to capture any aerosols. Cage changes are conducted in a HEPA filtered change station and bedding is autoclaved prior to being dumped. ▪ Animal experiments with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved (Chris Bosio abstained) **PRD#13-195** with the following minor modifications: 1. Add to the recommendations section: Intranasal inoculations must be conducted in a BSC. 2. Add to the recommendations section: Inocula must be double contained for transport between the BSL-2 and ABSL-2 facilities. 3. Add to the recommendations section: Anyone previously vaccinated against *B. pertussis* over 3 years ago and working directly with *B. pertussis* or working in the same space (lab or animal facility) as others performing work will be offered the Tdap vaccine by RML OMS. 4. Add to the recommendations section: Employees who have never been vaccinated and/or refuse vaccination are required to wear an N95 respirator while working with *B. pertussis*.
Item 2:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal)</u> ▪ Feldmann (LV) ▪ **PRD#17-138: Arenaviruses** (non-select agent viruses: IPPY, Mopeia, Mobala, Pichinde, Tacaribe, LCMV) ▪ Becky Anderson presented the risk assessment. Becky Anderson informed the committee that this is a renewal of the current Arenavirus PRD, with the only new work added being primary cells from Mastomys rodents. The goals of these studies are to understand the pathogenesis of Arenaviruses for vaccine and treatment development. The disease depends on the specific virus and can vary greatly in severity. IPPY & Mobala virus have not been linked to human disease. Tacaribe has low pathogenicity in primates & humans. Mopeia virus is

	closely related to Lassa virus, sharing 75% amino acid identity, and is also isolated from the same reservoir. However, Mopeia virus is naturally attenuated and nonpathogenic for humans. Pichinde virus has had asymptomatic infections reported in humans. ▪ LCMV infection in immunocompetent adults may be asymptomatic. Nearly one third of all infections are limited to a non-specific, self-limited viral syndrome with symptoms such as fever, cough, malaise, myalgia, headache, photophobia, nausea, vomiting, adenopathy, and sore throat. The illness can progress to include meningitis or meningoencephalitis, and other less common neurologic symptoms such as paralysis, sensorineural hearing loss, and Guillain-Barré type syndrome. LCMV infection is usually non-fatal, with a mortality rate of less than 1%, and recovery from even severe disease occurs without sequelae in most cases. ▪ Congenital LCMV infection can produce a spectrum of pathologic effects, from minimal to severe, depending on the developmental stage of the fetus at the time of infection. In some cases, infection may result in abortion, hydrocephalus, chorioretinitis, and/or mental retardation of the infant. The mortality rate of infants diagnosed with congenital LCMV is approximately 35%. Among survivors of congenital LCMV infection, two thirds have long-term neurologic abnormalities, including microcephaly, mental retardation, cerebral palsy, seizures, and visual impairment. ▪ The primary lab hazards include: generation of aerosols, parenteral contact, and accidental needle stick. Treatment with ribavirin has been shown to inactivate arenaviruses in vitro and may improve symptoms under clinical conditions. ▪ The containment levels include: a. IPPY-BSL-2 b. Pichinde-BSL-2 c. Tacaribe-BSL-2 d. Mopeia-BSL-3 e. Mobala-BSL-3 f. <u>LCMV : BSL-2 with additional practices</u> all work with infectious material is conducted in a biosafety cabinet, centrifugation of infectious materials must be carried out in sealed safety cups or removable rotors that can be loaded and unloaded in a biosafety cabinet. g. Women who are pregnant or are thinking of becoming pregnant are encouraged to notify the Laboratory Supervisor and the RML OMS Nurse. This is in order to assure that they are aware of any potential risks to themselves or the fetus and to determine if any additional risk reduction measures should be taken. Becky Anderson informed the committee that this statement needs to be added to the recommendations section.

	▪ No animal studies were proposed, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Andrea Marzi abstained) **PRD#17-138** with the following minor modifications: 1. Add to the recommendations section the precautions for pregnant women working with LCMV.
Item 3:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Feldmann (LV) ▪ **RD#17-418**: Molecular characterization of viral proteins of pathogenic RNA viruses ▪ Reviewers: Chris Bosio, Scott Kobayashi ▪ **Summary:** The RD renewal describes CCHFV minigenomes, virus like particles (VLPs), and reverse genetics systems. ▪ Chris Bosio summarized the RD. Chris Bosio informed the committee that this is a renewal and that most of the content was previously reviewed and approved. The purpose of this work is to study the molecular biology of CCHFV. They will be using minigenomes, VLPs, and reverse genetics. The only new elements are the addition of a pT7 vector system that is like the other approved systems. It requires multiple RNAs to function which do not overlap in their viral sequence so there is no risk for homologous recombination to produce infectious virus or replicating virus. The other new element is the V5 tag, which is a reporter tag. In the registration they mention they will perform animal studies in the future, but currently there are no animal studies attached. ▪ The NIH Guidelines were appropriate and there were no dual use concerns. ▪ Scott Kobayashi had no additional comments or concerns. ▪ No animal studies were proposed, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Andrea Marzi abstained) **RD#17-418** as written. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 and BSL-4 under III-D-1-a, III-D-3-c, III-D-2-a and III-E-1 of the NIH Guidelines.

Item 4:	**Working Group Summary** ▪ Bob Heinzen reviewed the Working Group summary with the committee. Dana Scott, Clay Jarrett, and Scott Kobayashi were the working group members that reviewed the inactivation methods from Ted Hackstadt's lab. ▪ The Hackstadt lab tested the ability of Trizol LS to inactivate *Rickettsia rickettsii*. They showed in two different experiments that all the bacteria was inactivated. ▪ The requests the Working Group made were to have the Hackstadt lab: a. Clarify in 6.4 if the tubes are wiped down prior to being stored at -80C. b. On page 24, correct 5.2.1 to 6.2.1. ▪ These changes were made to the SOP and the validation protocol. ▪ See summary attached. Action: The committee unanimously approved the Working Group recommendation that Trizol LS completely inactivated *R. rickettsii* and approved the validation studies as written.
Item 5:	**Working Group Summary** ▪ Bob Heinzen reviewed the Working Group summary with the committee. Karin Peterson, Bob Heinzen, and Chris Bosio were the working group members that reviewed the inactivation methods from Heinz Feldmann's lab. ▪ The Feldman lab tested the ability of gamma irradiation to inactivate *Coronaviruses and Orthomyxoviruses*. They showed in triplicate that all the virus was inactivated. ▪ The requests the Working Group made were to have the Feldmann lab: a. In the table, change "Minimum Dose" to "Minimum Inactivation Dose". b. In the table, change, "Required Dose" to "2X Minimum Inactivating Dose". c. Make the indicated changes in red to the following statement: *"Additionally, individual samples which have tested negative by qRT-PCR or infectivity assays can be irradiated with the Minimum Inactivating Dose at the discretion of the Chief Scientist of the MCL, and must be approved in advance."* ▪ These changes were made to the SOP and the validation protocol. ▪ Bob Heinzen informed the committee that he was concerned there was not a statement that made it clear in the SOP that the 2X Minimum inactivating dose was the standard, and that when there is no viable virus, THEN they can use the Minimum Dose. The committee agreed that a sentence should be added to

	6.15 to clarify. ▪ See summary attached. Action: The committee unanimously approved the Working Group recommendation that gamma irradiation completely inactivated *Coronaviruses and Orthomyxoviruses* and approved the validation studies with the following modification to SOP#4-28-17: 1. Add a sentence to 6.15 stating that the 2X Minimum Inactivating Dose is required unless it has been determined that there is no virus remaining by PCR or viability assay.
Item 6:	**Standard Operating Procedures: (b)(6) SOP, *Coxiella burnetti, Rickettsia spp*. (Update)** ▪ Becky Anderson informed the committee that the request made by the IBC WG have been made to the (b)(6) SOP. The procedures outlined in the SOP match the validation procedures used with Trizol LS on *Rickettsia spp*. ▪ Alida Merritt pointed out that "insure" should be changed to "ensure" in 6.4. Action: The committee unanimously approved (b)(6) **SOP, *Coxiella burnetti, Rickettsia spp*. (Update)** with the following minor modifications: 1. Change "insure" to "ensure" in section 6.4.
Item 7:	**Standard Operating Procedures: SOP#4-28-27 Removal of Specimens for Irradiator (Update)** ▪ Bob Heinzen informed the committee that the irradiation SOP was updated in response to the IBC requests described in the Working Group summary. ▪ He also noted that the sentence to clarify when the 2X Minimum Inactivating Dose is required will be added to 6.15. Action: The committee unanimously approved **SOP#4-28-27 Removal of Specimens for Irradiator (Update)** with the following minor modifications: 1. Add a sentence to 6.15 stating that the 2X Minimum Inactivating Dose is required unless it has been determined that there is no virus remaining by PCR or viability assay.
Item 8:	**Standard Operating Procedures: SOP#4-28-60 Aerosol Exposure System Operation (Update)** ▪ Bob Heinzen informed the committee that the aerosol exposure SOP was updated in response to the IBC requests and that (b)(6) and (b)(6) (b)(6) had completed the testing of the caging system that was requested by the IBC. This testing was to determine if the transmission caging was contained and did not have any detectable leaks when virus or fluorescein was

introduced into the system.

- (b)(6) and Becky Anderson described the setup for the fluorescein testing. Initial tests were set up to use the normal collison nebulizer and aerosolize fluorescein. Testing was conducted, but no fluorescein was detected inside or outside of the caging system. It was discussed that perhaps the particles were too small and/or the volume was too low to detect the fluorescein. Instead, (b)(6) used a nebulizer inside the cage that could nebulize 50 mL of fluorescein. This worked well and the fluorescein was easily visible in the caging system. Pictures and video were presented to the IBC that demonstrated this testing method. It was clear that fluorescein was covered the internal areas of the caging, but no fluorescein was detected on the exterior of the caging. All doors and seals were monitored and nothing was visually observed.
- Becky Anderson stated that the only place they could see fluorescein was on the air intake HEPA filter on the cage door. There were a few droplets that could be seen on the external side of the HEPA filter. This may have occurred because liquid droplets hit the HEPA filter from the nebulizer. This probably does not mean there was breakthrough of the filter, but she recommended performing a HEPA filter change on the door after each aerosol challenge. A filter change would not be required when natural transmission was being tested. The committee agree with this addition to the SOP.
- Nancy Hoe asked what the concentration of fluorescein was. (b)(6) stated that is was 1 g/mL. They used 50 mL three separate times with the nebulizer.
- (b)(6) then presented his results for testing with a non-Select Agent virus. This test used the normal collison nebulizer for testing conditions that they will use in their aerosol experiments. All Glass Impingers (AGI) and gelatin filters were placed on the exhaust HEPA of the blower unit and at the two sampling ports on the transmission tube. (b)(6) performed four separate runs consecutively, and continuously sampled with the AGI and gelatin filters during all four runs. After the final run, (b)(6) swabbed the caging seals and the HEPA at the air intake on the caging door. These samples were collected and analyzed by qRT-PCR. The results demonstrated that the virus was detectable within the caging system through the sample ports, but was not detected at any of the seals or either HEPA filter tested.
- Clay Jarrett was absent, but provided comments to (b)(6) by email. He asked about the transport box shown on page 12. He stated that it was hard to imagine that this box could create an airtight seal. (b)(6) stated that the lid has a foam gasket that connects the lid to the box and a clamp that holds it tightly in place. This was a commercially purchased product. The committee discussed the utility of the box and agreed that the box is only used for very short durations to transport the animal to/from the animal holding room to an

	adjacent animal holding room and the proposed box was acceptable for this use. ▪ The committee discussed that they were pleased with both methods of testing and the results of the testing. The committee also agreed that even though the testing looks good, the conclusion is still to use bioBUBBLEs during the aerosol challenge part of the experiment. The SOP was updated to include a description of bioBUBBLE usage. Action: The committee unanimously approved **SOP#4-28-60 Aerosol Exposure System Operation (Update)** with the following minor modifications: 1. Add a statement that the HEPA filter on the door of the infected cage will be changed after every aerosol challenge.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Nancy Hoe presented the BSO report. ▪ Nancy Hoe reviewed the Inspection Report received from CDC Division of Select Agents and Toxins.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ Not present.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ Completed the (b)(6) shutdown in May, this is ahead of the normal schedule.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present at close of meeting
Around the room	▪ None.

Other issues	▪ None.

Next Meeting:

- Date: 7/20/17
- Place: Library conference room
- Time: 1:00 PM

RML Biosafety Committee Meeting
June 15, 2017
Biosafety Officer/Responsible Official Report

1) Requests approved by BSO since last meeting:

a) Summer Student Projects

i) *Steele-Mortimer*

(1) (b)(6) *– identification of structural differences between wild type Salmonella enterica serovar Typhimurium SL1344 (a lab strain) and various mutants, - approved 5/30/17*

ii) *DeLeo*

(1) (b)(6) *– growth and characterization of study Klebsiella pneumoniae – approved 6/7/17*

2) ***New requests approved by committee via electronic review:***

a) *None*

3) ***New requests***

a) *Pathogen Registration Documents*

i) ***New***

(a) *Bosio (LB)*

(a) ***PRD 17-195:*** *Bordetella pertussis*

ii) ***Renewal***

(a) *Feldmann (LV)*

(a) ***PRD 17-138****: Arenaviruses (exempt)*

(i) Ippy, Mobala, Pichinde, Tacaribe, Mopeia, LCMV

b) *Registration Documents for Recombinant Nucleic Acid Experiments*

i) ***Renewal***

(a) *Feldmann (LV)*

(a) ***RD-17-418****: CCHFV minigenomes, VLPs, and reverse genetic systems*

c) *Working Group Recommendations after Review of Inactivation Validation Studies*

i) *Hackstadt:*

(a) *R. rickettsia: inactivation by Trizol*

ii) *Feldmann*

(a) *Inactivation of Bunyaviridae, Paramyxoviridae, Arenaviridae, and Filoviridae by irradiation*

(a) *Addendum: add inactivation of coronaviridae and orthomyxoviridae by irradiation*

d) *Standard Operating Procedures*

(a) ***Updated***

(a) ***SOPs Coxiella burnetii, Rickettsia spp. BSL-3***

(i) Add Trizol inactivation procedures for R. Rickettsia

(b) ***SOP 4-28-27 Removal of Specimens for Irradiator***

(i) *Add irradiation conditions for coronaviridae and orthomyxoviridae, include terms "minimum inactivating dose" and "2X minimum inactivating dose"*

(b) ***Tabled – re-submitted for review***

(a) *SOP#4-28-60: NHP Transmission Caging Operation for Aerosol Exposure*

4) ***Animal Study Protocols Review***

Title	***Associated PRD***	***Associated RD***	***Reviewer***
Development of animal infection models to study Klebsiella pneumoniae virulence and potential treatments – pilot study	*16-180 (Klebsiella pneumoniae)*	*NA*	*N. Hoe*
Crimean Congo hemorrhagic fever virus pathogenesis in TKO-humanized mice	*13-92 (CCHFV)*	*NA*	*M. Brose*
Testing the efficacy of the VSV-Marburg vaccine in STAT2 knock-out hamsters	*13-90 (MARV) 13-82 (rVSV))*	*15-404*	*R. Anderson*
Assessing the extent and duration of spirochetemia of Borrelia crocidurae following experimental inoculation of Mastomys natalensis	*14-160 (Borrelia crocidurae)*	*NA*	*R. Anderson*
The roles of macrophages/monocytes in Ebola virus pathogenesis in hamsters	*13-90 (MA-EBOV)*	*14-426*	*M. Brose*
Investigation of blood brain barrier and blood cerebrospinal fluid barrier leakage in Salmonella enterica serovar Typhimurium infected mice.	*12-44 (Salmonella typhimurium)*	*NA*	*N.Hoe*

5) ***Biosafety Training Performed –Megan Morgan, Rebecca Anderson***

Type of Training	***Number of Sessions***	***Number of Employees Trained***
Select Agent initial	*1*	*1*
BSL-3 Visitor	*2*	*6*
BSL-3 Laboratory Biosafety	*1*	*1*
BSL-4 Laboratory Biosafety	*9*	*3*
BSL-4 Refresher	*1*	*2*

6) ***Safety Audits and Inspections***

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

a) *Biological Incident Report: None*

RML Biosafety Committee Meeting
June 15, 2017
Biosafety Officer/Responsible Official Report

7) ***Select Agent Issues***
   a) *Results of DSAT MCL Annual Inspection*

8) ***Other Issues***
   a) *none*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 07/20/17
Meeting Time: 1:03 PM **Adjourned:** 2:50 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Kevin Mora	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Karin Peterson	☒	☐
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Dana Scott	☒	☐
Alan Applebury	☐	☒	Nancy Hoe	☒	☐	Alexandra Scranton	☐	☒
Chris Bosio	☐	☒	Chris Hoffman	☒	☐			
Marshall Bloom (EO)	☐	☒	Clay Jarrett	☐	☒			
Teresa Borino	☒	☒	Josh Kellar (EO)	☐	☒			
Megan Brose	☒	☐	Scott Kobayashi	☒	☐			
Carol Calderwood	☐	☒	Jamie Lovaglio	☒	☐			
Marcie Caldwell (EO)	☐	☒	Andrea Marzi	☐	☒			
Paul Carlson	☐	☒	Alida Merritt	☐	☒			

(P=present; A=absent)

Guests (b)(6)

Minutes: Meeting minutes from 6/15/17 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** ▪ No comments. Action: Meeting minutes for 5/18/17 were unanimously approved as written.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment) ▪ Peterson (LPVD) ▪ **PRD#12-103 Amend: La Crosse virus** ▪ Becky Anderson presented the risk assessment. The amendment is to add

	human plasma, serum, and cerebral spinal fluid (CSF) to the PRD. The plasma and serum samples will be analyzed for California Serogroup Orthobunyaviruses by neutralization assays or ELISA assays. The CSF samples will be analyzed for virus by real-time PCR analysis using primers specific to the different California Serogroup Viruses. The three most common blood borne pathogens that may be in the human samples include: Hepatitis B virus (HBV), Hepatitis C virus, and HIV. HBV is the most common of the three and causes a serious form of hepatitis. The symptoms include: jaundice, fatigue, abdominal pain, loss of appetite, intermittent nausea, and vomiting. It can also lead to chronic liver disease, liver cancer, and death. There is a vaccine available for HBV, the vaccine is offered free of charge at RML through the OMS Nurses. Hepatitis C virus symptoms include jaundice, fatigue, abdominal pain, loss of appetite, intermittent nausea, and vomiting. It can also lead to chronic liver disease and death. HIV is the virus that leads to AIDS. Antivirals are administered in some cases of exposure. There is a vaccine available through OMS for HBV. The primary lab hazards include accidental needle stick, parenteral inoculation, and generation of aerosols. ▪ Becky Anderson pointed out that the following wording needs to be added to the recommendations section of the PRD: All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 375-9755. ▪ BSL-2 is appropriate for work with human blood and body fluids. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **PRD#12-103 Amend** with the following minor modifications: 1. Add to the recommendations section wording for work with human blood and body fluids.
Item 2:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal)</u> ▪ Hackstadt (LB) ▪ **PRD#17-35: Chlamydia spp.** ▪ Becky Anderson presented the risk assessment. This is a renewal for the following Chlamydia strains: *C. caviae, C. muridarum, C. pneumoniae, C. psittaci.* The proposed research is focused on 1.) the cellular interactions that promote entry and intracellular growth, primarily those controlled by secreted chlamydial effector proteins and 2.) regulation of vesicular interactions of the chlamydial inclusion with the host cell by secreted

chlamydial proteins. The disease severity depends on the strain worked with.

- *C. caviae*-infects guinea pigs and causes ocular disease and conjunctivitis in guinea pigs. It is used as a model for human Chlamydial infections.
- *C. muridarum*-infects mice and hamsters, it is not known to be infectious to humans.
- *C. psittaci* infections are known as parrot disease or ornithosis because the infection can be acquired from birds, typically pet birds. Illness in humans include respiratory symptoms ranging from cough to severe chronic pneumonia. Symptoms include fever, chills, headache, myalgia, non-productive cough, difficulty breathing and GI symptoms. Infections generally last 10 to 14 days. With antibiotic treatment, the mortality rate is 1%.
- *C. pneumoniae*- causes mild pneumonia or bronchitis in adolescents and young adults. Older adults can experience more severe disease and repeated infections.
- There are 18 serovars of *C. trachomatis*, 4 cause trachoma, 5 cause lymphogranuloma venereum (LGV) and the remaining serovars cause a variety of STDs. *C. trachoma* can cause a variety of clinical diseases including genital tract infections, inclusion conjunctivitis, trachoma, pneumonia in infants and lymphogranuloma venereum (LGV).

- Chlamydia infections are sensitive to antibiotic treatment with doxycycline, tetracycline, erythromycin, and azithromycin. The primary lab hazards include accidental needle stick; direct and indirect exposure of mucous membranes of the eyes, nose, and mouth to infected fluids; infectious aerosols are also a potential source of infection.
- Nancy Hoe added that women need to be aware of the hazards of working with *Chlamydia psittaci*. This should be added to the recommendations section.
- Nancy Hoe informed the committee that the SOP should also be updated to include:
  - Add eye protection to #6 PPE section.
  - Add the other Chlamydia strains to the SOP in Section A.1.
- Sue Priola noted on page 3 of the SOP, update LICP to LB.
- BSL-2 with BSL-3 practices is appropriate for work with Chlamydia spp.
- No animal studies were submitted, reviewed, or approved.
- The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.

Action: The committee unanimously approved **PRD#17-35** with the following minor modifications:

1. Add precautions for pregnant women working with *Chlamydia psittaci* to the

	recommendations section. 2. Update the Chlamydia SOP to include: a. Add eye protection to #6 PPE section. b. Add other strains to the SOP in Section A.1. c. On page 3 of the SOP, update LICP to LB.
Item 3:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Hackstadt (LB) ▪ **PRD#17-37: *Chlamydia trachomatis*** ▪ Becky Anderson presented the risk assessment. The information was discussed at the same time as PRD#17-35 and the information is included in Item 2. ▪ Becky Anderson stated that for this PRD, for animal work with mice, all infection and control solutions will be prepared and administered by laboratory personnel wearing protective clothing, gloves, and safety goggles or a face shield. ▪ Scott Kobayashi pointed out a typo in the Synopsis section, "molecular" was spelled wrong. ▪ Nancy Hoe pointed out that (b)(6) should be added to the PRD. ▪ Nancy Hoe noted that the same changes to the SOP that were discussed for PRD#17-35 should be addressed and the updated SOP attached to this PRD as well. ▪ BSL-2 with BSL-3 practices is appropriate for work with *Chlamydia trachomatis*. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#17-37** with the following minor modifications: 1. Correct the misspelling in the Synopsis section. 2. Add (b)(6) to the PRD. 3. Add the updated Chlamydia SOP.
Item 4:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Feldmann (LV) ▪ **PRD#17-83: Human blood and body fluid** ▪ Becky Anderson presented the risk assessment. The risk assessment is the same as was presented for Karin Peterson's amendment to PRD#12-103 to add human blood and body fluid. See Item 1 for more detail.

	▪ BSL-2 is appropriate for work with human blood and body fluids. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#17-83** as written.
Item 5:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Hinnebusch (LZP) ▪ **PRD#17-05: *Yersinia enterocolitica*** ▪ Becky Anderson presented the risk assessment. The proposed studies are to use *Yersinia enterocolitica* for comparison studies with *Y. pestis* and *Y pseudotuberculosis* for *in vitro* assays and flea infections. *Y. enterocolitica* infection is characterized by enteritis, enterocolitis (especially in children), fever, watery stools, abdominal pain and acute mesenteric lymphadenitis. In rare cases, complications can include meningitis, endophthalmitis, conjunctivitis, myocarditis, pneumonia, pulmonary abscess, hepatitis, cholangitis, etc. If left untreated, the mortality rate can be up to 50%. Typically infections are self-limiting, but antibiotic treatment may be necessary for more severe cases. *Y. enterocolitica* is sensitive to many antibiotics: aminoglycosides, doxycycline, trimethoprim-sulfamethoxazole, or fluoroquinolones may be used. The natural route of transmission is fecal/oral from animal to human or through consumption of undercooked pork. Nosocomial infections and transmission by infected blood products have also been reported. The primary lab hazards include: ingestion and sharp injuries, frequent hand washing is recommended. ▪ BSL-2 is appropriate for work with *Y. enterocolitica*. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#17-05** as written.
Item 6:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New) ▪ Evans (LPVD) ▪ **PRD#17-196: Murine gammaretroviruses** ▪ Becky Anderson presented the risk assessment. The registration is for murine gammaretroviruses including: Friend, Moloney, Akv, Dr- and Mo- recombinants generated naturally in mice. The proposed studies are to study mixed retrovirus infection including interactions of exogenous retroviruses with endogenous retroviruses of the host. The listed viruses are ecotropic and only

	infect mice. To date, there have been no documented cases of human disease. Infections with these viruses in mice result in systemic hypergammaglobulanemia, splenomegaly, T and B cell dysfunction and eventually neurological disorder. Several strains cause neurodegenerative disease (Friend & Moloney temp sensitive mutants). The primary lab hazards include sharps injuries and generation of aerosols. ▪ Sue Priola pointed out that in the Eukaryote Cell section, the Evans lab will be working with human cells so the biosafety level should be changed from BSL-1 to BSL-2. ▪ BSL-1 is appropriate for work with murine gammaretroviruses. If working with human cells, BSL-2 procedures should be followed. If performing aerosol generating procedures, they should be conducted in a BSC. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **PRD#17-196** with the following minor modifications: 1. In the Eukaryote Cell section, change BSL-1 to BSL-2.
Item 7:	<u>Registration Documents for Recombinant DNA Experiments (New)</u> ▪ Evans (LPVD) ▪ **RD#17-216**: Construction of murine cells expressing Staphylococcal Protein A ▪ Reviewers: Scott Kobayashi, Bob Heinzen ▪ **Summary:** The RD describes construction of murine cells that will express Staphylococcal Protein A ▪ Scott Kobayashi summarized the RD. The Evan's lab will be making mouse cell lines that express the immunoglobin binding domain of the Staphylococcal Protein A. The Evan's lab will clone a portion of the protein A into the plasmids that are listed in the RD. They will use a replication defective leukemia virus to transfect the murine cells. This construct will result in protein A expression on the surface of the murine cells. ▪ Scott Kobayashi stated that there was no description of the defective leukemia virus. Karin Peterson agreed that more information on the virus needed to be added. Specifically, what is the replication-defective retroviral vector being used and are there associated vector maps? What murine retroviral envelope proteins are expressed in Psi2 and PA317 cells (ecotropic and/or amphotropic), what will be the cell tropism of the replication defective viruses generated in the packaging cells, can they infect human cells? ▪ Nancy Hoe pointed out that the NIH Guidelines in the Eukaryote Cell section

	need to be changed from III-D-2-a to III-D-3-e. ▪ The NIH Guidelines were appropriate and there were no dual use concerns. ▪ Bob Heinzen had no additional comments or concerns. ▪ No animal studies were proposed, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **RD#17-216** with the following minor modifications: 1. Add more detail to the RD regarding the replication defective retroviral vector. 2. Change NIH Guidelines in the Eukaryote Cell section from III-D-2-a to III-D-3-e. Research using prokaryotic hosts is approved at BSL-1 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-1 under III-D-3-e of the NIH Guidelines.
Item 8:	<u>Registration Documents for Recombinant DNA Experiments (New)</u> ▪ Feldmann (LV) ▪ **RD#17-452**: Use of an Alphavirus replicon system to produce vaccines ▪ Reviewers: Karin Peterson, Sue Priola ▪ **Summary:** The RD describes using replication-deficient alphavirus replicon system to express viral proteins as vaccine candidates. ▪ Sue Priola summarized the RD. They will use alphaviruses to express viral proteins of interest. There are two different types of systems, attenuated Venezuelan Equine Encephalitis virus (VEE) or Ross River virus. There are three plasmids for the replicon system that will be used. Two other plasmids have capsid and glycoproteins, they must use all three plasmids in cells to generate a viral particle that is capable of infecting but not replicating. The safety aspect in this system is that they would need two recombination events to generate virus and the attached study describes this. The committee discussed that the Eukaryote Cell section describes using any mammalian or insect cell line commercially available. The committee agreed that they were alright with leaving the wording as is. Sue Priola informed the committee that the attached ASP describes vaccinating animals at BSL-2 which is appropriate for the Alphavirus and that when the animals are challenged this would be at the approved biosafety level for the challenge virus, which is a suitable way to state the change in biosafety level. ▪ Sue Priola noted that the vectors for the VEE system are not clearly included,

	unless they are the same for both VEE and Ross River virus. This should be clarified. ▪ Nancy Hoe informed the committee that the VEE strain being used is exempt from the Select Agent regulations. ▪ The NIH Guidelines were appropriate and there were no dual use concerns. ▪ Karin Peterson had no additional comments or concerns. ▪ No animal studies were proposed, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved unanimously approved **RD#17-452** with the following minor modification: 1. Add or clarify the vectors for the VEE system. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a and III-E-1 of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a and III-D-3-a of the NIH Guidelines.
Item 9:	**Working Group Summary** ▪ Sue Priola reviewed the Working Group summary with the committee. Karin Peterson, Chris Bosio, and Andrea Marzi were the working group members that reviewed the inactivation methods from Bob Heinzen's lab. ▪ The Heinzen lab tested the ability of boiling, fixation with 4% PFA or formaldehyde, or sterile filtration to inactivate or remove *Coxiella burnetii* from samples. They showed in two different experiments that all the bacteria was inactivated or physically removed (filtration). ▪ The suggestions the Working Group made were to have the Heinzen lab: a. Require a minimum sample boiling time of 5 minutes (i.e. 5-times higher than the amount needed to inactivate *C. burnetii*) b. Require a minimum of 12-hour fixation in 4% paraformaldehyde or formaldehyde. c. Reduce the level of experimental detail in the associated SOPs where possible/practical. ▪ See summary attached. Action: The committee unanimously approved the Working Group recommendation that boiling, fixation with 4% PFA or formaldehyde, or sterile filtration completely inactivated or removed *C. burnetii* from the sample and approved the validation studies as written.

Item 10:	**Exposure Control Plan (Annual Review)** ▪ Becky Anderson presented the updates to the committee. Becky Anderson also informed the committee of the safer sharps devices that were reviewed by RML employees this year as part of the annual review. The group reviewed three different types of retractable needles. This group of employees that reviewed the sharps work in the ABSL-3 and did not like the design that to activate the safety mechanism, they needed to expel any remaining inoculum first. This dislike was stated for all three safety syringes tested. ▪ (b)(6) was not in attendance, but submitted the following questions to Sue Priola by email. Instructions on calling the RML OMS nurse have been deleted with the comment that this is not the worker's responsibility section on page 7. If it is not their responsibility, whose is it? The committee discussed and agreed that this statement should stay in this section, but that it should be moved up to the Workers section after bullet three. ▪ (b)(6) wrote in her email that the edit to section 2 on page 7 is not very clear why "it is strongly suggested that RML workers" was deleted. The committee discussed and agreed that the meaning is not as strong with this deletion and should be changed back to the original version. ▪ The committee also discussed the edit to bullet one in the Worker's section and agreed that "must" should not be deleted from the sentence and the wording should return to the original version. Action: The committee unanimously approved **Exposure Control Plan (Annual Review)** with the following minor modifications: 1. Keep "Must" in the first bullet of the Worker's section on page 7. 2. Move the statement, "During work hours (8AM to 5PM), the RML OMS nurse. . ." under the third bullet in the Worker's section on page 7. 3. Return the wording to original for, "It is strongly suggested that RML workers disclose their place of employment . . ." on page 7 in the Worker's section.
Item 11:	**Standard Operating Procedures (b)(6) SOP, *Coxiella burnetii, Rickettsia spp*. (Update)** ▪ Sue Priola informed the committee that the procedures outlined in the SOP match the validation procedures used with boiling, fixation with 4% PFA or formaldehyde, or sterile filtration on *C. burnetii*. ▪ Sue Priola asked Bob Heinzen if he wanted to change the boiling time from 20 minutes to 5 minutes as that would still give him a safety margin over the validated inactivation time, but would not be as long as 20 minutes. Bob Heinzen agreed that the boiling times in the SOP could be changed to state, "at least 5 minutes".

	▪ The committee discussed with Bob Heinzen the possibility of changing the minimum fixation time to 12 hours with 4% PFA or formaldehyde. Bob Heinzen decided to leave it as written. ▪ Sue Priola also asked Bob Heinzen if he wanted to remove some detail from the associated SOPs where possible/practical. Bob Heinzen decided to leave it as written for now, but with the thought that in the future it may be changed to allow for flexibility with new staining procedures. ▪ There were no additional comments or concerns. Action: The committee unanimously approved (b)(6) **SOP, *Coxiella burnetii, Rickettsia spp*. (Update)** with the following minor modifications: 1. Change the boiling time from 20 minutes to, "at least 5 minutes".
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Nancy Hoe presented the BSO report. ▪ Nancy Hoe reviewed an incident that involved a clean needle stick in the ABSL-4. This needle stick was reported to CDC DSAT and follow-up is ongoing. ▪ Nancy Hoe informed the committee of the OIG's final review of NIH's shipping and transfer procedures of infectious and inactivated Select Agents.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ Not present.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ (b)(6) is currently shutdown and repairs on the autoclave are being performed.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ None.

Other issues	▪ None.

Next Meeting:

- Date: 8/17/17

- Place: Library conference room
- Time: 1:00 PM

RML Biosafety Committee Meeting
July 20, 2017
Biosafety Officer/Responsible Official Report

1) ***Requests approved by BSO since last meeting:***
   a) *None*
2) ***New requests approved by committee via electronic review:***
   a) *None*

3) ***New requests***
   a) *Pathogen Registration Documents*
      i) ***Amend***
         (a) *Peterson (LVPD)*
            (a) ***PRD 12-103****: La Cross virus (LACV)*
               (i) Add human plasm/serum, and cerebral spinal fluid
      ii) ***Renewal***
         (a) *Hackstadt (LB)*
            (a) ***PRD-17-35****: Chlamydia spp. (C. caviae GPIC, C. muridarum MoPn, C. pneumoniae AR-39, C. psittaci Mn*
            (b) ***PRD-17-37****: Chlamydia trachomatis (serovars A, B, D, G, and L2)*
         (b) *Feldmann (LV)*
            (a) ***PRD-17-83****: Human and NHP blood and body fluids*
         (c) *Hinnebusch (LZP)*
            (a) ***PRD-17-05:*** *Yersinia enterocolitica*
      iii) ***New***
         (a) *Evans (LPVD)*
            (a) ***PRD-17-196:*** *Murine Gammaretroviruses*

   b) *Registration Documents for Recombinant Nucleic Acid Experiments*
      i) ***Renewal***
         (a) ***Evans (LPVD)***
            (a) ***RD-17-216:*** *construction of murine cells expressing Staphylococcal Protein A*
      ii) ***New***
         (a) *Feldmann (LV)*
            (a) ***RD-17-452****: Use of an Alphavirus replicon system to produce vaccines*

   c) *Working Group Recommendations after Review of Inactivation Validation Studies*
      i) *Heinzen*
         (a) *Inactivation of Coxiella burnetii by boiling, fixation in 4% paraformaldehyde, sterile filtration*

d) *Annual review of the RML Biological Exposure Control Plan*

e) *Standard Operating Procedures*

(a) ***Updated***

(a) ***SOPs Coxiella burnetii, Rickettsia spp. BSL-3***

(i) Update SOP BSL-3-Cb-5 Inactivation of Coxiella burnetiid and subcomponents for removal from the BSL-3 laboratory

4) ***Animal Study Protocols Review***

Title	***Associated PRD***	***Associated RD***	***Reviewer***
Collection of Normal Tissues from Mice	*NA*	*NA*	*N. Hoe*
Investigating Phenotypic Range of Highly Pathogenic Influenza in CC Mice	*12-131 (1918 Influenza) 13-123 (H5N1)*	*15-433*	*M. Brose*
Strain-dependent differences in severity of MERS-CoV disease in the common marmoset	*17-143 (MERS-CoV)*	*NA*	*N. Hoe*

5) ***Biosafety Training Performed –Megan Morgan, Rebecca Anderson***

Type of Training	***Number of Sessions***	***Number of Employees Trained***
Select Agent initial	*1*	*2*
Visitor	*3*	*4*
BSL-3 Laboratory Biosafety	*3*	*4*
BSL-4 Laboratory Biosafety	*8*	*2*
Biosafety Briefs	*3*	*WIPs*

6) ***Safety Audits and Inspections***

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

a) *Biological Incident Report:*

i) *Needlestick in ABSL-4*

7) ***Select Agent Issues***

a) *None*

8) ***Other Issues***

a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 08/18/17
Meeting Time: 1:02 PM **Adjourned:** 2:35 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Kevin Mora	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Karin Peterson	☒	☐
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Dana Scott	☒	☐
Alan Applebury	☐	☒	Nancy Hoe	☒	☐	Alexandra Scranton	☐	☒
Chris Bosio	☒	☐	Chris Hoffman	☐	☒			
Marshall Bloom (EO)	☒	☐	Clay Jarrett	☒	☐			
Teresa Borino	☐	☒	Josh Kellar (EO)	☐	☒			
Megan Brose	☐	☒	Scott Kobayashi	☒	☐			
Carol Calderwood	☐	☒	Jamie Lovaglio	☒	☐			
Marcie Caldwell (EO)	☐	☒	Andrea Marzi	☒	☐			
Paul Carlson	☒	☐	Alida Merritt	☐	☒			

(P=present; A=absent)

Guests: (b)(6)

Minutes: Meeting minutes from 7/20/17 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** ▪ Sue Priola pointed out a minor clarification for page 9, Item 10, bullet 3. The way the sentence was written was not clear. Sue Priola provided a re-write. Action: Meeting minutes for 7/20/17 were unanimously approved with the above minor modification.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New) ▪ Haigh (LPVD)

	▪ **PRD#17-197: Human Transmissible Spongiform Encephalopathy (TSE)** ▪ Becky Anderson presented the risk assessment. The purpose of the study is to monitor TSE spread and toxic changes in human neurons and cerebral organoids (mini-brains) exposed to different human TSE sources. For CJD there is a gradual onset of confusion, progressive dementia, myoclonic jerks with spasticity, wasting and coma; slight elevation of CSF proteins; death usually occurs in less than 1 year; 10% cases have family history of dementia; amorphous amyloid plaques in cerebellum of 15% of cases. Gerstmann-Straussler-Scheinker (GSS) is an inherited disease that generally develops between the ages of 35 and 50 years. Affected people may experience: progressive ataxia, including clumsiness, unsteadiness, and difficulty walking, cognitive dysfunction leading to slowness of thought processing and dementia of different degrees, slurred speech, abnormal eye movements, rigid muscle tone, visual disturbances, lack of coordination in swallowing, deafness, and Parkinsonian features. The first symptoms of fatal familial insomnia (FFI), also an inherited disease usually begin between the ages of 32 and 62 (mean average 51 years), but have been reported to begin as early as 18 to as late as 72. People survive on average 60 months. It is important to note that insomnia is not always the first symptom of FFI; sometimes the first symptom is progressive dementia. Other symptoms may include panic attacks, phobias, weight loss, lack of appetite, and having a body temperature which is too low or too high. CJD is not known to be transmitted through the air or other forms of casual contact. Exposure to brain tissue and spinal cord fluid from infected individuals should be avoided to prevent transmission of the disease through these materials. ▪ In some cases, CJD has spread to other people from grafts of dura mater (a tissue that covers the brain), transplanted corneas, implantation of inadequately sterilized electrodes in the brain, and injections of contaminated pituitary growth hormone derived from human pituitary glands taken from cadavers. Primary lab hazards include: accidental parenteral inoculation, ingestion, or sharps injuries. ▪ BSL-2 with the following precautions is appropriate for work with human TSEs. Work will be performed in a restricted access lab, PPE includes a gown, respirator, and gloves. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **PRD#17-197** as written.
Item 2:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New)</u> ▪ Haigh (LPVD)

	▪ **PRD#17-198: Animal Transmissible Spongiform Encephalopathy (TSE)** ▪ Becky Anderson presented the risk assessment. The purpose of this registration is to study the pathogenesis of prion disease in animal cell culture models. Transmissible spongiform encephalopathies (TSE) are a group of fatal neurodegenerative diseases that can affect both humans and animals. This registration is for the listed animal TSEs. ▪ Signs of scrapie vary widely among individual animals and develops very slowly. Due to damage to nerve cells, affected animals usually show behavioral changes, tremor (especially of head and neck), severe itching, and locomotor incoordination that progresses to recumbency and death. ▪ Signs of Chronic Wasting Disease (CWD) include excessive salivation, loss of appetite, progressive weight loss, excessive thirst and urination, listlessness, teeth grinding, holding the head in a lowered position and drooping ears. CWD is a slowly progressive disease; infected deer may not show signs of the disease for 18 or more months. ▪ There is no known transmission of the listed agents to humans, however, accidental sharps injuries and production of aerosols should be avoided. ▪ BSL-2 is appropriate for work with the listed animal TSE agents. This work is segregated from the human TSE agents that are worked with in the restricted access BSL-2 lab. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **PRD#17-198** as written.
Item 3:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New)</u> ▪ Haigh (LPVD) ▪ **PRD#17-199: Human Blood and Body fluids** ▪ Becky Anderson presented the risk assessment. The Haigh lab will work with human neurons and cerebral organoids (mini-brains). They propose to monitor disease spread and toxic changes in human neurons and cerebral organoids exposed to different human prion sources. When working with human blood and body fluids the most common bloodborne pathogens are: HBV, HCV, and HIV. HBV is the most common of the three and causes a serious form of hepatitis. The symptoms include: jaundice, fatigue, abdominal pain, loss of appetite, intermittent nausea, vomiting. It can also lead to chronic liver disease, liver cancer, and death. There is a vaccine available for HBV, the vaccine is offered free of charge at RML through the OMS Nurses. HCV symptoms include jaundice, fatigue, abdominal pain, loss of appetite, intermittent nausea, and vomiting. HCV can also lead to chronic liver disease

	and death. HIV is the virus that leads to AIDS. Exposures to human blood and body fluid may be treated with anti-virals depending on the exposure. The primary lab hazards include: accidental sharps injuries, parenteral inoculation, and generation of aerosols. ▪ Sue Priola pointed out that the title is confusing and should be changed to Human blood and body fluids. ▪ Sue Priola also noted in the Eukaryote Cell section that the "BSL2/3 facility" should be changed to "Restricted access (b)(6) ▪ BSL-2 is appropriate for work with human blood and body fluid. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#17-199** with the following minor modifications: 1. Change the title to human blood and body fluids. 2. In the Eukaryote Cell section, change "BSL2/3 facility" to "Restricted access (b)(6)
Item 4:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New) ▪ Munster (LV) ▪ **PRD#17-200: Various bacteria (*E. coli, S. aureus, S. pyogenes, K. pneumonia, P. aeruginosa, B. fragilis*)** ▪ Becky Anderson presented the risk assessment. The proposed work is to utilize the bacteria to perform optimization/validation experiments to ensure they can obtain host and bacterial DNA alongside the typical viral RNA from blood samples. The listed bacteria can all cause disease in humans, however *K. pneumoniae* and *P. aeruginosa* are opportunistic pathogens and pose a greater risk to immunocompromised persons. Becky Anderson stated that it is recommended to add precautions for both to the recommendations section of the PRD. The primary lab hazards include ingestion, generation of aerosols and accidental sharps injuries. ▪ Scott Kobayashi questioned why only the *K. pneumoniae* and *P. aeruginosa* are a risk for immunocompromised persons. All of the bacteria can cause disease in humans and if you are immunocompromised, you would be at risk for any of these bacterial infections. The committee discussed and agreed that this wording should not be added to any of the PRDs anymore. ▪ Nancy Hoe stated that a bite/scratch kit should be in the lab for work with non-human primate blood and body fluids. This can be added to the recommendations section. ▪ Sue Priola stated that the specific strains should be added to the registration.

	▪ BSL-2 is appropriate for work with the above listed bacteria. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#17-200** with minor modifications: 1. Delete from the recommendations section precautions for immunocompromised persons. 2. Add to the recommendations section, that a bite/scratch kit must be in the lab where work with non-human primate blood and body fluid are worked with. 3. Specify which bacterial strains will be worked with.
Item 5:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Rosa (LZP) ▪ **RD#15-314 Amend**: Genetic manipulation of Leptospira spp. ▪ Reviewers: Dana Scott, Andrea Marzi ▪ **Summary:** The RD amendment is to add rabbits to the RD. ▪ Dana Scott summarized the RD. The amendment is to add rabbits to the current RD. They will use purified *E. coli* recombinant protein mixed with adjuvant to produce antibodies in rabbits. There are no dual use concerns with the work and the NIH Guidelines are appropriate. ▪ Andrea Marzi had no additional comments or concerns. ▪ No animal studies were proposed, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#15-314 Amend** as written. Research using prokaryotic hosts is approved at BSL-2 under section III-D-1-a and III-D-2-a of the NIH Guidelines.
Item 6:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Heinzen (LB) ▪ **RD#15-123 Amend**: Mechanisms of pathogen vacuole biogenesis ▪ Reviewers: Chris Bosio, Scott Kobayashi ▪ **Summary:** The RD describes adding genes from *Ehrlichia chaffeensis* into avirulent *C. burnetii* Nine Mile phase II.

	▪ Chris Bosio summarized the RD. Chris Bosio informed the committee that the amendment is to add individual genes from *Ehrlichia chaffeensis* into *C. burnetii* to see if the genes are secreted in the Type IV secretion system. The genes to be cloned are predicted effector proteins as identified bioinformatically. ▪ The NIH Guidelines were appropriate and there were no dual use concerns. ▪ Sue Priola asked if all the vector maps in the original RD would be used for the new work. Bob Heinzen informed the committee that there is no change in the vector maps that will be used and the previous ones attached are accurate. ▪ Scott Kobayashi had no additional comments or concerns. ▪ No animal studies were proposed, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Bob Heinzen abstained) **RD#15-123 Amend** as written. Research using prokaryotic hosts is approved at BSL-2 under section III-D-1-a and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a and Appendix G-II-B of the NIH Guidelines.
Item 7:	Registration Documents for Recombinant DNA Experiments (New) ▪ De Leo (LB) ▪ **RD#17-316**: Characterization of *Klebsiella pneumoniae* antigens ▪ Reviewers: Bob Heinzen, Clay Jarrett ▪ **Summary:** The RD describes developing a gene deletion system for K. pneumoniae strains with broad antibiotic resistance. ▪ Bob Heinzen summarized the RD. This work proposed in the RD is to do genetics with antibiotic resistant *K. pneumoniae* where this field struggles to have selectable markers. They will use a commercial kit called Gene Bridges Quick & Easy *E. coli* Gene Deletion Kit. The gene of interest to delete will be PCR amplified for use in the Red/ET recombination system with an antibiotic resistance gene. This will result in an intermediate with antibiotic resistance. The antibiotic resistance gene can be removed from the bacterial chromosome by introduction of an additional plasmid encoding the FLP recombinase. The Red/ET and FLP recombinase plasmids are temperature sensitive replicons and can be cured from the host cell. Bob Heinzen questioned if any of the antibiotics used in selection are clinically relevant. Scott Kobayashi stated that many of the strains naturally acquire antibiotic resistance to the antibiotics that would be used for selection with this genetic system. Nancy Hoe questioned if the strains the de Leo lab plans to work with are already carbapenem resistant.

	Scott Kobayashi stated that they are all resistant. He stated that clinically they can treat strains that are tetracycline resistant with some of the newer tetracycline derivatives because they do not cross react with tetracycline. Bob Heinzen pointed out that there are 6 antibiotics listed for the Gene Bridge system in this RD. We need to determine if any of those are clinically relevant. ▪ Nancy Hoe read to the committee III-A-1-a of the NIH Guidelines. The committee discussed extensively that these antibiotics may be naturally acquired but expressed concern that they may still be used for treatment in certain cases. The committee agreed to table the registration until Nancy Hoe can contact OBA and ask for guidance on this registration. ▪ The committee discussed the dual use potential of the proposed work. The committee agreed that if there is no issue with the antibiotics used for selection, then there are no dual use concerns. The IBC will wait to hear a response from OBA regarding the use of the proposed antibiotics as selection markers. ▪ Clay Jarrett had no additional comments or concerns beyond those that were discussed as a committee. ▪ No animal studies were proposed, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee tabled (Scott Kobayashi abstained) **RD#17-316** until clarification from OBA is obtained. The IBC will electronically review the RD if OBA determines the proposed antibiotics may be used for selection markers in the submitted RD.
Item 8:	**Working Group Summary** ▪ Sue Priola reviewed the Working Group summary with the committee. Bob Heinzen and Scott Kobayashi were the working group members that reviewed the inactivation methods from Catharine Bosio's lab. ▪ The Bosio lab tested the ability of 100% methanol or 1% Vesphene IIse to inactivate *F. tularensis* in samples. They showed in two different experiments that all the bacteria were inactivated. ▪ The suggestions the Working Group made were to have the Bosio lab: a. Specify the percentage of methanol used in the SOP. b. Treatment with 1% Vesphene IIse should be done for 5 minutes as an extra safety margin. ▪ See summary attached.

	Action: The committee unanimously approved the Working Group recommendation that 100% methanol and 1% Vesphene IIse completely inactivated *F. tularensis* and approved the validation studies as written.
Item 9:	**Standard Operating Procedures: (b)(6) SOP, *F. tularensis* (Update)** ▪ Sue Priola informed the committee that the procedures outlined in the SOP match the validation procedures used with *F. tularensis* by the Bosio lab. The changes that were requested by the Working Group have been made to the SOP. ▪ Sue Priola stated that the (b)(6) SOP should list the IBC approved disinfectants instead of having them in a paragraph. The way it is written is difficult to find the information quickly. ▪ Sue Priola also stated that "100%" is missing from a couple of locations on page 29. ▪ There were no additional comments or concerns. Action: The committee approved (Chris Bosio abstained) (b)(6) **SOP, *F. tularensis* (Update)** with the following minor modifications: 1. List the IBC approved disinfectants on page 6. 2. Add "100% to the appropriate places on page 28.
Item 10:	**Standard Operating Procedures: ABSL-3 SOP *Francisella tularensis* (Update)** ▪ Sue Priola informed the committee that the procedures outlined in the SOP match the validation procedures with Vesphene IIse. ▪ Andrea Marzi pointed out that the maximal load that can be inactivated with Roccal-D and Earth Sense is 10^9 bacteria, but for Vesphene IIse it is 10^8. The committee discussed that they cannot have anything greater than 10^8 that would need to be inactivated in the lab. Sue Priola will look at the other inactivation data and talk to the Bosio lab. The group agreed that there should be consistency between the disinfectants. ▪ There were no additional comments or concerns. Action: The committee approved (Chris Bosio abstained) **ABSL-3 SOP *Francisella tularensis* (Update)** with the following minor modifications: 1. Sue Priola will follow-up with the Bosio lab regarding the differences in the maximal load that can be inactivated with the IBC approved disinfectants. a. Upon discussion with Catherine Bosio, it was determined that there was not a specific reason that the lab tested 10^8 CFU for Vesphene vs. 10^9 CFU with the other disinfectants. Catharine Bosio stated that there would not be a scenario that would require disinfection of greater than

	10^8 CFU/mL with Vesphene. The SOP was finalized as written.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Nancy Hoe presented the BSO report. ▪ Nancy Hoe reviewed an incident that involved a glove tear in the ABSL-4. This glove tear was reported to CDC DSAT and has been closed out by CDC DSAT. ▪ Nancy Hoe provided annual IBC training to the committee.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ We have had some issues with lab items being sent off to the laundry service in laundry loads. Employees are reminded to make sure nothing goes offsite. ▪ There was a chemical burn in the water treatment area where an employee was working with a hose that was over pressurized and sprayed chemical on their arm. They sustained minor chemical burns to their arm. ▪ There was a mouse bite in (b)(6) with an uninfected mouse. Paul Carlson will investigate and follow-up on the incident. ▪ A wild bat was found today on the side of one of the campus buildings. Safety staff makes sure bats are removed if they are near any entrances to buildings. If there are not by an entrance, the policy is to leave them alone. Please report if you see any bats near the entrances to buildings.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ Not present
Report	**Associate Director Report/Marshall Bloom** ▪ Not present at close of meeting.
Around the room	▪ None.

Other issues	▪ None.

Next Meeting:

- Date: 9/21/17
- Place: Library conference room

- Time: 1:00 PM

RML Biosafety Committee Meeting
August 17, 2017
Biosafety Officer/Responsible Official Report

1) ***Requests approved by BSO since last meeting:***
   a) *None*
2) ***New requests approved by committee via electronic review:***
   a) *Updates to SOP 4-28-44 Husbandry and Manipulation of Swine in Level Biocontainment*
      i) *Modify to allow option of using open caging or open caging within a ventilated enclosure such as a BioBUBBLE (approved 8/11/17)*
3) ***New requests***
   a) *Pathogen Registration Documents*
      i) ***New***
         (a) *Haigh (LPVD)*
            (a) ***PRD 17-197****: Transmissible spongiform encephalopathies (sporadic CJD, genetic FFI, GSS and CJD types, variant CJD*
            (b) ***PRD 17-198****: Transmissible spongiform encephalopathies (mouse-adapted scrapie, chronic wasting disease)*
            (c) ***PRD 17-199****: Human blood and body fluids*
         (b) *Munster (LV)*
            (a) ***PRD 17-200:*** *Assorted bacteria (E. coli, S. aureus, S. pyogenes, K. pneumonia, P. aeruginosa, and B. fragilis)*
   b) *Registration Documents for Recombinant Nucleic Acid Experiments*
      i) ***Amend***
         (a) *Rosa (LZP)*
            (a) ***RD-15-314:*** *Genetic manipulation of Leptospires*
               (i) Add rabbits for antibody production
         (b) *Heinzen (LB)*
            (a) ***RD-15-123****: Introduction of Anaplasma phagocytophilum and Orientia tsutsugamushi genes into avirulent Coxiella burnetii Nine Mile phase II*
               (i) Add work with Ehrlichia chaffeensis
      ii) ***New***
         (a) *DeLeo (LB)*
            (a) ***RD-17-316****: Characterization of K. pneumoniae antigens*
   c) *Working Group Recommendations after Review of Inactivation Validation Studies*
      i) *Bosio*
         (a) *Inactivation of Francisella tularensis with 100% methanol; 1% Vesphene IIse*
   d) *Standard Operating Procedures*
         (a) ***Updated***
            (a) ***SOPs for Francisella tularensis BSL-3***

(i) *Update SOP BSL-3-C-8 Inactivation of Francisella spp.; define approved disinfectants; modify text throughout to indicate "appropriate disinfectant"*

(b) ***SOPs for Francisella tularensis ABSL-3***

(i) *define approved disinfectants; modify text throughout to indicate "appropriate disinfectant"*

4) ***Animal Study Protocols Review***

Title	***Associated PRD***	***Associated RD***	***Reviewer***
Efficacy testing of human antibodies against Andes virus in the hamster HCPS model	*12-81 (Hantavirus)*	*NA*	*N. Hoe*
Assess the contribution of circulating T cells in tularemia using mouse parabiosis	*13-73 (F. tularensis exempt)*	*NA*	*N. Hoe*
Exploring the role of the receptor/ligand pair, CD47 & SIRPα, in immune cell function using a model of murine retrovirus infection.	*16-187 (Friend virus)*	*NA*	*N. Hoe*
TKO-BLT mice to study the HIV-1 reservoir using in vivo viral outgrowth assays.	*12-55 (HIV-1)*	*NA*	*N. Hoe*
Comparative pathogenesis of Crimean Congo Hemorrhagic Fever strain Hoti and 10200 in mice	*13-92 (CCHFV)*	*NA*	*R. Anderson*
Mastomys natalanesis transciptional responses following Lassa virus infection	*13-94 (Lassa virus)*	*NA*	*N. Hoe*
Efficacy of the VSV-Lassa vaccine in the Cynomolgus macaque model of Lassa fever: comparison between GMP-produced seed and original vaccine stock	*13-94 (Lassa virus) 13-82 (VSV)*	*15-404*	*N. Hoe*

5) ***Biosafety Training Performed –Megan Morgan, Rebecca Anderson, Nancy Hoe***

Type of Training	***Number of Sessions***	***Number of Employees Trained***
Select Agent initial	*1*	*2*
Visitor	*1*	*6*
BSL-3 Visitor	*1*	*3*
ABSL-3 additional: cage changing procedures	*1*	*9*
BSL-4 Laboratory Biosafety	*2*	*1*
BSL-4 Refresher	*2*	*2*
Lab Support Personnel	*1*	*1*

6) ***Safety Audits and Inspections***

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

a) *Biological Incident Report:*

i) *Glove tear in ABSL-4*

7) ***Select Agent Issues-****None*

8) ***Other Issues -****None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 09/21/2017
Meeting Time: 1:02 PM **Adjourned:** 2:10 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Kevin Mora	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Karin Peterson	☒	☐
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Dana Scott	☐	☒
Alan Applebury	☐	☒	Nancy Hoe	☐	☒	Alexandra Scranton	☐	☒
Chris Bosio	☒	☐	Chris Hoffman	☐	☒			
Marshall Bloom (EO)	☐	☐	Clay Jarrett	☒	☐			
Teresa Borino	☒	☐	Josh Kellar (EO)	☐	☒			
Megan Brose	☐	☒	Scott Kobayashi	☒	☐			
Carol Calderwood	☐	☒	Jamie Lovaglio	☐	☒			
Marcie Caldwell (EO)	☐	☒	Andrea Marzi	☒	☐			
Paul Carlson	☐	☒	Alida Merritt	☐	☒			

(P=present; A=absent)

Guests: (b)(6)

Minutes: Meeting minutes from 8/17/17 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** ▪ Clay Jarrett pointed out that he was present for the last meeting. ▪ Sue Priola noted a minor typo. Action: Meeting minutes for 8/17/17 were unanimously approved with the above minor modifications. **Evans RD 17-216** ▪ Sue Priola informed the committee that at July IBC meeting additional information was requested from Dr. Evans on his RD. Upon obtaining the additional information, the biosafety level needs to be adjusted from BSL-1 to BSL-2. Sue Priola wanted to make sure the IBC reviewed and approved the change to the biosafety level for the Eukaryote Cell section on the RD. Action: The committee unanimously approved **PRD#17-197** as written with the

	biosafety level changed to BSL-2.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New)</u> ▪ Fischer (RTB) ▪ **PRD#17-201: Murine Cytomegalovirus (MCMV)** ▪ Becky Anderson presented the risk assessment. The proposed studies are to test the effects of glutaraldehyde and paraformaldehyde on the high resolution structure of mouse CMV compared to unfixed mouse CMV. Murine CMV is host specific for mice. Infected mice are asymptomatic, although experimentally, mouse genotypes and viral strains can influence virus infectivity and organ damage. Depending on the route of inoculation, mice develop systemic viremia either from parenteral inoculation or following replication from the primary site of infection. Virus replication occurs in salivary glands, liver, spleen, adrenal glands, lymph nodes, kidney, lung, intestine and pancreas. MCMV is not a human pathogen so there is no risk of transmission to humans. Mouse to mouse transmission occurs through contact with virus in saliva and urine. The primary laboratory hazards include generation of aerosols, parenteral inoculation, and sharps injuries. ▪ BSL-2 according to the attached SOP is appropriate for work with MCMV. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **PRD#17-201** as written.
Item 2:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renew)</u> ▪ Hinnebusch (LPVD) ▪ **PRD#17-144: *Proteus mirabilis*** ▪ Becky Anderson presented the risk assessment. The proposed studies are to determine if bacterial urease is toxic to fleas. *Proteus mirabilis* is well-known as the species that swarms across agar surfaces, overtaking any other species present in the process. *Proteus* spp. are commonly associated with complicated urinary tract infections (UTIs). They generally affect the upper

	urinary tract, causing infections such as urolithiasis (stone formation in kidney or bladder), cystitis, and acute pyelonephritis. Other infections include septicemia and wound infections. *P. mirabilis* is susceptible to broad-spectrum antibiotics including: cephalosporins, aminoglycosides, and imipenem, trimethoprim-sulfamethoxazole, ampicillin, amoxicillin, and piperacillin. *P. mirabilis* is resistant to tetracycline and nitrofuratoin, while 10-20% are resistant to ampicillin or cephalexin. The natural route of transmission occurs when *P. mirabilis* (part of the normal intestinal flora) colonizes another location of the body. This can happen with contaminated catheters or by accidental parenteral inoculation. The primary lab hazards include: parenteral inoculation, accidental needle stick, and aerosol generation. ▪ BSL-2 is appropriate for work with *P. mirabilis*. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Chris Bosio and Clay Jarrett abstained) **PRD#17-144** as written.
Item 3:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renew) ▪ Feldmann (LV) ▪ **PRD#17-81: Hantavirus** ▪ Becky Anderson presented the risk assessment. The proposed studies are to elucidate mechanisms of pathogenesis with both *in vitro* and *in vivo* studies. The proposed studies will evaluate virus multiplication, the innate immune response, various animal models to monitor disease course and study potential treatments and finally develop and characterize reassortant viruses (co-infections with different strains). Hantavirus infection can lead to two different syndromes: hantavirus pulmonary syndrome (HPS) or Hemorrhagic fever with renal syndrome (HFRS). ▪ HPS has a fatality rate of 40%; symptoms appear 1 to 6 weeks after being exposed to the virus. The symptoms can include: tiredness, dizziness, fever and chills, muscle aches and headaches, nausea and vomiting, stomach pain, coughing. More severe symptoms may include: shortness of breath, severe difficulty breathing. HFRS can manifest as mild, moderate or severe disease, depending upon the causative virus, the case fatality rate is 5-15%. Symptoms of haemorrhagic fever with renal syndrome: symptoms appear 1 to 2 weeks after exposure. They can include: intense headaches, back and stomach pain, fever, chills, nausea, blurred vision. Additional symptoms may include: flushed face, inflamed or red eyes, and rash. ▪ Becky Anderson informed the committee that this renewal combines a PRD for

	Feldmann and a PRD for Ebihara that Feldmann took over as PI when Ebihara left RML. ▪ BSL-3 is appropriate for work with Hantavirus. All work involving inoculation of virus-containing samples into rodent species permissive for chronic infection should be conducted at ABSL-4, all animal work with Hantavirus is performed at ABSL-4. ▪ Animal studies with hamsters, ferrets, deer mice, rabbits, and NHPs were proposed. ▪ The committee discussed the dual-use potential of these experiments. Questions 1 was marked yes on the PRD. The committee discussed the explanation the PI provided and the committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Andrea Marzi abstained) **PRD#17-81** as written.
Item 4:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renew) ▪ Best (LV) ▪ **PRD#17-112: Langat virus** ▪ Becky Anderson presented the risk assessment for all four Best PRDs that were up for renewal. The proposed studies for the listed viruses are to understand the mechanisms that Flaviviruses use to evade the host innate immune response. ▪ **Langat**: Incidence of human disease with Langat virus is extremely low. Langat has been tested as a live vaccine for TBEV, Langat strain TP21 vaccination resulted in meningoencephalitis with permanent neurological sequelae in <0.005% of patients vaccinated (35 of ~650,000 patients), however there was a very low frequency of encephalitis. ▪ **Kunjin**: Mild disease consists of lymphadenopathy, fever, lethargy, rash, muscle weakness and fatigue. Less common is a more severe disease where development of encephalitis occurs requiring hospitalization. ▪ **Dengue**: An acute febrile disease characterized by the sudden onset of fever for 3 to 5 days, with an intense headache, myalgia, arthralgia, retro-orbital pain, anorexia and rash, symptoms are usually self-limiting; dengue hemorrhagic fever, a more severe manifestation on second exposure is characterized by abnormal vascular permeability, decreased blood volume and abnormal clotting mechanisms; fatality as high as 40-50%; infection with one serotype does not offer cross protection to another serotype. ▪ **Powassan virus**: acute inflammatory disease of short duration involving parts of brain, spinal cord and meninges; asymptomatic and mild cases present with febrile head ache or aseptic meningitis; severe infections with stupor, disorientation, coma, tremors, convulsions and spastic paralysis; high incidence of neurologic sequelae.

	▪ The natural route of transmission is depends on the virus. Kunjin & Dengue: through an infected mosquito bite (*Culex annulirostris* or *Aedes aegypti* respectively). For Langat and Powassan virus: through an infected tick (Langat: *Ixodes granulatus* and *haemaphysalis* spp) (Powassan: *Ixodes cookie*, *Ixodes marxi, Ixodes spinipalpus*). There are no specific treatments for the above listed viruses, supportive care is offered. The primary lab hazards include: accidental parenteral inoculation, contact with broken skin or mucous membranes, and accidental needle sticks ▪ Sue Priola noted that the PRD describes work with human blood or body fluid but the precautions are not listed in the recommendations section, this needs to be added. ▪ For Langat virus: BSL-2, lab coat and gloves, all work is to be performed in a BSC with the use of sealed centrifuge cups or rotors. Everything should be sealed prior to removal from the BSC, this includes sealed/gasketed safety cups for centrifuges, parafilming of microtitre plates etc. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#17-112** with minor modifications: 1. Add Human blood and body fluids precautions to the recommendations section.
Item 5:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renew) ▪ Best (LV) ▪ **PRD#17-113: Kunjin virus** ▪ Becky Anderson presented the risk assessment. See risk assessment described in Item 4. ▪ For Kunjin virus: BSL-2, lab coat and gloves, all work is to be performed in a BSC with the use of sealed centrifuge cups or rotors. Everything should be sealed prior to removal from the BSC, this includes sealed/gasketed safety cups for centrifuges, parafilming of microtitre plates etc. ▪ Sue Priola noted that the PRD describes work with human blood or body fluid but the precautions are not listed in the recommendations section, this needs to be added. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#17-113** with minor

	modifications: 1. Add Human blood and body fluids precautions to the recommendations section.
Item 6:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renew)</u> ▪ Best (LV) ▪ **PRD#17-140: Dengue virus** ▪ Becky Anderson presented the risk assessment. See risk assessment described in Item 4. ▪ For Dengue virus: BSL-2, lab coat and gloves, all work is to be performed in a BSC with the use of sealed centrifuge cups or rotors. Everything should be sealed prior to removal from the BSC, this includes sealed/gasketed safety cups for centrifuges, parafilming of microtitre plates etc. ▪ Dengue virus employees should be informed of the following risks of working with Dengue virus: There is an increased severity of disease upon second exposure to dengue virus, as well as working with multiple serotypes increases your risk for disease. Becky Anderson stated that this should be added to the recommendations section. ▪ Sue Priola noted that the PRD describes work with human blood or body fluid but the precautions are not listed in the recommendations section, this needs to be added. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. Dual use question 7C was answered Yes. The committee discussed the response the PI provided and the committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved (Karin Peterson abstained) **PRD#17-140** with minor modifications: 1. Add Human blood and body fluids precautions to the recommendations section. 2. Add the precautions for employees working with Dengue virus to the recommendations section.
Item 7:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renew)</u> ▪ Best (LV) ▪ **PRD#17-107: Powassan virus** ▪ Becky Anderson presented the risk assessment. See risk assessment described

	in Item 4. ▪ BSL-3 is appropriate for work with Powassan virus. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#17-107** as written.
Item 8:	Registration Documents for Recombinant DNA Experiments (New) ▪ Bloom (LV) ▪ **RD#17-452**: Infection of cell lines with recombinant Flaviviruses encoding various micro RNAs. ▪ Reviewers: Karin Peterson, Sue Priola ▪ **Summary:** The RD describes using recombinant Zika virus strains to study the pathogenesis of infection in humans and animals. ▪ Karin Peterson summarized the RD. The RD is to use recombinant Zika virus for vaccine development. The constructs are already made by the Pletnev lab and they had their proper approvals to make these constructs (attached to Bloom RD). The Pletnev lab will share these constructs with the Bloom lab. The vector maps are attached and described, but there is also a table that lists Zika micro RNAs, but it is not referenced in the RD, this should be better described. Marshall Bloom described the attachment and will add those comments to the RD. ▪ Sue Priola added that there are no dual use concerns and the NIH Guidelines are appropriate. ▪ No animal studies were proposed, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#17-452** with minor modifications: 1. Add a description to the RD about the attached table. Research using eukaryotic cells is approved at BSL-2 under III-D-3-a of the NIH Guidelines.
Item 9:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Heinzen (LB) ▪ **RD#14-106 Amend**: Genetic transformation of *Coxiella burnetii*

	▪ Reviewers: Chris Bosio, Scott Kobayashi ▪ **Summary:** The RD amendment describes treating *Coxiella burnetii* with tunicamycin. ▪ Chris Bosio summarized the RD. The amendment is to treat *C. burnetii* with tunicamycin. Tunicamycin inhibits N-glycosylation so it inhibits glycoprotein synthesis. Treatment of human cells with tunicamycin causes cell cycle arrest in G1 phase. Treatment of *C. burnetii* with tunicamycin is proposed to truncate LPS and possibly convert phase I Coxiella to phase II Coxiella. Tunicamycin is toxic to cells and is not clinically used to treat Q fever. Chris Bosio asked Bob Heinzen how they will use tunicamycin. Bob Heinzen informed the committee that the bacteria will be treated directly with the tunicamycin. ▪ Scott Kobayashi had no additional comments or concerns. ▪ Sue Priola pointed out that there is a typo in the NIH Guidelines for the Eukaryote Cells Section of the RD. III-D-1-q should be III-D-1-a. ▪ No animal studies were proposed, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#14-106 Amend** with minor modifications: 1. Fix the typo for the NIH Guidelines in the Eukaryote Cell Section. Research using eukaryotic cells is approved at BSL-2 or BSL-3 under III-D-1-a, Appendix G-II-c of the NIH Guidelines.
Item 10:	**BSL-3 Operations and Safety Procedures (Annual Review)** ▪ Becky Anderson summarized the updates to the BSL-3 OSP. ▪ There were no additional comments or concerns. Action: The committee unanimously approved **BSL-3 Operations and Safety Procedures (Annual Review)** as written.
Item 11:	**ABSL-3 Operations and Safety Procedures (Annual Review)** ▪ Becky Anderson summarized the updates to the ABSL-3 OSP. ▪ Bob Heinzen pointed out on page 47 there is still a reference to the freezer lock that has now been removed. This reference should be deleted. ▪ There were no additional comments or concerns. Action: The committee approved **ABSL-3 Operations and Safety Procedures (Annual Review)** with the following minor modifications:

	1. Delete the reference to the freezer lock on page 47.
Item 12:	**RML IBC Charter (Update)** ▪ Sue Priola summarized the updates to the IBC Charter. The biggest change was to include an SOP for reviewing and approving inactivation methods for infectious material for BSL-3 and BSL-4. ▪ Becky Anderson noted in the delegation of authority section, it should state that the BSO may approve additional routes of inoculation for animal studies at BSL-1-4, not just BSL-4. ▪ Marshall Bloom pointed out on page 5 that the "Associate Director" should be changed to "Associate Director for Scientific Management". ▪ There were no additional comments or concerns. Action: The committee unanimously approved **RML IBC Charter (Update)** With minor modifications: 1. Change BSL-4 to BSL-1-4 for the BSO approval of additional route of inoculation. 2. Change "Associate Director" to "Associate Director for Scientific Management".
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Becky Anderson presented the BSO report. ▪ Becky Anderson reviewed an incident that involved a cut with scissors while the employee was cleaning them after dissecting tissues from NHPs that were infected with Zika virus.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ Not present.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ Not present.
Report	**Associate Director Report/Marshall Bloom** ▪ The PREPARE clinical trial that includes testing of VSV-Ebola will be offered to RML BSL-4 employees. The study coordinator will give a video presentation to RML employees on Wednesday September 27th.
Around the room	▪ None.

Other issues	▪ None.

Next Meeting:

- Date: 10/19/17
- Place: Library conference room
- Time: 1:00 PM

RML Biosafety Committee Meeting
September 21, 2017
Biosafety Officer/Responsible Official Report

1) ***Requests approved by BSO since last meeting:***
   a) *None*
2) ***New requests approved by committee via electronic review:***
   i) *None*
3) ***New requests***
   a) *Pathogen Registration Documents*
      i) ***New***
         (a) *Fischer (RTB)*
            (a) ***PRD 17-201****: murine cytomegalovirus*
      ii) ***Renew***
         (a) *Hinnebusch (LZP)*
            (a) ***PRD-17-44****: Proteus mirabilis*
         (b) *Feldmann (LV)*
            (a) ***PRD-17-81:*** *Hantavirus*
         (c) *Best (LV)*
            (a) ***PRD-17-112:*** *Langat virus*
            (b) ***PRD-17-113:*** *Kunjin virus*
            (c) ***PRD-17-140:*** *Dengue virus*
            (d) ***PRD-17-107:*** *Powassan virus*
   b) *Registration Documents for Recombinant Nucleic Acid Experiments*
      i) ***Amend***
         (a) *Heinzen (LB)*
            (a) ***RD-14-106****: Genetic transformation of Coxiella burnetii*
               (i) Conversion of phase I to phase II Coxiella using tunicamycin
      ii) ***New***
         (a) *Bloom (LV)*
            (a) ***RD-17-452****: Infection of cell lines with recombinant Flaviviruses encoding various micro RNAs*
   c) *Standard Operating Procedures*
            (a) ***Annual Review***
               (i) BSL-3 Operations and Safety Procedures (OSP)
               (ii) ABSL-3 Operations and Safety Procedures (OSP)

RML Biosafety Committee Meeting
September 21, 2017
Biosafety Officer/Responsible Official Report

4) ***Animal Study Protocols Review***

Title	*Associated PRD*	*Associated RD*	*Reviewer*
Contribution of bacterial membrane lipids in virulence of Francisella tularensis in mice	*13-71 (F. tularensis)*	*13-125*	*N. Hoe*
Determination of the minimum time to immunity of a VSV-based vaccine against Zika virus infection in mice	*13-82 (VSV) 16-182 (Zika virus)*	*15-404*	*N. Hoe*
Mapping of a susceptibility allele for Ebola hemorrhagic fever pathogenesis and resistance in mice	*13-90 (Ebola virus)*	*NA*	*R. Anderson*
The effect of TRAIL-short blockade on HIV-1 viral control in TKO-BLT mice.	*12-55 (HIV-1)*	*NA*	*N. Hoe*
Prevention of CD4+ T cell depletion by pyroptosis in TKO-BLT mice	*12-55 (HIV-1)*	*NA*	*R. Anderson*
The role of age in the susceptibility of young pigs to Reston ebolavirus infection	*13-90 (Ebola virus)*	*NA*	*N. Hoe*
Regulatory and Effector T cell responses to a murine retrovirus in APOBEC3 knockout mice	*16-187 (Friend virus)*	*NA*	*N. Hoe*
The Role of IL-6 and TNFa in Modulating Regulatory and Effector T cell Responses to a Murine Retrovirus in APOBEC3 knockout mice	*16-187 (Friend virus)*	*NA*	*N. Hoe*
Evaluation of beta gluten compound (IRI-1681) as a therapeutic for Ebola virus infection in a mouse model.	*13-90 (Ebola virus)*	*NA*	*R. Anderson*
Investigating the Role of MAVS in Lassa Virus Pathogenesis	*13-94 (Arenaviridae)*	*NA*	*R. Anderson*

5) ***Biosafety Training Performed – Rebecca Anderson, Nancy Hoe***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
Select Agent refresher	*4*	*93*
BSL-4 Annual Refresher	*3*	*46*
Select Agent Visitor	*1*	*1*

6) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
a) *Biological Incident Report:*
   i) *Scissor stick in ABSL-2*

7) ***Select Agent Issues-****None*

8) ***Other Issues -****None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 10/19/2017
Meeting Time: 1:05 PM **Adjourned:** 1:40 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Kevin Mora	☐	☒
Bob Heinzen, Vice Chair	☐	☒	Frank DeLeo (EO)	☐	☒	Karin Peterson	☐	☒
Becky Anderson (EO)	☐	☒	Heinz Feldmann (EO)	☐	☒	Dana Scott	☐	☒
Alan Applebury	☐	☒	Nancy Hoe	☒	☐	Alexandra Scranton	☐	☒
Chris Bosio	☐	☒	Chris Hoffman	☐	☒			
Marshall Bloom (EO)	☐	☒	Clay Jarrett	☒	☐			
Teresa Borino	☐	☒	Josh Kellar (EO)	☐	☒			
Megan Brose	☐	☒	Scott Kobayashi	☒	☐			
Carol Calderwood	☐	☒	Jamie Lovaglio	☐	☒			
Marcie Caldwell (EO)	☐	☒	Andrea Marzi	☒	☐			
Paul Carlson	☐	☒	Alida Merritt	☐	☒			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 9/21/17 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** ▪ (b)(6) s name was misspelled. ▪ Nancy Hoe noted that the wrong document was listed as being approved under item 11 on page 8. It should be "ABSL-3 Operations and Safety Procedures". Action: Meeting minutes for 8/17/17 were unanimously approved with the above minor modifications.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amend) ▪ Feldmann (LV) ▪ **PRD#16-182: Zika virus** ▪ Nancy Hoe presented a summary of the requested amendment. The investigator is proposing to add a mouse-adapted (MA) strain of Zika virus. The MA-Zika virus was generated by (b)(6) at Washington University School of Medicine in St. Louis. The Dakar strain was passaged twice in Rag1-/- mice to create a mouse adapted variant this is more pathogenic in mice. This virus is not lethal for WT B6 mice, but does reach higher viral titers in target organs including brain and testes. All recombinant work was done according to IBC approved protocols. ▪ BSL-2/ABSL-2 with the additional precautions that are currently part of the approved PRD are recommended. ▪ Currently approved animal models are mice, hamsters, guinea pigs, and non-human primates. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Andrea Marzi abstaining) the amendment to **PRD#16-182** as written.
Item 2:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amend) ▪ Feldmann (LV) ▪ **PRD#13-92: Crimean-Congo Hemorrhagic Fever virus (CCHFV)** ▪ Nancy Hoe presented a summary of the proposed amendment. An Animal Study Proposal (ASP) has been submitted to the RML ACUC for review that requires an update to the Dual-Use questionnaire for this PRD. The goal of the proposed animal study is to generate a strain of CCHFV that can cause disease in wild-type laboratory strains of mice. This will be accomplished by passaging the virus in immunodeficient mice. To date, wild-type laboratory strains of mice are refractory to infection with CCHFV and exhibit mild-to-absent clinical signs of disease in addition to minimal viral replication. A mouse-adapted strain of CCHFV that could cause disease in immunocompetent mice would enable studies of vaccines and therapeutics against this virus. The investigator had updated the dual-use questionnaire by checking

	"yes" for question 1 regarding enhancing the harmful consequences of the agent. They stated that mouse adaptation has already been used for filoviruses, and adaptation of these viruses to rodents did not change the phenotype of the adapted viruses. In addition, mouse-adapted Ebola virus has been shown to be attenuated in non-human primates, therefore it is not expected that mouse adaptation of CCHFV will enhance the virulence of this virus for humans or other animals. The main vector and reservoir of CCHFV are ticks of the *Hyalomma* genus, and it is not expected, based on results with other viruses, that mouse adaptation of CCHFV will enhance fitness of the virus for ticks. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that the proposed project might enhance the virulence of the agent for mice, but did not feel the proposed work was DURC. ▪ BSL-4/ABSL-4 are the currently-approved biosafety levels for this work. The committee agreed these were still appropriate. ▪ Currently approved animal models are mice, hamsters, and non-human primates. Action: The committee approved (Andrea Marzi abstaining) the amendment to **PRD#13-92** as written.
Item 3:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renew) ▪ Feldmann (LV) ▪ **PRD#17-143: Coronavirus (exempt)** ▪ Nancy Hoe presented the risk assessment. The proposed studies are to study and characterize the following coronaviruses *in vitro* and *in vivo*: a. MERS CoV: Most individuals confirmed to have MERS-CoV infection have had severe acute respiratory illness with symptoms of fever, cough, and shortness of breath. Some individuals also had gastrointestinal symptoms including diarrhea, nausea, and vomiting. More severe complications can follow infection, such as pneumonia and kidney failure. Approximately 3 to 4 of every 10 individuals infected with MERS have died, although most deaths occur in people with underlying medical conditions. b. Human coronaviruses (HCoV-229E, HCoV-NL-63, HCoV-HKV1): The human BSL-2 coronaviruses cause 10-15% of the common cold cases. Depending on the virus, they can cause bronchitis, gastroenteritis, upper and/or lower respiratory tract infection, rhinorrhea, sneezing, sore throat, and cough. Human to human transmission occurs

	through infectious aerosols, contaminated surfaces, and fecal/oral routes. c. Bat coronaviruses (WIV1 SARs-like, SHC014 SARS-like, KU4-MERS like): None of the listed viruses are currently known to cause disease in humans. They have been identified by sequence only in the same bats that carry SARS-CoV and prepared as recombinant clones by (b)(6) They can infect and replicate in human airway epithelial cells. ▪ The primary lab hazards are accidental parenteral inoculation, contact with broken skin or mucous membranes, and accidental needle stick. There are no vaccines or specific treatments available. ▪ BSL-2 is recommended for work with the human coronaviruses. BSL-3 is recommended for all laboratory work with MERS CoV and bat Coronaviruses, and BSL-4/ABSL-4 for animal work due to space constraints. ▪ Animal studies with mice, bats, pigs, sheep, goats, and NHPs are proposed. BSL-4 SOPs for the animal work are in place. ▪ There were no dual use questions marked yes. The committee discussed the dual-use potential of these experiments and agreed that there were no dual-use concerns with the proposal. ▪ Sue Priola asked had his institutional IBC approval been obtained. She requested that Dr. Feldmann request a statement from (b)(6) stating that he has IBC approval to create the recombinant viruses. ▪ Nancy Hoe will update the name of the PRD to "Coronaviruses (exempt)" in PI-Dashboard to distinguish it from the select agent SARS-CoV. Action: The committee approved (Andrea Marzi abstained) **PRD#17-143** with the following changes/recommendations: 1) Dr. Feldmann will obtain a statement from (b)(6) that he has IBC approval to create the recombinant viruses. 2) The name of the PRD will be updated to "Coronaviruses (exempt)" in PI-Dashboard to distinguish it from the select agent SARS-CoV
Item 4:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renew) ▪ Best (LV) ▪ **PRD#17-108: West Nile virus** ▪ Nancy Hoe presented the risk assessment. The proposed studies are to understand the events associated with the host immune responses that are important for virus clearance and to understand how Flaviviruses evade

	these host responses to infection. ▪ Most individuals infected with WNV remain asymptomatic. Of those infected, approximately 20% developed West Nile fever. West Nile fever is typically a mild illness lasting 3 to 6 days. The main symptoms are sudden onset of fever with chills, rash, malaise, headache, backache, arthralgia, myalgia, and eye pain. Meningitis, encephalitis, and/or acute flaccid paralysis develop in less than 1% of WNV-infected individuals. The overall case fatality rate ranges from 4-14% in individuals exhibiting neuroinvasive disease. No specific treatments are available. Transmission is usually through the bite of an infected mosquito, but human-to-human transmission can occur through breast milk, organ transplantation, blood transfusions, and vertical transmission. The primary lab hazards are accidental parenteral inoculation, contact with broken skin or mucous membranes, and accidental needle stick. ▪ BSL-3/ABSL-3 is recommended for work with the virus. There are approved SOPs in place. Standard precautions for working with human blood and body fluids are also recommended as work will be performed with primary human dendritic cells. ▪ Animal studies with mice were proposed. ▪ There were no dual use questions marked yes. The committee discussed the dual-use potential of these experiments and agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#17-108** as written.
Item 5:	Registration Documents for Recombinant DNA Experiments (Amend) ▪ Feldmann (LV) ▪ **RD#17-431**: Molecular characterization of viral proteins of pathogenic RNA viruses ▪ Reviewers: Dana Scott, Sue Priola ▪ **Summary:** The original RD describes the cloning of viral genes and expression of viral proteins to characterize viral protein functions and viral protein/host cellular protein interactions. ▪ Dana Scott was absent so Sue Priola summarized the proposed amendment to the RD. The investigator is adding 2 plasmids, pCR-XL-2 TOPO and pCR-Blunt II-TOPO, for subcloning, and adding hamsters as an animal model. ▪ Sue Priola stated that no dual use questions were marked yes and the NIH Guidelines are appropriate. ▪ Animal studies with hamsters were proposed.

	▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Andrea Marzi abstained) **RD#17-431** as written. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a, and eukaryotic cells is approved at BSL-2 under sections III-D-2-a and III-E-1 of the NIH Guidelines.
Item 6:	**Working Group Summary** ▪ Sue Priola reviewed the Working Group (WG) summary with the committee. Karin Peterson and Clay Jarrett were the WG members that reviewed the inactivation methods from Catharine Bosio's lab. ▪ The Bosio lab performed validation studies to demonstrate that incubating *Francisella tularensis* strain SchuS4 at 65° for 1 hour in 6mM Tris pH 6.8/10mM EDTA/2% SDS completely inactivated infectivity. This method is used to isolate *F. tularensis* capsule. ▪ The data presented indicated the method could inactivate 13-28 x 10^{10} CFU/ml of SchuS4. ▪ The WG also reviewed the associated BSL-3 SOP and made several requests for changes: o As one time point was tested, the WG requested that the SOP reflect a 2-hour incubation at 65°C to provide a safety margin. o The SOP state the pH of the Tris solution ▪ The WG also suggested that section of the SOP on the isolation of *F. tularensis* lipids could be combined with this procedure as they are essentially the same. ▪ See attached summary Action: The committee unanimously approved the Working Group recommendation that incubation at 65° for 1 hour in 6mM Tris pH 6.8/10mM EDTA/2% SDS completely inactivated infectivity of *F. tularensis* and approved the validation studies as written.
Item 7:	**Standard Operating Procedures:** (b)(6) **SOP, *F. tularensis* (Update)** ▪ Sue Priola summarized the updates to the BSL-3 OSP. ▪ Sue Priola informed the committee that the procedures outlined in the SOP match the validation procedures used with *F. tularensis* by the Bosio lab. The changes that were requested by the Working Group have been

	made to the SOP. ▪ The change suggested by the WG to consolidate the 2 methods (described in Item 6) were not made as the starting materials are different. ▪ There were no additional comments or concerns. Action: The committee unanimously approved (b)(6) **SOP, *F. tularensis* (Update)** as written.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Nancy Hoe presented the BSO report (see attached)
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ Not present.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ Not present.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present
Around the room	▪ None.

Other issues	▪ None.

Next Meeting:

- Date: 11/16/17
- Place: Library conference room
- Time: 1:00 PM

RML Biosafety Committee Meeting
October 19, 2017
Biosafety Officer/Responsible Official Report

1) ***Requests approved by BSO since last meeting:***
   a) *None*
2) ***New requests approved by committee via electronic review:***
   i) *None*
3) ***New requests***
   a) *Pathogen Registration Documents*
      i) ***Amend***
         (a) *Feldmann (LV)*
            (a) ***PRD 16-182****: Zika virus*
               (i) Add a mouse-adapted strain
            (b) ***PRD-13-92****: CCHFV*
               (i) Generation of a mouse-adapted strain
      ii) ***Renew***
         (a) *Feldmann (LV)*
            (a) ***PRD-17-143:*** *Coronavirus (exempt)*
         (b) *Best (LV)*
            (a) ***PRD-17-108****: West Nile Virus*
   b) *Registration Documents for Recombinant Nucleic Acid Experiments*
      i) ***Amend***
         (a) *Feldmann (LV)*
            (a) ***RD-17-431****: Molecular characterization of viral proteins of pathogenic RNA viruses*
               (i) Add hamsters as an animal model
               (ii) Add two plasmids for sub-cloning
   c) *Working Group Summary*
      i) *Bosio*
         (a) *Inactivation of Francisella tularensis strain SchuS4 by treatment with 6mM Tris pH 6.8/10mM EDTA/2% SDS at 65°C for 1 hour*
   d) *Standard Operating Procedures*
      i) ***Update***
         (a) *BSL-3 SOP for Francisella tularensis*
            (a) *Add procedure for inactivating of Francisella tularensis strain SchuS4 by treatment with 6mM Tris pH 6.8/10mM EDTA/2% SDS*

RML Biosafety Committee Meeting
October 19, 2017
Biosafety Officer/Responsible Official Report

3) ***Animal Study Protocols Review***

Title	*Associated PRD*	*Associated RD*	*Reviewer*
Protective efficacy of a novel subunit vaccine approach against Ebola virus in hamsters	*13-90 (Ebola) 13-82 (VSV)*	*15-404 17-431*	*R. Anderson*
Passage of Crimean Congo Hemorrhagic Fever in Rag2-/- mice	*13-92 (CCHFV)*		*N. Hoe*
Complementation of rickettsial virulence determinants in Guinea pigs	*14-38 (Rickettsia rickettsia)*	*14-110*	*R. Anderson*

4) ***Biosafety Training Performed – Rebecca Anderson, Nancy Hoe***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
New Employee	*1*	*1*
BSL-3 Laboratory	*3*	*4*
Visitor	*3*	*4*
Biosafety Briefs	*2*	*2 WIPs*
Bite/Scratch Procedure – exercise	*2*	*18*

5) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
a) *Biological Incident Report:*
   i) *None*

6) ***Select Agent Issues-****None*

7) ***Other Issues -****None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 11/16/2017
Meeting Time: 1:02 PM **Adjourned:** 1:37 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Kevin Mora	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Karin Peterson	☒	☐
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Dana Scott	☒	☐
Alan Applebury	☐	☒	Nancy Hoe	☒	☐	Alexandra Scranton	☐	☒
Chris Bosio	☒	☐	Chris Hoffman	☐	☒			
Marshall Bloom (EO)	☐	☒	Clay Jarrett	☒	☐			
Teresa Borino	☒	☐	Josh Kellar (EO)	☐	☒			
Megan Brose	☒	☐	Scott Kobayashi	☒	☐			
Carol Calderwood	☐	☒	Jamie Lovaglio	☒	☐			
Marcie Caldwell (EO)	☐	☒	Andrea Marzi	☒	☐			
Paul Carlson	☐	☒	Alida Merritt	☐	☒			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 10/19/17 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** ▪ Bob Heinzen pointed out that there was typo on page 5, "transmissions" should be "transmission". ▪ Sue Priola noted a couple of minor typos. Action: Meeting minutes for 10/19/17 were unanimously approved with the above minor modifications.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals

(Renewal)

- Feldmann (LV)
- **PRD#17-123: Phlebovirus**
- Becky Anderson presented the risk assessment. The proposed studies are to develop an understanding of the molecular basis of phlebovirus viral life cycle, pathogenesis, and mechanisms of virulence acquisition and evolution. Some Phleboviruses are known to be human pathogens and to cause phlebotomus fever. The listed human pathogenic phleboviruses transmitted by mosquito only cause self-limiting illness with symptoms such as fever, headache, photophobia, conjunctivitis, nausea, stiff neck, and back/joint pains. The illness temporally lasts 2-4 days and is followed by a period of weakness and other symptoms during convalescence. The clinical course is generally benign, and the patient fully recovers within 7-30 days. Human pathogenic viruses can also produce minimal symptoms remaining unrecognized unless seroconversion is detected. Rarely, infection with Tuscana virus can cause severe illness with aseptic meningitis/encephalitis and systemic symptoms. No fatal cases have been reported.
    - SFTSV presents with non-specific symptoms including fever and gastrointestinal symptoms. Multiorgan failure develops rapidly in most patients. Case fatality rates are 2.25 to 12% (transmitted by ticks).
    - Heartland virus- symptoms include fever, headaches, fatigue, muscle aches, and diarrhea (transmitted by ticks).
    - Malsoor virus-not known to be a human pathogen, but BSL-3 because of close genetic relationship to SFTSV.
    - Bhanja virus-results in a febrile illness and encephalitis in humans (transmitted by ticks).
- The natural route of transmission is through tick or mosquito bites. The primary lab hazards include: parenteral inoculation, accidental sharps injuries, and generation of aerosols. There are no vaccines or post exposure treatments available, treatment currently involves palliative care.
- Alex Scranton submitted questions to Sue Priola by email. Alex Scranton questioned why on page 3 that the Agent Inactivation section did not match what was listed in the comment section of the Cell Sorting description where it states that 10% bleach or 70% ethanol will be used for disinfection and inactivation. The committee discussed and agreed that the wording in the Cell sorting section was misleading and will delete, “and inactivation” from the sentence that describes bleach and ethanol.
- Alex Scranton submitted a second question as to why the PRD states that

	field tick samples will be in enhanced BSL-2, but the next page states "BSL3 viruses will be handled in the BSL-3 lab". Nancy Hoe stated that no active work with any samples is performed until the sequencing of viruses is complete. Once they have the sequence information, the samples can be worked with at the appropriate biosafety level. Additionally, they have yet to isolate a BSL-3 virus from the tick samples. ▪ BSL-2/ABSL-2 is approved for all viruses on the PRD except: SFTSV, Heartland, Malsoor, and Bhanja virus, these viruses are approved for BSL-3/ABSL-3. ▪ Currently approved animal models are mice and non-human primates. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Andrea Marzi abstaining) **PRD#17-123** as written.
Item 2:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Feldmann (LV) ▪ **PRD#17-132: Non-Select Agent Influenza viruses** ▪ Becky Anderson presented the risk assessment. The proposed studies are to characterize various seasonal and pandemic influenza A viruses. Experiments may include assessment of replication kinetics, RNA isolation, and *in vivo* animal studies. Influenza virus infections are characterized by an acute viral disease of the upper respiratory tract characterized by fever, headache, myalgia, malaise, sore throat, non-productive cough, sneezing and nasal discharge. Pulmonary complications of influenza include pneumonia (viral and bacterial), croup, asthma and bronchitis. Myocarditis and pericarditis are occasional cardiac complications. Fatality due to influenza is generally low, except in those with chronic lung or heart conditions. Secondary bacterial pneumonia after influenza is a leading cause of mortality worldwide. The current PRD has not changed except for the addition of some bat strains and bat cells to culture the viruses in. The bat strains included in this renewal do not infect human cells *in vitro* and are only known to be found in bats. The natural route of transmission for influenza virus is by aerosols and droplets (from coughing and sneezing) or from contact transmission from contaminated surfaces. Primary lab hazards include accidental needle sticks, generation of aerosols, and parenteral inoculation. Treatment of influenza infections typically includes fluids and rest. Some antiviral agents (mainly oseltamivir) may be employed to treat infection.

	▪ The following biosafety levels are currently approved: Circulating human strains (e.g. H1/H3/B): BSL-2/ABSL-2 Low pathogenicity avian influenza (LPAI): H1-4, H6, H8-16: BSL-2/ABSL-2 Equine and Swine influenza: BSL-2/ABSL-2 Bat influenza strains: H17, H18, N10, N11: BSL-2/ABSL-2. Non-contemporary, wild-type human influenza (H2N2): BSL-3/ABSL-3 (some experiments performed at BSL-4/ABSL-4) Human and swine origin H1N1: BSL-3/ABSL-3 (some experiments performed at BSL-4/ABSL-4) ▪ Currently approved animal models are mice, ferrets, and non-human primates. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal Action: The committee approved (Andrea Marzi abstaining) **PRD#17-132** as written.
Item 3:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Feldmann (LV) ▪ **PRD#17-202: Influenza viruses (H5Nx, H7Nx, H7N9, and Reconstructed 1918 Influenza virus)** ▪ Becky Anderson presented the risk assessment. This renewal combines PRD#12-131 and PRD#13-123. There was confusion with the PRD numbers on animal study protocols, so the new combined PRD is now PRD#17-202. The proposed studies include studying the listed influenza viruses *in vitro* and *in vivo*. Avian influenza A viruses are referred to as low pathogenic avian influenza (LPAI) and highly pathogenic avian influenza (HPAI), based on the severity of illness caused in poultry. To date, only H5 and H7 subtypes have been shown to be HPAI, although not all H5 and H7 viruses are highly virulent. ▪ Human infections from influenza A virus subtypes H5, H7 and H9 range from eye infections (conjunctivitis) to influenza-like illness symptoms to severe respiratory illness. Symptoms of H5N1 range from typical flu-like symptoms (e.g., fever, sore throat, cough, and muscle aches) to pneumonia, acute respiratory distress syndrome, multiple organ failure, lymphopenia, elevated liver enzyme levels and abnormal clotting profiles, diarrhea, vomiting, abdominal pain, pleuritic pain, and bleeding from the nose and gums. The H5N1 mortality rate is estimated at 59%. ▪ H7N9-is a low pathogenicity avian influenza, causes severe respiratory illness in human's. The initial symptoms include fever, cough and shortness of

	breath. There have been 135 laboratory confirmed cases with 44 deaths (mortality 32%). Reconstructed 1918 Influenza virus presents with abrupt onset of fever with temperature >100.4 F, dry cough, chest pain, myalgias. Case fatality rate in US during the pandemic was 2.5%. ▪ The natural route of transmission includes aerosol, close contact with sick or infected poultry, and some human to human transmission. Primary lab hazards include accidental needle sticks, generation of aerosols, and parenteral inoculation. There are no vaccines or specific treatments available. Various subtypes are sensitive to neuraminidase inhibitors if treatment is necessary. ▪ The biosafety level varies slightly between the agents but is BSL-3 enhanced for HPAI, 1918, and H7N9. Some of the enhancements include: decontamination of laboratory liquid effluents and the capability to shower out of the lab or animal facility. ▪ Recommendations: a. The agents will be approved at BSL-3 enhanced, but to meet the facility requirements, work will be conducted at BSL-4/ABSL-4. b. Please be aware there is potential for reassortants and therefore work with H5 and H7 should be physically and/or temporally separated. c. Reconstructed 1918 Influenza virus will be kept physically separate from other high pathogenicity influenza strains. d. If any of the viruses are to be sent to lower containment, they have to be kept physically separate from Rift Valley Fever Virus e. Nucleic acids and proteins from HPAI are not regulated as SA, but are regulated pursuant to 9 CFR Part 122 (i.e. permits are required for import or transport w/in US). ▪ Animal studies with ferrets, mice, poultry, and NHPs are proposed. BSL-4 SOPs for the animal work are in place. ▪ Sue Priola asked if poultry could be listed or if it should be more specific? Nancy Hoe said that is the way the CDC DSAT registration lists the animal species so it is good to be consistent. ▪ There were no dual use questions marked yes. The committee discussed the dual-use potential of these experiments and agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Andrea Marzi abstained) **PRD#17-202** with the following changes/recommendations: 1. Correct the PRD numbers that were combined to make the current PRD#17-

	202. After further review, the PRD numbers listed were accurate. No changes were necessary.
Item 4:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal)</u> ▪ Feldmann (LV) ▪ **PRD#17-145: SARS-CoV** ▪ Becky Anderson presented the risk assessment. The proposed studies are to perform *in vitro* assays to study viral growth kinetics in the presence of various antiviral compounds. Animal studies will also be conducted to determine efficacy of various antiviral compounds *in vivo*. SARS-CoV infections result in a respiratory syndrome that initially presents with a fever greater than 100.4 degrees F, accompanied with myalgia, malaise, chills, and a non-productive cough. Within 2 to 7 days, respiratory symptoms follow including a dry cough, shortness of breath, and difficulty breathing or hypoxia. Some cases become more severe and patients require oxygen support and mechanical ventilation. Case fatality rate is 14 to 15% overall. Case fatality rate for older persons is greater than 50%. Transmission occurs through human to human contact via direct contact with mucous membranes, respiratory droplets and/or infected body fluids, or contact with fomites. SARS treatment is focused on supportive care. Ribavirin, corticosteroids, lopinavir, ritonavir, type 1 interferon, intravenous immunoglobulin, and SARS convalescent plasma have all be used to treat patients infected with SARS-CoV, but it has not been determined how beneficial each of these treatments have been. Primary lab hazards include inhalation from aerosols, accidental parenteral inoculation, and accidental needle sticks. ▪ BSL-3/ABSL-3 is recommended for work with the virus. For logistical reasons, experiments with SARS-CoV are performed in the BSL-4/ABSL-4. ▪ Animal studies with mice and non-human primates were proposed. ▪ There were no dual use questions marked yes. The committee discussed the dual-use potential of these experiments and agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved (Andrea Marzi abstained) **PRD#17-145** as written.
Item 5:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal)</u> ▪ Bosio (LB) ▪ **PRD#17-203: *Staphylococcus aureus* (MRSA, VISA, MSSA)**

	▪ Becky Anderson presented the risk assessment. The proposed studies are to assess the metabolic capacity of *S. aureus*. The Bosio lab will test the ability of *S. aureus* to utilize different compounds for generating energy using the Seahorse XFe96 analyzer. *S. aureus* is an opportunistic pathogen that can cause a variety of self-limiting to life-threatening diseases in humans. *S. aureus* is one of the most common causes of skin, soft-tissue, and nosocomial infection. The bacteria are a leading cause of food poisoning, resulting from the consumption of food contaminated with enterotoxins. Staphylococcal food intoxication involves rapid onset of nausea, vomiting, abdominal pain, cramps, and diarrhea. Symptoms usually resolve after 24 hours. The strains to be used include, methicillin resistant *S. aureus*, vancomycin intermediate *S. aureus*, and methicillin sensitive *S. aureus*. Antibiotics such as cloxacillin and cephalexin are commonly used to treat staph infections. Vancomycin which is administered intravenously is used to treat MRSA. The natural route of transmission is ingestion of contaminated food, vertical transmission, human to human transmission if in contact with purulent lesions. Primary lab hazards include inhalation from aerosols, accidental parenteral inoculation, and accidental needle sticks. ▪ BSL-2 is appropriate for the prosed studies. ▪ No animal studies were proposed. ▪ There were no dual use questions marked yes. The committee discussed the dual-use potential of these experiments and agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved (Chris Bosio abstained) **PRD#17-203** as written.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Nancy Hoe presented the BSO report (see attached)
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ Not present.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ Nothing to report.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present
Around the room	▪ None.

Other issues	▪ None.

Next Meeting:

- Date: 12/21/17 May not occur if no submitted registrations.
- Place: Library conference room
- Time: 1:00 PM

RML Biosafety Committee Meeting
November 16, 2017
Biosafety Officer/Responsible Official Report

1) Requests approved by BSO since last meeting:

a) None

2) ***New requests approved by committee via electronic review:***

i) *None*

3) ***New requests***

a) *Pathogen Registration Documents*

i) ***Renew***

(a) *Feldmann (LV)*

(a) ***PRD-17-123:*** *Phlebovirus*

(b) ***PRD-17-132****: Influenza A viruses: Influenza A subtypes H1-H18 with the exception of 1918 (H1N1) and HPAI subtypes H5 and H7 and Low pathogenic avian influenza H7N9*

(i) Addition of bat influenza strains: H17, H18, N10, N11

(c) ***PRD-17-202****: Influenza A viruses: HPAI subtype H5Nx, HPAI subtype H7Nx, Reconstructed 1918 H1N1, LPAI H7N9*

(i) Previous PRDs for HPAI and 1918 are not combined in this PRD

(d) ***PRD-17-145****: SARS-CoV*

ii) ***New***

(a) *Bosio (LB)*

(a) ***PRD-17-203****: Staphylococus aureus*

2) ***Animal Study Protocols Review***

Title	***Associated PRD***	***Associated RD***	***Reviewer***
Effects of Ab opsonization on neutrophil recruitment to draining lymph nodes in response to virulent Y. pestis	*13-04 (Y. pestis)*	*N/A*	*N. Hoe*
Determining the Role of Beclin 1 complex on Ebola virus infection	*13-90 (Ebola)*	*N/A*	*N. Hoe*
Polyclonal antibody production in rabbits to Borrelia species	*N/A*	*14-319*	*R. Anderson*

3) ***Biosafety Training Performed – Rebecca Anderson, Megan Brose***

Type of Training	***Number of Sessions***	***Number of Employees Trained***
Select Agent Initial	*1*	*2*
BSL-4 Refresher	*1*	*1*
Visitor	*1*	*1*
Biosafety Briefs	*1*	*RMVB*

4) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
   a) *Biological Incident Report:*
      i) *None*

5) ***Select Agent Issues-****None*

6) ***Other Issues -****None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 12/15/2017
Meeting Time: 10:03 AM **Adjourned:** 10:45 AM
(b)(6)

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Kevin Mora	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Karin Peterson	☐	☒
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Dana Scott	☐	☒
Alan Applebury	☐	☒	Nancy Hoe	☒	☐	Alexandra Scranton	☒	☐
Chris Bosio	☐	☒	Chris Hoffman	☐	☒			
Marshall Bloom (EO)	☒	☐	Clay Jarrett	☒	☐			
Teresa Borino	☐	☒	Josh Kellar (EO)	☐	☒			
Megan Brose	☒	☐	Scott Kobayashi	☒	☐			
Carol Calderwood	☐	☒	Jamie Lovaglio	☐	☒			
Marcie Caldwell (EO)	☐	☒	Andrea Marzi	☐	☒			
Paul Carlson	☐	☒	Alida Merritt	☒	☐			

(P=present; A=absent)
Guests (b)(6) **Alex Scranton participated via phone**

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes** ▪ Since this was not a regularly scheduled committee meeting, the minutes from the previous meeting were not reviewed. The minutes from the November 16th meeting will be reviewed at the January 18th, 2018 meeting.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	<u>Purpose of Special Committee Meeting</u> ▪ This meeting was called to review an incident involving the creation of non-approved strains of *Francisella tularensis* and to discuss the potential for non-compliance with the NIH Office of Biotechnology Activities (OBA) recombinant guidelines and the CDC Division of Select Agents. ▪ No human pathogen or recombinant DNA registrations were reviewed at this meeting.

Incident Report

- Nancy Hoe presented the incident report to the committee. See safety incident investigation form for detailed information.
- On December 13, 2017, (b)(6) (b)(6) that over the period of July – November 2017, the (b)(6) had created specific recombinant strains of *Francisella tularensis* strain Schu4 without prior approval of the RML IBC.
- As described in RD-13-125, (b)(6) currently has approval for the following nucleic acid inserts:
  - *gfp-mut3*, encoding the Green Fluorescent Protein,
  - *dsred*$_{m+}$ and *mCherry* encoding a Red Fluorescent Protein
  - various *F. tularensis* chromosomal fragments used for allelic replacement
  - single *F. tularensis* genes encoding various proteins identified as involved in intracellular pathogenesis
  - chimeric fusions of *F. tularensis* genes with a Bordetella pertussis *cyaA* fragment
  - chimeric fusions of *F. tularensis* genes with a *bla* fragment
- The 5 constructs that were created by the (b)(6) all contain a single *E. coli* gene per strain. The inserted genes are involved in phospholipid biosynthesis (*plsY, plsC, acpP*, and *plsX*) and were constructed to study the contribution of phospholipid biosynthesis to *F. tularensis* virulence. *F. tularensis* has long acyl chains on their fatty acids and the (b)(6) hypothesized that if the *E. coli* homologs were inserted, they could make *F. tularensis* less immunosuppressive. Ultimately, they expected the strains to have a decrease in virulence.
- The knock out of the specific genes was expected to be lethal, so they (b)(6) inserted *E.coli* homologs into *F. tularensis*. The strains were constructed with previously approved allelic exchange methods and/or expression plasmids and approved antibiotic resistance markers of *F. tularensis* SchuS4 (RD-13-125). Once these strains were created, they were added to the Select Agent inventory.
- (b)(6) elf-reported the oversight on 12/13/17 once she realized that the lab did not have approval to create the above listed strains. At that time, all work with the strains was immediately terminated.
- This incident does not involve a theft, loss, or release of a Select Agent and does not involve a restricted experiment as defined by the Select Agent regulations (42 CFR Part 73).
- Notifications were made the following day to: Dr. Sue Priola, RML IBC

	Chair, Jeff Potts, NIH Biorisk Manager, and Dr. Marshall Bloom, RML Associate Director for Science Management, NIAID. Dr. Bloom also notified Dr. Karyl Barron of the NIAID Division of Intramural Research ▪ Nancy Hoe Reviewed the relevant sections of the NIH Guidelines with the committee. <u>Questions from the Committee Members</u> ▪ Alida Merritt asked how the incident was discovered. Nancy Hoe informed the committee that one of the (b)(6) members went to another Select Agent lab for advice on constructing other mutant strains and that lab member mentioned that they need to be sure they have IBC approvals in place prior to starting the new work. At this time, the (b)(6) (b)(6) then reviewed their RD to verify what approvals they had. It was then that they realized they did not have approval to insert *E. coli* genes into *F. tularensis*. Marshall Bloom added that if the knock-out of these genes was not lethal, the lab probably would never had thought to insert the same gene from a non-pathogenic bacteria.
	<u>Questions for the Committee</u> Sue Priola posed 5 questions for the committee to address. 1. Was there, or was there not, a failure to comply with OBA/NIH recombinant DNA guidelines? a. The committee agreed that there was a failure to comply with the NIH rDNA Guidelines. 2. Was there, or was there not, a failure to comply with DSAT Select Agent regulations? a. The committee agreed that there was not a failure to comply with Select Agent regulations. There was no theft, loss, or release. All experiments were performed at the appropriate biosafety level (BSL-3), and the strains were properly logged into the inventory as soon as they were created. 3. If the answer to either question 1 or 2 is yes, do the incidents described indicate a deliberate attempt to circumvent the OBA/NIH recombinant DNA Guidelines or the CDC DSAT Select Agent regulations? a. No, the committee agreed that this was not a deliberate attempt. (b)(6) (b)(6) thought she had approval to perform the experiments. To further the case, the PI self-reported as soon as she realized that the strains were created without proper approval in place. 4. Does the IBC consider this incident significant enough to report to the Office of Science Policy (OSP)?

	a. The committee discussed this topic extensively. The committee agreed that according to the NIH rDNA Guidelines, ANY incidence of non-compliance must be reported and thus this incident must be reported. The group agreed that Nancy Hoe, the Biosafety Officer would report the incident to OBA. b. The committee also discussed if this was a "significant" incident. The committee agreed that this was not a significant incident because the PI thought they had approval to make the strains, there was no deliberate attempt to circumvent the NIH rDNA guidelines, the PI self-reported the incident, and the strains that were created had genes inserted from a non-pathogenic bacteria. The committee agreed that there were no dual use concerns with the strains that were created. The committee agreed that the PI self-reporting proves that the culture of biosafety at RML works. No punitive actions are warranted for this incident. 5. What, if any, action(s) does the committee recommend? a. Rebecca Anderson will work with the PI (b)(6) to update RD-13-125 with the relevant information to prepare a submission to the IBC for the January meeting. b. Nancy Hoe will send out an email to all RML PIs reminding them of their responsibilities under the NIH rDNA Guidelines. This email will also give examples of what needs to be submitted to the IBC, and the PIs will be reminded to review their RD periodically with their staff. c. Sue Priola will write a formal letter to (b)(6) to inform her of the discussion and the actions requested by the committee. d. The committee agreed with all the actions that had already been taken.
Around the room	▪ Marshall Bloom questioned if reporting to CDC DSAT needs to occur. Nancy Hoe stated that the decision is up to her as the RO. Nancy Hoe informed the committee she will report by email a summary of the incident and actions taken by the committee.

Other issues	▪ None.

Next Meeting:

- Date: 1/18/18
- Place: Library conference room
- Time: 1:00 PM

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 01/18/2018
Meeting Time: 1:02 PM **Adjourned:** 1:59 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☒	Bruce Chesebro (EO)	☐	☒	Karin Peterson	☒	☐
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Dana Scott	☒	☐
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Alexandra Scranton	☐	☒
Alan Applebury	☐	☒	Nancy Hoe	☒	☐	Brian Vickrey (EO)	☐	☒
Chris Bosio	☒	☐	Chris Hoffman	☐	☒			
Marshall Bloom (EO)	☐	☒	Clay Jarrett	☒	☐			
Teresa Borino	☐	☒	Josh Kellar (EO)	☐	☒			
Megan Brose	☒	☐	Scott Kobayashi	☒	☐			
Carol Calderwood	☐	☒	Jamie Lovaglio	☐	☒			
Marcie Caldwell (EO)	☐	☒	Andrea Marzi	☒	☐			
Paul Carlson	☒	☐	Alida Merritt	☐	☒			

(P=present; A=absent)

Guests: (b)(6)

Minutes: Meeting minutes from 11/16/17 meeting

approved ☒ **not-approved** ☐

Special Meeting minutes from 12/15/17 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 11/16/17** ▪ Nancy Hoe pointed out on page 4, the first sentence should have "currently" placed before approved. ▪ Sue Priola pointed out minor typos. Action: Meeting minutes for 11/16/17 were unanimously approved with the above modifications.
Item 2:	**Minutes from 12/15/17** ▪ Nancy Hoe pointed out on page 3, in the Questions from the Committee Members section "went" was spelled wrong. ▪ On the top of page 4, "topic" was misspelled.

	▪ On page 4, Section 5.d. a statement should be added that the "Committee agreed with all the actions that had already been taken prior to the special IBC meeting." ▪ Sue Priola pointed out minor typos. Action: Meeting minutes for 12/15/17 were unanimously approved with the above modifications.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Best (LV) ▪ **PRD#18-135: Tick borne encephalitis viruses (TBEVs)** ▪ Becky Anderson presented the risk assessment. She informed the committee that PRD 12-134, 12-136, and 12-139 are being combined into one PRD. The proposed studies are to understand the events associated with the host immune response that are important for virus clearance and to understand how TBEV evade these host responses to infection. ○ TBEV infections usually present as a mild, influenza-type illness or as benign, aseptic meningitis, but may result in fatal meningoencephalitis. Fever is often biphasic, and there may be severe headache and neck rigidity, with short term paralysis of the limbs, shoulders or less commonly the respiratory musculature. A few patients are left with residual paralysis. Previous infection leads to immunity. ○ For Omsk: Sudden onset of fever, chills, headache, pain in lower and upper extremities and severe prostration. A papulovesicular rash on the soft palate, cervical lymphadenopathy and conjunctival suffusion are usually present. Central nervous system abnormalities develop after one to two weeks, and severe cases present with hemorrhages - no cutaneous rash. Leukopenia and thrombocytopenia are noticeable. Estimated case fatalities are 1-10%. Previous infection leads to immunity. ○ For Kyasanur: Presents similar to Omsk. Bradycardia is frequently present along with inflammation of the conjunctivae. A mild meningoencephalitis frequently occurs. A small proportion of patients develop coma or bronchopneumonia prior to death. Estimated case fatality rate is between 1-10%. ▪ The natural route of transmission is by the bite of an infected tick. There is no evidence of human to human transmission. Primary lab hazards include:

	accidental parenteral inoculation; generation of aerosols, and droplet exposure of the mucous membranes. ▪ The biosafety level for work with the listed TBEV viruses is BSL-4. ▪ Nancy Hoe stated that Central European in the strain list should be changed to Siberian. ▪ Nancy How also stated that the "containment centrifuge" box should be checked. ▪ Animal experiments with mice and non-human primates were proposed. Animal work with non-human primates is **pending DSAT approval**. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#18-135** with the following minor modifications: 1. Change Central European virus to Siberian in the strain list. 2. Check the box for "Containment centrifuge".
Item 2:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Feldmann (LV) ▪ **RD#18-429**: Rabies as a vaccine vector ▪ Reviewers: Karin Peterson, Sue Priola ▪ **Summary:** The RD renewal describes using rabies virus as a vaccine vector. ▪ Karin Peterson summarized the RD. The RD is straight forward and describes work with rabies virus as a vaccine vector. They will use viral proteins from the list and insert into rabies virus to ultimately vaccinate hamsters. Karin Peterson questioned where the list of foreign genes was. Becky Anderson explained that the list that is referred to is the list of viral families stated in the third paragraph in the discussion section. Karin Person also stated that they may use more than one gene in the vaccine, but a statement should be made to make it clearer. Sue Priola suggested that a statement should say something like, "Multiple genes will be used, but will always be less than 2/3 of the viral genome". The committee agreed that should be added. ▪ Additionally, it was not clear until discussion with Andrea Marzi during the meeting that virus like particles will be generated with this RD. The committee agreed that a few sentences should be added to the Description section to describe that work. ▪ Sue Priola questioned the NIH Guidelines that were listed. She stated that the NIH Guidelines for the Research Product section should be changed to III-D-2-a and the NIH Guidelines for Eukaryote Cells should be changed to III-D-3-a. ▪ Animal studies with hamsters and non-human primates were proposed.

	▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Andrea Marzi abstained) **RD#18-429** with the following minor modifications: 1. Change the NIH Guidelines for the Research Product section to III-D-2-a and the NIH Guidelines for Eukaryote Cells section should be changed to III-D-3-a. 2. Add a sentence to the Description section stating that multiple genes will be used but will always be less than 2/3 of the viral genome. 3. Add a couple sentences to the Description section stating that virus like particles will also be generated. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-3-a of the NIH Guidelines.
Item 3:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Bosio (LB) ▪ **RD#18-125**: *F. tularensis* interaction with host cells ▪ Reviewers: Bob Heinzen, Scott Kobayashi ▪ **Summary:** The RD renewal describes generating mutants of *F. tularensis* to further understand the interaction with host cells. ▪ Bob Heinzen summarized the RD. This is the standard recombinant DNA protocol for the Bosio lab that uses many traditional methods for bacteriology. The changes to the renewal are listed in red. The primary concern with this type of work is the use of antibiotic markers. The ones stated are ok to use. Bob Heinzen stated that it was not clear why they wanted to modify the phospholipid biosynthesis genes of *F. tularensis*, there should be a short description added to explain rationale. Katy Bosio informed the committee why they wanted to modify them and will add that description to the RD. Bob Heinzen added that they will be using anhydrotetracycline, but it is not listed in the RD, that should be added as well. ▪ Nancy Hoe stated that it should be clear that the spectinomycin that will be used is only for LVS. A sentence should be added to the RD to clarify. The DSAT approval letter for approved antibiotics should also be added to the RD. ▪ Bob Heinzen questioned why plasmid maps for pEDL18 and pEDL56 were not attached. (b)(6) stated that they are derivatives of pEDL17 and the changes are described in the attached material. The committee agreed that this is fine the way it is written. Bob Heinzen stated that it was not necessary to include the nucleotide sequence in the attached material and it should be

	deleted. ▪ Scott Kobayashi stated that "gonorrhea" was spelled wrong and needs to be corrected. ▪ Sue Priola asked why the biosafety level is listed as BSL-3 for the cloning section. The committee agreed that it should be changed to BSL-2 only. ▪ The NIH Guidelines were appropriate and there were no dual use concerns. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Chris Bosio abstained) **RD#18-125** with the following modifications: 1. Add a description to describe the rationale for modifying the phospholipid biosynthesis genes. 2. Add to the RD that anhydrotetracycline will be used. 3. Add the DSAT letter listing approved antibiotics. 4. Delete the nucleotide sequence in the attached material. 5. Delete BSL-3 from the containment section in Section A. 6. Correct the spelling for gonorrhea. 7. Clarify that spectinomycin will only be used for LVS. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 and BSL-3 under III-D-1-a, and III-D1-b of the NIH Guidelines.
Item 4:	**Working Group Summary** ▪ Sue Priola reviewed the Working Group summary with the committee. Karin Peterson, Chris Bosio, and Bob Heinzen were the working group members that reviewed the inactivation methods from Heinz Feldmann's lab. ▪ The Feldmann lab tested the ability of gamma irradiation to inactivate TBEV. They used the same procedures that they have used for all the other viral families. In this case, they used Russian Spring Summer Encephalitis virus as the representative TBEV virus. They showed in two different experiments that all the virus was inactivated by gamma irradiation at the specified doses. ▪ The associated SOP was updated to reflect the addition of TBEV to the table of viruses approved for irradiation and the appropriate dose for inactivation. ▪ See summary attached.

	Action: The committee unanimously approved the Working Group recommendation that irradiation completely inactivated TBEV and approved the validation studies as written.
Item 5:	**Standard Operating Procedures: SOP#4-28-27 Removal of Specimens for Irradiator (Update)** ▪ Sue Priola informed the committee that the irradiation SOP has been updated to include gamma irradiation procedures for TBEV viruses. ▪ There were no comments or concerns with the SOP. Action: The committee unanimously approved **SOP#4-28-27 Removal of Specimens for Irradiator (Update)** as written.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Nancy Hoe presented the BSO report. ▪ Nancy Hoe reviewed the incident report that was submitted to OBA. ▪ Nancy Hoe informed the committee about the lifted ban on gain of function research.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ There have been a few slips, trips, and falls with the bad weather. There are Yak Tracks available if anyone wants them. ▪ The St. Patrick Hospital drill in December went well. ▪ There was a back injury where an employee improperly lifted.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ Planning annual shutdowns for first half of the year, both BSL-3 and BSL-4 ○ (b)(6); (b)(3):42 U.S.C. 262a(h) is down now and almost complete. ○ (b)(6) – Feb. 29-Mar. 2 ○ (b)(6); (b)(3):42 U.S.C. 262a(h) (Public Health Security and Bioterrorism – Feb. 1 ○ (b)(6) – Feb. 12-16 ○ (b)(6) – Mar. 12-16 ○ (b)(6) – Mar. 19-23 ○ (b)(6); (b)(3):42 U.S.C. – Mar. 26 ○ (b)(6) – Apr. 16 ○ (b)(6); (b)(3):42 – sometime in May ▪ Reviewed the FLCL Annual Report

Report	**Associate Director Report/Marshall Bloom** ▪ Not present
Around the room	▪ None.

Other issues	▪ None.

Next Meeting:

- Date: 2/15/18
- Place: Library conference room
- Time: 1:00 PM

RML Biosafety Committee Meeting
January 18, 2018
Biosafety Officer/Responsible Official Report

1) Requests approved by BSO since last meeting:

a) None

2) ***New requests approved by committee via electronic review:***

i) *Annual review of the MCL Operations and Safety Procedures*

(a) *review complete 12/18/17*

3) ***New requests***

a) *Pathogen Registration Documents*

i) ***Renew***

(a) *Best (LV)*

(a) ***PRD-18-135:*** *Flaviviruses (TBEV; Kyasenur Forest disease virus, Omsk hemorrhagic fever virus)*

(i) add work with non-human primates

b) *Registration Documents for Recombinant Nucleic Acid Experiments*

i) ***Renew***

(a) *Feldmann (LV)*

(a) ***RD-18-429****: RABV as a vaccine vector*

ii) *Bosio (LB)*

(a) ***PRD-18-125****: recombinant Francisella tularensis*

c) *Working Group Summary*

i) *Feldmann*

(a) *inactivation of TBEV viruses by gamma irradiation*

d) *Standard Operating Procedures*

i) *Update*

(a) *SOP 4-28-27: Removal of Specimens for the Irradiator*

(a) *add inactivation of TBEV viruses*

2) ***Animal Study Protocols Review***

Title	***Associated PRD***	***Associated RD***	***Reviewer***
Evaluation of the protective efficacy of a VSV-based Zika virus vaccine in pigtail macaques	*16-182 (Zika virus) 13-82 (VSV)*	*N/A*	*M. Brose*

RML Biosafety Committee Meeting
January 18, 2018
Biosafety Officer/Responsible Official Report

Title	***Associated PRD***	***Associated RD***	***Reviewer***
Characterization of distinct strains of Crimean Congo Hemorrhagic Fever in IFNAR-/- mice	*13-92 (CCHFV)*	*N/A*	*R. Anderson*
Evaluation of an adenovirus vaccine candidate for Crimean Congo Hemorrhagic Fever against a heterologous challenge in mice	*13-92 (CCHFV)*	*17-410*	*R. Anderson*
Small Rodent Trapping in Mali	*N/A*	*N/A*	*N. Hoe*

3) ***Biosafety Training Performed – Rebecca Anderson, Megan Brose***

Type of Training	***Number of Sessions***	***Number of Employees Trained***
Select Agent Initial	*1*	*3*
Laboratory Biosafety for Support Personnel	*2*	*2*
BSL-4 Refresher: Bite/Scratch	*4*	*26*
BSL-3/BSL-4 Refresher for NIH Police and Emergency Responders	*2*	*6*
Visitor	*1*	*1*
Biosafety Briefs	*2*	*WIPs*
Full-length Clone Lab Initial	*1*	*2*
Full-length Clone Lab Annual Refresher	*3*	*8*

4) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
a) *Biological Incident Report:*
   i) *None*

5) ***Select Agent Issues-****None*

6) ***Other Issues –***
a) *Government lifts pause on Gain-of-Function research*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 02/15/2018
Meeting Time: 1:03 PM **Adjourned:** 1:55 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Dana Scott	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Heinz Feldmann (EO)	☐	☒	Alexandra Scranton	☐	☒
Becky Anderson (EO)	☒	☐	Nancy Hoe	☒	☐	Brian Vickrey	☐	☒
Alan Applebury	☐	☒	Chris Hoffman	☐	☒			
Chris Bosio	☒	☐	Clay Jarrett	☒	☐			
Marshall Bloom (EO)	☐	☒	Josh Kellar (EO)	☐	☒			
Megan Brose	☐	☒	Scott Kobayashi	☐	☒			
Carol Calderwood	☐	☒	Jamie Lovaglio	☐	☒			
Marcie Caldwell (EO)	☐	☒	Andrea Marzi	☒	☐			
Paul Carlson	☒	☐	Alida Merritt	☒	☐			
Bruce Chesebro (EO)	☐	☒	Karin Peterson	☒	☐			

(P=present; A=absent)

Guests:

Minutes: Meeting minutes from 1/18/18 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 1/18/18** ▪ Nancy Hoe pointed out on page 2, the third bullet in Item 1 should be changed from "onto" to "into". ▪ Sue Priola pointed out minor typos. Action: Meeting minutes for 1/18/18 were unanimously approved with the above minor modifications.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New)

	▪ Bosio (LB) ▪ **PRD#18-202: *Yersinia pestis* (exempt)** ▪ Becky Anderson presented the risk assessment. The purpose of the Bosio study is to compare the pulmonary T cell response among animals vaccinated and challenged with attenuated *Y. pestis* to animals vaccinated and challenged with various strains of *F. tularensis*. The strains that they will work with are attenuated strains of *Y. pestis* and are not Select Agents. o Lcr- (low calcium response): KIM6 strains lack the Lcr plasmid (Lcr^-) are irreversibly attenuated due to the loss of a virulence plasmid. o Pgm- (pigmentation phenotype): Both KIM5 and KIM6 strains lack the Pgm virulence plasmid. Pgm^- mutants result in avirulence. These strains have been used for years as live human vaccines with no significant plague-associated problems. The mutation that occurs is due to the excision of about 102 kilobases of chromosomal DNA. ▪ KIM5 strain is the strain that caused a fatal laboratory acquired infection with *Y. pestis*. A postmortem diagnosis of hereditary hemochromatosis was made based on histopathologic, laboratory, and genetic testing. One possible explanation for the unexpected fatal outcome in this patient is that hemochromatosis-induced iron overload might have provided the lab strain (KIM5), which is attenuated in its ability to acquire iron, with sufficient iron to overcome its iron-acquisition defects and become virulent. Other than the described laboratory acquired infection, these strains are not known to cause disease in humans. The primary lab hazards include: parenteral contact, accidental sharps injuries, and exposure to aerosols. ▪ The biosafety level for work with the exempt strains of *Y. pestis* is BSL-2/ABSL-2. All procedures involving the administration of *Y. pestis* exempt strains to mice must be conducted in a Class II BSC in the procedure room. ▪ Animal experiments with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Chris Bosio abstained) **PRD#18-202** as written.
Item 2:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Hasenkrug (LPVD) ▪ **PRD#18-130: Epstein-Barr virus (EBV)** ▪ Becky Anderson presented the risk assessment. The Hasenkrug lab uses EBV to create immortalized EBV cell lines from humanized mice. Infection with EBV results in infectious mononucleosis in young adults that is characterized by fever, sore throat, abdominal discomfort, pharyngitis, tonsillitis, tender generalized lymphadenopathy. The disease generally lasts 1 to 4 weeks;

	however, symptoms can last for up to one year in some patients. Burkitt's Lymphoma can arise from early infection with EBV in B cells. EBV infections themselves are quite prevalent affecting more than 90% of individuals worldwide in the first 20 years of life. Treatment of infectious mononucleosis is mainly supportive. Viral replication can be inhibited by nucleoside analogues which can reduce or stop viral shedding but have no effect on the symptoms. Lymphoproliferative disorders associated with EBV can be treated with anti-CD20 monoclonal antibodies and EBV specific cytotoxic T lymphocytes along with anti-viral drugs. EBV is primarily transmitted through sexual contact or saliva and there is a possibility that it is spread through blood. The primary lab hazards include: accidental needle sticks, aerosolized material, and direct exposure to mucous membranes. ▪ The biosafety level for work with EBV is BSL-2. All work that generates aerosols must occur in a BSC. ▪ No animal studies were proposed, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#18-130** as written.
Item 3:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment) ▪ Feldmann (LV) ▪ **PRD#13-91 Amend: Henipaviruses (Nipah, Hendra, and Cedar)** ▪ Becky Anderson described the amendment and presented the risk assessment. The Feldmann lab would like to add bats to the Henipavirus PRD. The bats will specifically be added for Cedar virus only, which is a non-select agent virus. To add bats to Hendra and Nipah, the Feldmann lab would need to obtain DSAT approval. These studies will focus on characterizing the course of Cedar virus infection in a pteropid bat, *Rousettus aegyptiacus*, to identify the localization and timing of virus replication and shedding. The primary hazards of working with bats, include teeth and nails that pose a risk for bites and scratches. To mitigate these hazards, studies with Cedar virus will be conducted in the BSL-4 according to the IBC approved *SOP#4-28-56 Husbandry Procedures for Bats in Level 4 Biocontainment.* PPE will include: positive pressure suit and additional protective gloves (leather or sheep skin gloves) over the suit gloves when manually restraining bats. ▪ The biosafety level for work with Cedar virus is BSL-4/ABSL-4. ▪ Animal studies with bats were proposed for Cedar virus only. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Andrea Marzi abstained) **PRD#13-91 Amend** as

	written.
Item 4:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Feldmann (LV) ▪ **RD#15-404 Amend**: VSV-replication competent ▪ Reviewers: Karin Peterson, Sue Priola ▪ **Summary:** The amendment is to add Flaviviruses to the list of viruses being studied. ▪ Karin Peterson summarized the RD. The amendment is to add Flaviviruses to the list of viruses for this RD. Karin Peterson stated that Feldmann lab had already added Zika virus, but this did not include the other Flaviviruses that they have registered on their PRD. ▪ Sue Priola had no additional comments or concerns. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Andrea Marzi abstained) **RD#15-404 Amend** as written. Research using prokaryotic hosts is approved at BSL-2 under section III-D-1-a and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a and III-D-3-a of the NIH Guidelines.
Item 5:	**Standard Operating Procedures: BSL-3 Operations and Safety Procedures (Update)** ▪ Becky Anderson informed the committee that the Decontamination/Waste Handling section was updated to include disinfection procedures for data transfer devices and laptops or computers. ▪ Sue Priola pointed out that the additional wording would fit better in item 7.a. where contaminated equipment is discussed. The committee agreed with this change. ▪ There were no additional comments or concerns with the SOP. Action: The committee unanimously approved **BSL-3 Operations and Safety Procedures (Update)** with the following minor modification: 1. Move item 9 to 7.a. in the Decontamination/Waste handling section.
Item 6:	**Standard Operating Procedures: ABSL-3 Operations and Safety Procedures (Update)** ▪ Becky Anderson informed the committee that the Decontamination/Waste

	Handling section was updated to include disinfection procedures for data transfer devices and laptops or computers. ▪ There were no comments or concerns with the SOP. Action: The committee unanimously approved **ABSL-3 Operations and Safety Procedures (Update)** as written.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Nancy Hoe presented the BSO report.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ Paul Carlson informed the committee that there is a new pest management contract in place. Employees may see new cardboard traps placed throughout campus. Logbooks are available for employees to fill out if they see pests in specific areas.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ Not present
Report	**Associate Director Report/Marshall Bloom** ▪ Not present
Around the room	▪ None.

Other issues	▪ None.

Next Meeting:

- Date: 3/15/18
- Place: Library conference room
- Time: 1:00 PM

RML Biosafety Committee Meeting
February 15, 2018
Biosafety Officer/Responsible Official Report

1) ***Requests approved by BSO since last meeting:***
   a) *None*
2) ***New requests approved by committee via electronic review:***
   a) *None*
3) ***New requests***
   a) *Pathogen Registration Documents*
      i) ***New***
         (a) *Bosio (LB)*
            (a) ***PRD-18-202:*** *Attenuated strains of Yersinia pestis (exempt)*
      ii) ***Renew***
         (a) *Hasenkrug (LPVD)*
            (a) ***PRD-18-130****: EBV transformation of human B cells*
      iii) ***Amend***
         (a) *Feldmann (LV)*
            (a) ***PRD-13-91****: Paramyxoviridae, Henipavirus*
               (i) add bats for Cedar virus only
   b) *Registration Documents for Recombinant Nucleic Acid Experiments*
      i) ***Amend***
         (a) *Feldmann (LV)*
            (a) ***RD-15-404****: RSV Replication competent*
   c) *Standard Operating Procedures*
      i) *Update*
            (a) *BSL-3 Operations and Safety Procedures*
               (i) add removal procedures for data transfer devices
            (b) *ABSL-3 Operations and Safety Procedures*
               (i) add removal procedures for data transfer devices
2) ***Animal Study Protocols Review***

Title	***Associated PRD***	***Associated RD***	***Reviewer***
Murine pulmonary T cell responses to bacterial pathogens	*18-202* *(Y. pestis (exempt)pending* *13-73* *(F. tularensis LVS)*	*N/A*	*N. Hoe*

Title	*Associated PRD*	*Associated RD*	*Reviewer*
	13-71 (F. tularensis) 17-195 (Bordetella pertussis)		
Production of TKO-BLT mice 2	*12-104 (HBBF)*	*N/A*	*R. Anderson*
Cross-protection of Chimpanzee Adenovirus expressing MERS-CoV-Spike (ChAdOx1-MERS-S) Vaccine in transgenic hDPP4 mice	*12-143 (MERS-CoV)*	*17-410 14-444*	*N. Hoe*
Protective efficacy of the small molecule inhibitor HU2976 against Ebola virus infection in mice	*13-90 (Ebola virus)*	*N/A*	*M. Brose*
Studies of retinal damage in mice during prion disease	*16-90 (rodent-adapted scrapie agent)*	*N/A*	*R. Anderson*
Production of prion infected mouse tissues for in vitro experimentation	*16-90 (rodent-adapted scrapie agent)*	*N/A*	*R. Anderson*
Pathogen surveillance in small mammals in Western Montana	*N/A*	*N/A*	*M. Brose*

3) ***Biosafety Training Performed – Rebecca Anderson, Megan Brose***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
Select Agent Initial	*1*	*4*
Laboratory Biosafety for Support Personnel	*1*	*4*
BSL-4 Refresher: Bite/Scratch	*2*	*2*
Visitor		
Biosafety Briefs		

4) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
   a) *Biological Incident Report:*
      i) *None*

5) ***Select Agent Issues-****None*

6) ***Other Issues –***
   a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 04/19/2018
Meeting Time: 1:03 PM **Adjourned:** 2:15 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☒	Bruce Chesebro (EO)	☐	☒	Karin Peterson	☒	☐
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Dana Scott	☐	☒
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Alexandra Scranton	☐	☒
Alan Applebury	☐	☒	Nancy Hoe	☒	☐	Brian Vickrey	☐	☒
Chris Bosio	☒	☐	Chris Hoffman	☐	☒			
Marshall Bloom (EO)	☐	☒	Clay Jarrett	☒	☐			
Teresa Borino	☐	☒	Josh Kellar (EO)	☐	☒			
Megan Brose	☒	☐	Scott Kobayashi	☒	☐			
Carol Calderwood	☐	☒	Jamie Lovaglio	☒	☐			
Marcie Caldwell (EO)	☐	☒	Andrea Marzi	☒	☐			
Paul Carlson	☒	☐	Alida Merritt	☐	☒			

(P=present; A=absent)

Guests: (b)(6)

Minutes: Meeting minutes from 2/15/18 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 2/15/18** ▪ Nancy Hoe pointed out on page 2, the third bullet should state that the strains are not only attenuated, but also not Select Agents. ▪ Sue Priola indicated on page 4, the fifth bullet down, that the wording suggests work was occurring prior to approval-this needs to be clarified. Becky Anderson stated that they do work with various Flavivirus strains on an IBC approved PRD but now want to add recombinant work with those previously approved strains. The committee agreed the wording needs to be updated to clarify what was already approved. Action: Meeting minutes for 2/15/18 were unanimously approved with the above modifications.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment)</u> ▪ Feldmann (LV) ▪ **PRD#17-143 Amend: Coronaviruses** ▪ Becky Anderson presented the risk assessment. She informed the committee that the PRD was being updated to include additional coronaviruses listed below: o HKU5 virus with SARS spike protein ectodomain, BSL3, cat #NR-48814, recombinant o Avian coronavirus Massachusetts, BSL2, cat# NR-43284 o Murine coronavirus icA59, BSL2, cat# NR-43000, recombinant o Canine coronavirus UCD1, BSL2, cat # NR-868 o Bat SARS-like coronavirus, with SARS spike receptor binding domain, BSL3, cat# NR-44009, o recombinant o Porcine respiratory coronavirus ISU1, BSL2, cat# NR-43286 o Bovine coronavirus Mebus, BSL2, cat# NR-445 o Alphacoronavirus Purdue P115, BSL2, cat# NR-43285 o MERS-CoV recombinant infectious clone with ORF5 red fluorescent protein replacement, BSL3, cat# NR-48813, recombinant. ▪ The proposed studies are to add the listed coronaviruses to develop various assays. One example listed was to develop a pan-coronavirus assay to use to detect Coronaviruses in samples obtained from field work. The disease caused by the Coronaviruses depends on the virus listed, many of the listed viruses do not cause disease in humans. Those that are already human pathogens for BSL-3 or have components of BSL-3 viruses are also classified at BSL-3. The natural route of transmission depends on the specific virus, but may include: respiratory secretions, blood, and feces. Primary lab hazards include: parenteral contact, accidental sharps injuries, and exposure to aerosols. For the human disease-causing Coronaviruses, there are not specific treatments available, typically treatment is supportive care. Antivirals and steroids may be given to reduce lung swelling. ▪ The biosafety level for work with the listed Coronaviruses is BSL-2 to BSL-3 as listed on the PRD for each strain. ▪ Alex Scranton submitted questions by email to Sue Priola. Alex Scranton questioned why the note listed at the bottom of the amendment stated some viruses may be worked with in the BSL4 for safety considerations. She asked if the IBC should have more detail before approving the amendment on what the safety considerations might entail. She asked for a better understanding of what is proposed before the work is approved. The committee discussed that often the Feldmann lab uses lower biosafety level viruses at the higher

	biosafety level so they can compare them in experiments or they choose to use them in the BSL-4 because of animal facilities or equipment. The committee discussed and agreed that the PI does not need to include that statement. The "note" will be removed from the registration. ▪ Alex Scranton also questioned why the biosafety level listed at the top of page 3 states BSL-2 when there are also BSL-3 pathogens listed on the registration. Becky Anderson stated that you can only enter one biosafety level in the software, which is a limitation of the program. PIs are directed to put the lowest biosafety level and then all pathogens are listed in the recommendations section to indicate the biosafety level for each individual pathogen. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Andrea Marzi abstained) **PRD#17-143 Amend** with the following minor modifications: 1. Delete the note at the bottom of the Amend Registration section.
Item 2:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment) ▪ De Leo (LB) ▪ **PRD#16-180 Amend: *Klebsiella pneumoniae*** ▪ Becky Anderson presented the risk assessment. The amendment is to add animal work with non-human primates (NHPs). The primary lab hazards for working with NHPs are bites and scratches from infected NHPs. To mitigate these hazards, animals are housed in NHP wing of (b)(6) All personnel on the ASP are trained on NHP handling procedures. PPE for these areas includes: lab coat/disposable gown, surgical mask, eye protection or face shield, and two pair of gloves. ▪ The biosafety level for work with *Klebsiella pneumoniae* is BSL-2/ABSL-2. Additional precautions have been added to state: *K. pneumoniae* infection can result in respiratory disease with potential for droplets, therefore additional mucous membrane protection such as surgical mask and goggles or face shield, front cover disposable gown and shoe covers should be worn when entering the room. The footbath may be placed outside the room and gloves will be disinfected or changed frequently. ▪ Nancy Hoe stated that the wording for placement of the footbath should be changed to "animal room" instead of just "room" in the additional precautions listed. ▪ Animal studies with NHPs were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.

	Action: The committee approved (Scott Kobayashi abstained) **PRD#16-180 Amend** with the following minor modifications: 1. Update the wording for the placement of the footbath to "animal room" instead of just "room" in the additional precautions listed.
Item 3:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Feldmann (LV) ▪ **PRD#18-82: Vesicular Stomatitis Virus (VSV)** ▪ Becky Anderson presented the risk assessment. She informed the committee that this is a renewal for VSV and the only changes to the PRD are noted at the top of the Purpose section of the registration. These changes include the addition of a route of inoculation for mice and the addition of bats as an animal species. ▪ The proposed studies are to use VSV to study protein function from other viruses. Other studies are focused on developing vaccines that use VSV to express immunogens from candidate viruses. ▪ Most human infections with Indiana VSV serotype appear to be subclinical. In patients that do show clinical manifestations, the initial symptom is high fever that is often biphasic. Subsequent symptoms are "flu-like" including severe malaise, headaches, myalgia, arthralgia, retrosternal pain, eye aches, and nausea. Vesicle formation on the oral mucosa, lips, and nose is possible, but these are rare symptoms. The natural route is by the bite of an infected sand fly, by direct contact with broken skin, or by the inhalation route. There is no documented evidence of person to person transmission of VSV. The primary lab hazards include: accidental sharps injuries, exposure of skin or mucous membranes to VSV, or generation of aerosols. ▪ Alex Scranton questioned by email the comments that were added in the animal section under "containment biosafety levels" and "practices biosafety levels" indicating that "..challenge may occur at ABSL-2 or ABSL-4 depending on the biosafety level of the virus". Alex Scranton asked if the IBC approved it as written did that grant the PI discretion to decide where vaccination and/or challenge takes place, or should the IBC approve the appropriate biosafety level for each activity for each virus. Additionally, the comment was added to sections inconsistently throughout the document. The committee agreed that the statement indicates that the challenge will occur at the biosafety level listed on the IBC-approved PRD of the challenge virus, and not at the PI's discretion. The committee agreed that it was fine to leave the comment in the document to acknowledge that the challenge may occur at a different biosafety level. The committee discussed that the consistency with where the statement was placed made it confusing and agreed that it should remain in the "containment" section, and be removed from the "practices" section. ▪ Alex Scranton also asked if the biosafety level should be listed in the table

	summarizing the ASPs. The committee agreed that it was not necessary to do so as the biosafety level is listed in each ASP and every new ASP gets reviewed by biosafety staff prior to being approved. ▪ The biosafety level for work with VSV is BSL-2/ABSL-2. ▪ Animal studies with guinea pigs, NHPs, hamsters, pigs, mice, and bats were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved (Andrea Marzi abstained) **PRD#18-82** with the following minor modifications: 1. Delete the comments in all BSL "practices" in the animal sections.
Item 4:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal)</u> ▪ Steele-Mortimer (LB) ▪ **PRD#18-44: *Salmonella enterica* serovar *Typhimurium*** ▪ Becky Anderson presented the risk assessment. She informed the committee that this is a renewal of the current PRD with no changes. The objective of the proposed studies is to study how serovar Typhimurim causes disease in humans using *in vitro* cell culture systems and animal models. ▪ Most people infected with Salmonella develop the following signs and symptoms 12-72 hours after being exposed to the bacteria: diarrhea, fever, and abdominal cramps. The illness usually lasts 4 to 7 days, and most people recover without treatment. In some people, the diarrhea may be so severe that the patient needs to be hospitalized. There are two strains that were added to this PRD previously by amendment. These strains are associated with invasive disease in immunocompromised people. In developed countries these infections are infrequent. However, in developing countries strains frequently cause severe illness, invasive infections, and possibly even death. These strains are currently circulating in Sub-Saharan Africa. The natural route of transmission is through person to person contact or by contaminated food or water. The primary lab hazards include: ingestion, parenteral inoculation, aerosol generation, and accidental needle stick. Treatment includes replacing fluids and electrolytes and IV fluids are given if a person becomes hospitalized. Antibiotic therapy is effective and may include: chloramphenicol, ampicillin, amoxicillin, or fluoroquinolones. ▪ Nancy Hoe pointed out in the Animal Use #4 section that the biosafety level listed is ABSL-3 and is not correct. She stated that these studies are carried out in the ABSL-3 facility, but the studies are not done at ABSL-3, they are conducted at ABSL-2. The biosafety level should be changed to ABSL-2. ▪ The biosafety level for work with *Salmonella enterica* serovar *Typhimurium is*

	BSL-2 with specific procedures conducted at BSL-2+ according to lab SOPs. ▪ Animal studies with mice and rabbits are proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#18-44** with the following minor modifications: 1. Change the biosafety level from ABSL-3 to ABSL-2 in Animal Use #4 Section.
Item 5:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Hasenkrug (LPVD) ▪ **PRD#18-55: HIV** ▪ Becky Anderson presented the risk assessment. She informed the committee that this is a renewal of the current PRD with no changes. The purpose of these studies is to test vaccines and therapeutics against HIV infection in humanized mice. ▪ The clinical features of HIV infection vary depending on the stage of the disease. Acute infection is accompanied by non-specific "flu-like" and "mononucleosis-like" symptoms such as myalgia, arthralgia, diarrhea, nausea, vomiting, headache, hepatosplenomegaly, weight loss, and neurological symptoms. Typically, when the patient's CD4+ T-cell count falls below 500 cells/µL, syndromes indicative of depressed cell mediated immunity can appear. Late-stage disease refers to the period when the patient's CD4+ T-cell count falls below 200 cells/µL. The natural route of transmission is through sexual activity, contaminated needles or blood products or from mother to infant during pregnancy, delivery or breastfeeding. The primary lab hazards include: accidental parenteral inoculation, contact with broken skin or mucous membranes, accidental needle stick, and exposure to aerosols. ▪ The biosafety level for work with HIV is BSL-2 with BSL-3 practices following SOPs for work with HIV. ▪ Nancy Hoe stated that the previous version of the HIV PRD had RMVB staff that take care of HIV infected animals listed in the Associated Researchers section to ensure that they receive HIV specific training. The committee agreed that RMVB staff should be added to the current version. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#18-55** with the following minor modifications: 1. Add to the list of Associated Researchers section members from RMVB that

	take care of HIV infected animals.
Item 6:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Hasenkrug (LPVD) ▪ **PRD#18-104: Human Blood and Body Fluids (HBBF)** ▪ Becky Anderson presented the risk assessment. She informed the committee that there are two PRDs for HBBF this month, one for Kim Hasenkrug and one for Bob Heinzen, therefore the risk assessment will be combined. The Hasenkrug lab proposes to generate humanized mice from human tissues (human thymus and liver are transplanted under the kidney capsule of mice). The Heinzen lab proposes to study the interactions of *C. burnetii* with human monocytes and macrophages. ▪ When working with HBBF, the pathogens that are of most concern are Hepatitis B virus (HBV), Hepatitis C Virus (HCV), and HIV. HBV is the most common of the three and causes a serious form of hepatitis. The symptoms include: jaundice, fatigue, abdominal pain, loss of appetite, intermittent nausea, and vomiting. It can also lead to chronic liver disease, liver cancer, and death. There is a vaccine available for HBV and the vaccine is offered free of charge at RML through the OMS Nurses. HCV symptoms include jaundice, fatigue, abdominal pain, loss of appetite, intermittent nausea, and vomiting. It can also lead to chronic liver disease and death. HIV is the virus that leads to AIDS. The primary lab hazards include: accidental needle stick, parenteral inoculation, and generation of aerosols. The most common route of transmission is through an accidental needle stick. ▪ The biosafety level for work with HBBF is BSL-2. ▪ Animal studies for mice were proposed for the Hasenkrug lab. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#18-104** as written.
Item 7:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Heinzen (LB) ▪ **PRD#18-104: Human Blood and Body Fluids (HBBF)** ▪ Becky Anderson presented the risk assessment described above. ▪ The biosafety level for work with HBBF is BSL-2. ▪ No animal studies were submitted, reviewed, or approved for the Heinzen lab. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.

	Action: The committee approved (Bob Heinzen abstained) **PRD#18-104** as written.
Item 8:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Heinzen (LB) ▪ **PRD#18-109: *Leishmania amazonensis*** ▪ Becky Anderson presented the risk assessment. The registration is being renewed and does not have any changes. The registration includes Leishmania expressing GFP and other fluorescent proteins that will be used to infect cells lines. Fluorescent Leishmania will be obtained from a collaborator and will not be genetically manipulated at RML. ▪ Infection in humans is not frequent, but a high percentage of cases develop into diffuse cutaneous infection. Cutaneous infections result from exposure to cuts or microabrasions on the skin and cause skin lesions but are not fatal. Treatment includes systemic agents such as antimony-based drugs, amphotericin, paromomycin, and oral miltefosine. The natural route of transmission is through the bite of an infected sand fly. The primary lab hazards include: parenteral inoculation, direct exposure to non-intact skin and aerosol exposure to mucous membranes. ▪ Paul Carlson pointed out that the project start date is listed as 1/1/2013 and needs to be updated. Becky Anderson stated that the duration of the project could be updated from 5 years to "ongoing". ▪ The biosafety level for work with *Leishmania amazonensis* is BSL-2. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Bob Heinzen abstained) **PRD#18-109** with the following minor modifications: 1. Change start date of project. 2. Update the duration of project to "ongoing".
Item 9:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ De Leo (LB) ▪ **PRD#18-1: *Staphylococcus aureus*** ▪ Becky Anderson presented the risk assessment. She informed the committee that this PRD is being renewed and there are no changes to the document. The proposed studies are to evaluate evasion of innate immunity by human bacterial pathogens. ▪ *Staphylococcus aureus* is an opportunistic pathogen that can cause a variety of

	self-limiting to life-threatening diseases in humans. *Staphylococcus aureus* is one of the most common causes of skin, soft-tissue, and nosocomial infection. The bacteria are a leading cause of food poisoning, resulting from the consumption of food contaminated with enterotoxins. Staphylococcal food intoxication involves rapid onset of nausea, vomiting, abdominal pain, cramps, and diarrhea. Symptoms usually resolve after 24 hours. Antibiotics such as cloxacillin and cephalexin are commonly used to treat staph infections. Vancomycin which is administered intravenously is used to treat MRSA. The natural route of transmission includes: ingestion of contaminated food, vertical transmission, human to human transmission if in contact with purulent lesions. The primary lab hazards include: ingestion of infected material, generation of aerosols, and accidental sharps injury. ▪ The biosafety level for *Staphylococcus aureus* is BSL-2/ABSL-2. ▪ The PRD also lists several additional pathogens. All the listed bacteria are BSL-2/ABSL-2. *Listeria monocytogenes* does have an additional precaution that needs to be added to the recommendations section. The precaution is, "Women of child bearing age are encouraged to discuss pregnancy with their supervisor or the RML OMSN to assure they are aware of any potential risks to themselves or the fetus and to determine if any additional risk reduction measures should be taken." ▪ Nancy Hoe pointed out that the permissible limit/Select Agent-exemption for Staphylococcal enterotoxins has changed from 5 mg to 100 mg and should be updated in the Description section. ▪ Animal studies with mice and rabbits are proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved (Scott Kobayashi abstained) **PRD#18-1** with the following minor modifications: 1. Add to the recommendations section the precautions for pregnant women working with *L. monocytogenes*. 2. Update the description section to list 100 mg instead of 5 mg.
Item 10:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal)</u> ▪ Priola (LPVD) ▪ **PRD#18-51: Transmissible spongiform encephalopathies (TSEs)** ▪ Becky Anderson presented the risk assessment. She informed the committee that this is another renewal with no changes to the document. The purpose of the study is to understand how human TSE agents or prions replicate and cause different forms of prion disease in humans. ▪ For CJD there is a gradual onset of confusion, progressive dementia, myoclonic

	jerks with spasticity, wasting and coma, as well as a slight elevation of CSF proteins. Death usually occurs in less than 1 year. Approximately 10% of cases have a family history of dementia and amorphous amyloid plaques in the cerebellum occur in about 15% of cases. Other TSE diseases have similar but different symptoms and course of disease. CJD is not known to be transmitted through the air or other forms of casual contact. Exposure to brain tissue and spinal cord fluid from infected individuals should be avoided to prevent transmission of the disease through these materials. Primary lab hazards include: accidental parenteral inoculation or ingestion. The risk of infection from aerosols, droplets, and exposure of intact skin, gastric, and mucous membranes is unknown. There is no specific treatment, just treatment for the symptoms. ▪ The biosafety level for work with the listed TSEs is BSL-2/ABSL-2 and work is conducted in a restricted access lab. PPE includes: gown, respirator, and gloves. ▪ Nancy Hoe pointed out that since this is a PRD, there is no need for NIH Guidelines to be listed, also the vector maps can be removed. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Sue Priola abstained) **PRD#18-51** with the following minor modifications: 1. Remove NIH Guidelines from the Eukaryote Cell section. 2. Remove vector maps from the registration.
Item 11:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Heinzen (LB) ▪ **RD#14-106 Amend**: Genetic transformation of *C. burnetii* ▪ Reviewers: Chris Bosio, Scott Kobayashi ▪ **Summary:** The RD amendment proposes the addition of counter-selectable markers, an additional site-directed recombination system, and an additional system for inducible gene expression. ▪ Chris Bosio summarized the RD. He stated that the amendment is to add tools for mutagenesis of *C. burnetii* that are similar to what the Heinzen lab already uses. They propose to add *ccdB* and gene *E* as counter-selectable markers as selection with s*acB* is not always 100%. Additionally, they want to add the Flp-*FRT* site-directed recombination system in addition to their currently approved Cre-*lox* system. Having the additional recombination system will allow them to create multiple large deletions in the same genome. The third part of the amendment is to add the theophylline-inducible synthetic riboswitch system. All genes will be cloned into approved plasmids containing approved antibiotic

	resistance or nutritional markers. ▪ Scott Kobayashi had no additional comments or concerns. ▪ Sue Priola pointed out in Section B, Physical Containment that BSL-2 is missing the "B". ▪ The NIH Guidelines were appropriate and there were no dual use concerns. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Bob Heinzen abstained) **RD#14-106 Amend** with the following modifications: 1. Add the "B" back to BSL-2 in the Physical Containment part of Section B. Research using prokaryotic hosts is approved at BSL-2 under section III-D-1-a and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 and BSL-3 under III-D-1-a, III-D-1-b, and Appendix G-II-C of the NIH Guidelines.
Item 12:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Bosio (LB) ▪ **RD#18-125 Amend**: *F. tularensis* interaction with host cells ▪ Reviewers: Andrea Marzi, Bob Heinzen ▪ **Summary:** The RD amendment expands the number of genes that can be inserted from *E. coli* and *Legionella pneumophila* into *F. tularensis*. ▪ Andrea Marzi summarized the RD amendment. The amendment just changes the wording from "single" to "multiple" for both *E. coli* and *L. pneumophila* phospholipid biosynthesis pathway genes that can be inserted into *F. tularensis*. The NIH Guidelines were appropriate and there were no dual use concerns. ▪ Bob Heinzen had no comments or concerns. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Chris Bosio abstained) **RD#18-125 Amend** as written. Research using prokaryotic hosts is approved at BSL-2 or BSL-3 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 and BSL-3 under III-D-1-a, and III-D1-b of the NIH Guidelines.

Item 13:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Feldmann (LV) ▪ **RD#15-404 Amend**: VSV Replication Competent ▪ Reviewers: Karin Peterson, Sue Priola ▪ **Summary:** The RD amendment is to add work with animals. ▪ Karin Peterson summarized the RD amendment. She stated that the amendment is to add a new route for mice (intradermal) and add animal work with a new species, bats. Karin Peterson had no concerns with the RD amendment. ▪ Sue Priola questioned why the ASP that is attached for work with mice did not include the intradermal route of inoculation. Megan Brose stated that she had reviewed the ASP and the route needed to be added because it was not approved by the IBC. Becky Anderson will work with the lab to make sure the appropriate ASP is attached to the RD renewal. ▪ Animal studies with mice and bats were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Andrea Marzi abstained) **RD#15-404 Amend** with the following minor modifications: 1. Ensure the proper ASP is attached for animal work with mice using the intradermal route of inoculation. Research using prokaryotic hosts is approved at BSL-2 under section III-D-1-a and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a and III-D-3-a of the NIH Guidelines.
Item 14:	**Standard Operating Procedures: (b)(6) SOP BSL-3-Cb-5 (Update)** ▪ Sue Priola informed the committee that the Heinzen lab added procedures in Section 14.0 of the SOP to prepare samples with paraformaldehyde that will then be used in animal experiments. These procedures have not been reviewed by an IBC working group, so samples treated with paraformaldehyde are not approved to be removed from the lab to a lower containment lab. This wording is added to the SOP to make it clear that it is not a validated inactivation procedure like the rest of the sections in the SOP. ▪ Alex Scranton submitted questions by email to Sue Priola. o Is there a significant difference between the new Section 14.0 and the older sections? o Once you have prepared the Coxiella with paraformaldehyde according to

	7.0 and 8.0, is it considered inactivated? Or do these sections similarly require the same restrictive language that is in section 14.0? ▪ Sue Priola and the committee discussed this extensively to make sure the wording is clear. Sections 7.0 and 8.0 as well as all other procedures in BSL-3-Cb-5 are Working Group reviewed and IBC approved inactivation procedures where samples can be removed from the BSL-3 lab to lower containment labs. Section 14.0 is different because the intent of the procedure is not to inactivate the samples and work with them at BSL-2, the intent is to kill the bacteria to use in animal experiments at ABSL-3. The committee discussed the wording and agreed that it was clear as stated. ▪ There were no additional comments or concerns with the SOP. Action: The committee unanimously approved (b)(6) **SOP BSL-3-Cb-5** as written.
Item 15:	**Standard Operating Procedures: SOP#4-28-43 Aerosol Exposure System Operation (Update)** ▪ Sue Priola informed the committee that the aerosol SOP has been updated to now include procedures for work with bats. The additions are listed in Sections 6.1 and 6.3.D. ▪ Alex Scranton emailed the following question/comment: o The SOP mentions that there will be green lights when things are working properly and red lights when they are out of limitations. It is unclear if red lights can be ignored or if all lights must be green before proceeding with the procedure. Also, it does not mention whether any adjustment made need to be recorded, would a red light be a malfunction? Would adjusting levels count as maintenance. Page 19 explains that records of malfunction and maintenance must be kept, although it is not specified how or where the documentation should be done. ▪ Becky Anderson stated that most of the green/red lights are associated with experimental parameters and being out of tolerance only leads to an issue with the experimental conditions. They do not result in a safety or containment issue. Becky Anderson emailed (b) (6) who was out of the country at the time of the meeting and he responded by email: o "The simple explanation is I have an excel spreadsheet to document all parts that are replaced, and the lights turn (red/green) based on parameters set by me during each experiment. They change each experiment, like humidity for instance. I have an aerosol run spreadsheet where I document all findings during the runs (and malfunctions). Each run is also saved on file and a printout summary can be shown for each experiment." ▪ The committee discussed if the wording for the red/green lights was acceptable and agreed that no changes were necessary. ▪ There were no additional comments or concerns with the SOP.

	Action: The committee unanimously approved **SOP#4-28-43 Aerosol Exposure System Operation** as written.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Nancy Hoe presented the BSO report. ▪ Nancy Hoe informed the committee about how the recent CDC DSAT inspection went.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ There have been three injuries since the last committee meeting: o An employee cut their index finder while necropsying a *Borrelia* infected mouse. o An employee sustained a contusion from a marmoset while anesthetizing the marmoset. The marmoset bit them but did not break the skin. o An employee received an injury from improper lifting technique. ▪ There was a fire alarm in (b)(6) due to burned popcorn. A few issues were identified that are being followed up. ▪ There was an ambulance call earlier in the week, however it was not work related.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ The BSL-3 (b)(6) annual shutdown is underway and will be complete tomorrow. ▪ Scientific Engineering Activities will be onsite April 30 to May 2 to complete their annual testing of our BSL-3 and BSL-4 facilities.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present
Around the room	▪ Nancy Hoe informed the committee that there will be a CDC Import permit inspection May 30 to June 1st. This will include inspections of labs in (b)(6) (BSL-2 and BSL-3) as well as animal holding areas in (b)(6)

Other issues	▪ None.

Next Meeting:

- Date: 5/17/18
- Place: Library conference room
- Time: 1:00 PM

RML Biosafety Committee Meeting
April 19, 2018
Biosafety Officer/Responsible Official Report

1) ***Requests approved by BSO since last meeting:***
   a) *None*
2) ***New requests approved by committee via electronic review:***
   a) *None*
3) ***New requests***
   a) *Pathogen Registration Documents*
      i) ***Amend***
         (a) *Feldmann (LV)*
            (a) ***PRD-17-143:*** *Coronavirus*
               (i) add strains
      ii) ***Renew***
         (a) *Feldmann (LV)*
            (a) ***PRD-18-82****: VSV*
         (b) *Steele-Mortimer (LB)*
            (a) ***PRD-18-44****: Salmonella typhimurium (and HBBF)*
         (c) *Hasenkrug (LPVD)*
            (a) ***PRD-18-55****: HIV*
            (b) ***PRD-18-104****: Human blood and body fluids*
         (d) *Heinzen (LB)*
            (a) ***PRD-18-153****: Human blood and body fluids*
            (b) ***PRD-18-109****: Leishmania amazonensis*
         (e) *DeLeo (LB)*
            (a) ***PRD-18-109****: Staphylococcus aureus*
         (f) *Priola (LPVD)*
            (a) ***PRD-18-51****: Human TSE agents*
   b) *Registration Documents for Recombinant Nucleic Acid Experiments*
      i) ***Amend***
         (a) *Heinzen (LB)*
            (a) ***RD-14-106****: Genetic transformation of Coxiella burnetii*
               (i) add ccdB, gene E as counter-selectable markers
               (ii) add Flp-FRT site-directed recombination system

(iii) add theophylline-inducible synthetic riboswitch-regulated protein expression system

(b) *Bosio (LB)*

(a) ***RD-18-125**: Cellular and molecular mechanisms of survival and replication of F. tularensis*

(i) add multiple E. coli or L. pneumophila genes to F. tularensis

(c) *Feldmann (LV)*

(a) ***RD-15-404**: RSV Replication competent*

(i) add bats as an animal model

(ii) i.d. as route of infection for mice

c) *Standard Operating Procedures*

i) *Update*

(a) ***BSL-3-Cb-5***

(a) *add paraformaldehyde inactivation (not for removal from containment)*

(b) *SOP#4-28-43 Aerosol Exposure System operation*

(a) *add bats*

2) ***Animal Study Protocols Review***

Title	***Associated PRD***	***Associated RD***	***Reviewer***
Surveillance for zoonotic viral pathogens in the Republic of Congo	*N/A*	*N/A*	*N. Hoe*
Evaluation of bacteriophage therapy for the treatment of Klebsiella pneumoniae infection in mice	*16-180 (Klebsiella pneumoniae)*	*N/A*	*M. Brose*
Treatment of lethal ZIKV infection with Favipiravir (T-705) and Ribavirin in IFNAR-/- mice	*16-182 (Zika virus)*	*N/A*	*N. Hoe*
ChAdOx1 MERS vaccine efficacy in the rhesus macaque model	*17-143 (MERS-CoV)*	*17-410*	*R. Anderson*
Efficacy of favipiravir treatment in a macaque model of Crimean Congo Hemorrhagic fever	*13-92 (CCHFV)*	*N/A*	*N. Hoe*
Determining the spatial and temporal dynamics of the MAVS-dependent innate response to virus infection in whole lymph nodes in mice	*13-82 (VSV exempt) 13-90 (Ebola virus)*	*15-404 14-407*	*N. Hoe*

3) ***Biosafety Training Performed – Rebecca Anderson, Megan Brose***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
Select Agent Initial	*1*	*4*
PPE for NIH Police/RML First Responders	*2*	*5*
BSL-3 Laboratory Biosafety	*3*	*3*
BSL-4 Laboratory Biosafety	*11*	*2*
Visitor (BSL-3, BSL-4)	*8*	*14*
Biosafety Briefs	*2*	*WIPs*

4) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
   a) *Biological Incident Report:*
      i) *None*

5) ***Select Agent Issues***
   a) *Summary of recent BSL-3/BSL-4 CDC DSAT inspection*

6) ***Other Issues –***
   a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 05/17/2018
Meeting Time: 1:02 PM **Adjourned:** 2:21 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Karin Peterson	☒	☐
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Dana Scott	☐	☒
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Alexandra Scranton	☐	☒
Alan Applebury	☐	☒	Nancy Hoe	☐	☒	Brian Vickrey	☐	☒
Chris Bosio	☒	☐	Chris Hoffman	☐	☒			
Marshall Bloom (EO)	☐	☒	Clay Jarrett	☒	☐			
Teresa Borino	☐	☒	Josh Kellar (EO)	☐	☒			
Megan Brose	☐	☒	Scott Kobayashi	☒	☐			
Carol Calderwood	☐	☒	Jamie Lovaglio	☐	☒			
Marcie Caldwell (EO)	☐	☒	Andrea Marzi	☒	☐			
Paul Carlson	☐	☒	Alida Merritt	☐	☒			

(P=present; A=absent)

Guests (b)(6)

Minutes: Meeting minutes from 4/19/18 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 4/19/18** ▪ Sue Priola pointed out minor typos Action: Meeting minutes for 4/19/18 were unanimously approved with the above minor corrections.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment) ▪ Feldmann (LV) ▪ **PRD#13-91 Amend: Paramyxoviridae, Henipavirus**

	▪ Becky Anderson presented the risk assessment. The Feldmann lab would like to add bats to the Henipavirus PRD. Animal work with bats will now be added to the entire PRD, DSAT approval was obtained 5/2/18. These studies will focus on characterizing the course of infection in a pteropid bat, *Rousettus aegyptiacus*, to identify the localization and timing of virus replication and shedding. Studies will be conducted in the BSL-4 according to IBC approved *SOP#4-28-56 Husbandry Procedures for Bats in Level 4 Biocontainment.* ▪ PPE includes: Positive pressure suit and additional protective gloves (leather or sheep skin gloves) over the suit gloves are worn when manually restraining bats ▪ The biosafety level for work with the listed Henipaviruses is BSL-4/ABSL-4. ▪ Animal studies with bats were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Andrea Marzi abstained) **PRD#13-91 Amend** as written.
Item 2:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New) ▪ Feldmann (LV) ▪ **PRD#18-203: Epstein Bar Virus (EBV)** ▪ Becky Anderson presented the risk assessment. The proposed studies are to create immortalized EBV lines from humanized mice. Infection with EBV results in infectious mononucleosis in young adults that is characterized by fever, sore throat, abdominal discomfort, pharyngitis, tonsillitis, and generalized lymphadenopathy. The disease generally lasts 1 to 4 weeks; however, symptoms can last for up to one year in some patients. Burkitt's Lymphoma can arise from early infection with EBV in B cells. EBV infections themselves are quite common and affect more than 90% of individuals worldwide in the first 20 years of life. Treatment of infectious mononucleosis is mainly supportive. Viral replication can be inhibited by nucleoside analogues which can reduce or stop viral shedding but have no effect on the symptoms. Lymphoproliferative disorders associated with EBV can be treated with anti-CD20 monoclonal antibodies and EBV specific cytotoxic T lymphocytes along with anti-viral drugs. EBV is primarily transmitted through sexual contact or saliva and there is a possibility that it is spread through blood. The primary lab hazards include: accidental needle sticks, aerosolized material, and direct exposure to mucous membranes. ▪ The biosafety level for work with EBV is BSL-2. All work that generates aerosols must occur in a BSC. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The

	committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#18-203** as written.
Item 3:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Rosa (LZP) ▪ **PRD#18-129: Leptospira spp.** ▪ Becky Anderson presented the risk assessment. The proposed studies are to cultivate and genetically manipulate Leptospira spp. to understand mechanisms of infection and pathogenicity. In humans, Leptospirosis can cause a wide range of symptoms, including: high fever, headache, chills, muscle aches, vomiting, jaundice (yellow skin and eyes), red eyes, abdominal pain, diarrhea, rash. The illness lasts from a few days to 3 weeks or longer. Without treatment, recovery may take several months. Treatment may include antibiotic treatment with: penicillin, streptomycin, erythromycin, or doxycycline. ▪ The biosafety level for work with Leptospira spp. is BSL-2/ABSL-2. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#18-129** as written.
Item 4:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Rosa (LZP) ▪ **PRD#18-24: *Borrelia burgdorferi*** ▪ Becky Anderson presented the risk assessment. The primary focus of the proposed research is to elucidate the mechanisms of adaptation and variation used by *B. burgdorferi* and thereby gain insight into virulence determinants required for infection by this pathogen. *B. burgdorferi* causes Lyme disease. It is a tickborne zoonotic disease characterized by distinctive skin lesions, can present with fever, chills, headache, fatigue, muscle and joint aches, and swollen lymph nodes. Erythema migrans (EM) rash is a common symptom: a. Occurs in approximately 70 to 80 percent of infected persons b. Begins at the site of a tick bite after a delay of 3 to 30 days (average is about 7 days) c. Expands gradually over a period of days reaching up to 12 inches or more (30 cm) across d. May feel warm to the touch but is rarely itchy or painful e. Sometimes clears as it enlarges, resulting in a target or “bull’s-eye”

	appearance f. May appear on any area of the body ▪ Approximately 10 to 20% of patients treated for Lyme disease with a recommended 2–4 week course of antibiotics will have lingering symptoms of fatigue, pain, or joint and muscle aches. In some cases, these can last for more than 6 months. Antibiotics commonly used are doxycycline and amoxicillin, erythromycin is used for those with allergies to penicillins or tetracyclines. ▪ The biosafety level for work with *Borrelia burgdorferi is* BSL-2. ▪ Animal studies with rabbits is proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#18-24** as written.
Item 5:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Heinzen (LV) ▪ **PRD#18-70: *Coxiella burnetii* (exempt, non-select agent)** ▪ Becky Anderson presented the risk assessment. The proposed studies are to define host-pathogen interactions and the developmental biology of *C. burnetii*. To develop genetic systems and identify genes involved in the infectious process. *C. burnetii* is the causative agent of Q fever and has 2 phase variants. Phase I is a highly virulent variant and phase II is an attenuated variant of C. *burnetii*. Attenuation of virulent *C. burnetii* was achieved by a ~26-kb chromosomal deletion that eliminates multiple genes involved in LPS biosynthesis. The phase II variant does not express the O side chain and several sugar residues in the core structure because of the major deletion of genes involved with LPS biosynthesis. This deletion results in a strain that is avirulent for immunocompetent mice and guinea pigs. Pathogenesis in humans is unknown; to date there have been no reported infections of humans with avirulent *C. burnetii*. The primary lab hazards include: parenteral inoculation, aerosols, and accidental needlesticks or sharp injuries. The current PRD also lists *C. trachomatis* L2, *C. muridarum*, and various *L. pneumophila*, none of which require additional precautions beyond BSL-2. The PRD also states that there will be no centrifugation of *C. trachomatis* L2. ▪ Sue Priola pointed out that the Animal Use 1 Section incorrectly lists mice when it should be guinea pigs according to the attached ASP. ▪ The biosafety level for work with *C. burnetii* is BSL-2. ▪ Animal studies with guinea pigs were proposed. ▪ The committee discussed the dual-use potential of these experiments. The

	committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Bob Heinzen abstained) **PRD#18-70** with the following minor modifications: 1. Change the animal species listed in Animal Use 1 section from mice to guinea pigs.
Item 6:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Peterson (LPVD) ▪ **PRD#18-103: La Crosse virus and California Serogroup viruses** ▪ Becky Anderson presented the risk assessment. The proposed studies are to examine the different California Serogroup (CSG) viruses in cell culture experiments and in mice to study the mechanisms behind viral pathogenesis. o LaCrosse virus- fever, headache, nausea, vomiting, and tiredness. Severe neurovinasive disease and/or encephalitis may develop. Mostly occurs in Midwestern, mid-Atlantic, and southeastern states. o Jamestown Canyon Virus- fever, headache, flu-like illness. Severe cases may involve the Central nervous system meningitis or encephalitis. Thirty one cases in US from 2000-2013. No fatalities have been reported. Infections have been diagnosed in the United States. o Tahyna Virus (TAHV)- Human illness from infection with TAHV has been reported as manifesting in undifferentiated fever and influenza-like symptoms; the infection may also cause pneumonia and pleurisy, acute arthritis, pharyngitis, and, occasionally, central nervous system involvement. No fatalities have been reported. Cases of Tahnya virus have been reported in Europe, Asia, or Africa. o Snowshoe hare virus-Fever headache, nausea. Few cases of encephalitis. Predominately found in the North America region. o Inkoo virus-infects humans with neurological symptoms. No fatalities to date, this virus is found in Northern Europe. ▪ Transmission is through the bite of an infected mosquito. Currently, there is no vaccine and there are no specific treatments, care includes treating the symptoms of infection. The primary lab hazards include: accidental needle stick and parenteral inoculation. ▪ Sue Priola pointed out that the PRD describes work with human cells, so the human blood and body fluids precautions should be added to the recommendations section. ▪ Sue Priola also noted that the additional CSG viruses should be listed in the Pathogen and/or Toxin section of the registration. ▪ The biosafety level for work with CSG viruses is BSL-2. ▪ Animal studies for mice, NHP, and rabbits were proposed.

	▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Karin Peterson abstained) **PRD#18-103** with the following minor modifications: 1. Add the human blood and body fluid precautions to the recommendations section. 2. Add the other viruses listed in the Synopsis section to the Pathogen and/or Toxin section.
Item 7:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Fischer (RTB) ▪ **PRD#18-151: Influenza A & B** ▪ Becky Anderson presented the risk assessment. The proposed studies are to isolate virus from chicken eggs to study by electron microscopy to obtain 2D and 3D images of the viruses in the presence and absence of antibodies. Four microliters of virus in suspension will be applied to grids within the Vitrobot and frozen with liquid ethane. The Fischer lab will follow BL2 SOPs posted in lab. Both Influenza A and B lead to acute viral disease of the upper respiratory tract characterized by fever, headache, myalgia, malaise, sore throat, non-productive cough, sneezing and nasal discharge. Fatality due to influenza is generally low, except in those with chronic lung or heart conditions. Secondary bacterial pneumonia after influenza is a leading cause of mortality. Seasonal influenza viruses are sensitive to the neuraminidase inhibitors oseltamivir (Tamiflu), and zanamivir (Relenza), and to amantadine, and rimantadine,. The natural route of transmission is by aerosols and droplets and/or contact with contaminated surfaces. Influenza viruses are highly communicable. The primary lab hazards include: parenteral inoculation, generation of aerosols, and accidental needlesticks and sharp injuries. ▪ The biosafety level for work with the listed Influenza strains is BSL-2 following the lab specific SOP. Vaccination with the seasonal influenza vaccine is recommended. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#18-151** as written.
Item 8:	Registration Documents for Recombinant DNA Experiments (New) ▪ Peterson (LPVD)

	▪ **RD#18-225**: Recombinant California Serogroup viruses ▪ Reviewers: Andrea Marzi, Sue Priola ▪ **Summary:** The RD describes the generation of recombinant California Serogroup (CSG) viruses. ▪ Andrea Marzi summarized the RD. She informed the committee that the Peterson lab will use reverse genetics on the CSG viruses. They will use La Crosse virus as the backbone to determine specific virulence and genetic factors of the CSG viruses that mediate differences in pathogenicity and host immune response. They attached the maps for the plasmids carrying the three genomic segments of La Crosse virus, L, M, and S segments. They will swap out portions of La Crosse virus sequences with the homologous regions of the other CSG viruses. The recombinant plasmids will then be used to generate recombinant viruses that can be used *in vitro* and *in vivo* in mice. The NIH Guidelines are appropriate, and Andrea Marzi had no dual use concerns. ▪ Sue Priola had no additional comments or concerns. ▪ The NIH Guidelines were appropriate and there were no dual use concerns. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Karin Peterson abstained) **RD#18-225** as written. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-2-a of the NIH Guidelines.
Item 9:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Steele-Mortimer (LB) ▪ **RD#14-126 Amend**: Salmonella cancer vaccine ▪ Reviewers: Chris Bosio, Clay Jarrett ▪ **Summary:** The amendment to the RD is to add animal work with mice. ▪ Chris Bosio summarized the RD. The amendment to the RD is to add mice. They will use mice to evaluate the recombinant attenuated Salmonella delivery system. ▪ Clay Jarret had no additional comments or concerns. ▪ The NIH Guidelines were appropriate and there were no dual use concerns. ▪ Animal studies with mice were proposed.

	▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#14-126 Amend** as written. Research using prokaryotic hosts is approved at BSL-2 under section III-D-1-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a of the NIH Guidelines.
Item 10:	**Working Group Summary** ▪ Sue Priola reviewed the Working Group summary with the committee. Karin Peterson, Scott Kobayashi, and Bob Heinzen were the working group members that reviewed the inactivation methods from Katy Bosio's lab. ▪ The Bosio lab tested the ability of 100% methanol to inactivate *F. tularensis* grown on agar plates. They showed in three different experiments that all the bacteria were inactivated. ▪ The associated SOP was updated to reflect the addition of 100% methanol to inactivate *F. tularensis*. ▪ See summary attached. Action: The committee unanimously approved the Working Group recommendation that 100% methanol completely inactivated *F. tularensis* and approved the validation studies as written.
Item 11:	**Standard Operating Procedures (b)(6) SOP BSL3-C-8 (Update)** ▪ Sue Priola informed the committee that the inactivation procedures described in the working group summary were accurately listed in the SOP update. ▪ There were no additional comments or concerns with the SOP. Action: The committee unanimously approved (b)(6) **SOP BSL3-C-8** as written.
Item 12:	**Trizol Inactivation of Ebola virus** ▪ Sue Priola informed the committee that the data for the Trizol inactivation was submitted too late to convene a working group, so the IBC would review the data as a committee. ▪ Sue Priola summarized the experimental parameters and the results to the committee. The Feldmann lab used Ebola virus as a surrogate for all the BSL-4 enveloped negative strand viruses in the Trizol inactivation experiments. ▪ Sue Priola asked (b) (6) f the data has been replicated since they validated it. (b) (6) stated that the testing of Trizol has been repeated many times and all experimental replicates were effective at inactivating Ebola

	virus.
Item 13:	**Standard Operating Procedures: SOP#4-28-32 Removal of Specimens for Nucleic Acid Extraction (Update)** ▪ Sue Priola informed the committee that the SOP has been updated to reflect the Trizol inactivation procedures. ▪ There were no additional comments or concerns with the SOP. Action: The committee unanimously approved **SOP#4-28-32 Removal of Specimens for Nucleic Acid Extraction (Update)** as written.
Item 14:	**Standard Operating Procedures: BSL-3 Operations and Safety Procedures for** (b)(6) **(Update)** ▪ Becky Anderson informed the committee that the BSL-3 users wanted to update the PPE section to make it clearer when to wear the two levels of PPE. The updated section is highlighted in red. ▪ There were no additional comments or concerns with the SOP. Action: The committee unanimously approved **BSL-3 Operations and Safety Procedures for** (b)(6) as written.
Item 15:	**Standard Operating Procedures: SOP#4-28-4 BSL-4 Daily External Systems Safety Checklist (Update)** ▪ Becky Anderson informed the committee that the updates were in response to the recent CDC DSAT inspection. The inspectors stated that the daily checklist was not clear on what systems were critical for entry. The SOP and the checklist have been updated to make this clearer. Previously, there was also a User's Guide to the checklist, this has now been added to the SOP so there is only one document for all the checklist information. ▪ There were no additional comments or concerns with the SOP. Action: The committee unanimously **SOP#4-28-4 BSL-4 Daily External Systems Safety Checklist** as written.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Nancy Hoe was not present. ▪ Becky Anderson also informed the committee that the CDC DSAT inspection report responses were submitted on May 11. ▪ Becky Anderson informed the committee that RML received our 3-year renewal for the Select Agent Registration. This renewal is contingent upon close-out of the March 2018 inspection.

Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ Not present.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ Not present.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ None.

Other issues	▪ None.

Next Meeting:

- Date: 6/21/18
- Place: Library conference room
- Time: 1:00 PM

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 06/21/2018
Meeting Time: 1:02 PM **Adjourned:** 2:15 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Karin Peterson	☒	☐
Bob Heinzen, Vice Chair	☐	☒	Frank DeLeo (EO)	☐	☒	Greg Saturday	☒	☐
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Alexandra Scranton	☐	☒
Alan Applebury	☐	☒	Nancy Hoe	☒	☐	Brian Vickrey	☐	☒
Chris Bosio	☒	☐	Chris Hoffman	☐	☒			
Marshall Bloom (EO)	☐	☒	Clay Jarrett	☒	☐			
Megan Brose	☒	☐	Josh Kellar (EO)	☐	☒			
Larry Brouwer	☒	☐	Scott Kobayashi	☒	☐			
Carol Calderwood	☐	☒	Jamie Lovaglio	☒	☐			
Marcie Caldwell (EO)	☐	☒	Andrea Marzi	☐	☒			
Paul Carlson	☐	☒	Alida Merritt	☐	☒			

(P=present; A=absent)

Guests (b)(6)

Minutes: Meeting minutes from 5/17/18 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 5/17/18** ▪ Sue Priola pointed out minor typos Action: Meeting minutes for 5/17/18 were unanimously approved with the minor corrections.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renew) ▪ Bloom (LV) ▪ **PRD#18-204: Kunjin virus**

	▪ Becky Anderson presented the risk assessment. The purpose of this work is to examine and characterize changes caused by acute or persistent Kunjin virus infection in mammalian or arthropod cells. Infection with Kunjin virus typically leads to mild disease with lymphadenopathy, fever, lethargy, rash, muscle weakness and fatigue. Less common is a more severe disease where development of encephalitis occurs requiring hospitalization. There are no specific treatments or vaccines available, supportive care is given. Primary lab hazards include: accidental parenteral inoculation, contact with broken skin or mucous membranes, and accidental needle sticks. All work with infectious material should be performed in a BSC with the use of sealed centrifuge cups or rotors. This was not included in the recommendations section prior to the meeting but needs to be added. ▪ Sue Priola pointed out that the registration lists "Yes" for vector maps being uploaded. They are not uploaded and do not need to be. Change the "yes" to "no". ▪ No animal studies were submitted, reviewed, or approved. ▪ The biosafety level for work with Kunjin virus is BSL-2. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **PRD#18-204** with minor modifications: 1. Add the recommendations section the requirement to work with infectious material in a BSC and use sealed centrifuge cups or rotors. 2. Change the "Yes" to "No" for vector maps uploaded.
Item 2:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal)</u> ▪ Hinnebusch (LZP) ▪ **PRD#18-86: Human blood and body fluids (HBBF)** ▪ Becky Anderson presented the risk assessment. The proposed studies are focused on understanding the interaction of *Y. pestis* with human white blood cells in order to understand how the bacteria resist being killed by white blood cells. Additionally, the Hinnebusch lab infects fleas by allowing them to feed on blood from a variety of animals, including human blood containing *Y. pestis* (exempt strains). ▪ When working with HBBF, the pathogens that are of most concern are Hepatitis B virus (HBV), Hepatitis C Virus (HCV), and HIV. HBV is the most common of the three and causes a serious form of hepatitis. The symptoms include: jaundice, fatigue, abdominal pain, loss of appetite, intermittent nausea, and vomiting. It can also lead to chronic liver disease, liver cancer, and death. There is a vaccine

	available for HBV and the vaccine is offered free of charge at RML through the OMS Nurses. HCV symptoms include jaundice, fatigue, abdominal pain, loss of appetite, intermittent nausea, and vomiting. It can also lead to chronic liver disease and death. HIV is the virus that leads to AIDS. The primary lab hazards include: accidental needle stick, parenteral inoculation, and generation of aerosols. The most common route of transmission is through an accidental needle stick. ▪ Scott Kobayashi pointed out that LHBP in the synopsis section should be changed to LB. ▪ The biosafety level for work with HBBF is BSL-2. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved (Chris Bosio, Clay Jarrett abstained) **PRD#18-86** with the following minor modifications: 1. Change LHBP to LB in the synopsis section.
Item 3:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal)</u> ▪ Hinnebusch (LZP) ▪ **PRD#18-07: *Yersinia pseudotuberculosis*** ▪ Becky Anderson presented the risk assessment. *Y. psuedotuberculosis* is very closely related to *Y. pestis* but is not transmitted by fleas. The proposed studies are to identify and characterize the genetic changes between the two bacteria that were required for the evolution of the flea-borne transmission route. *Y. pseudotuberculosis* is a rare cause of acute enteric disease with symptoms such as acute mesenteric lymphadenitis and gastroenteritis associated with abdominal pain and fever (diarrhea is unusual). One to 3 weeks after the acute phase of the disease, post-infectious complications can occur, such as reactive arthritis and erythema nodosum. The arthritic phase of the disease can last up to 6 months. Other complications include lesions to lymph nodes, spleen and liver, as well as septicemia in immunocompromised patients. The disease is most common in children and young adults. Immunocompromised individuals are at a greater risk of severe disease or death. Infections are usually self-limiting, but *Y. psuedotuberculosis* is susceptible to ampicillin, third generation cephalosporins, aminoglycosides, tetracyclines, and chloramphenicol. The natural route of transmission is through the fecal-oral route, consumption of contaminated food and/or water, or contact with infectious soil. The primary lab hazards include: accidental sharps injuries, ingestion, or generation of aerosols.

	▪ The biosafety level for work with *Y. pseudotuberculosis* is BSL-2/ABSL-2. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Chris Bosio, Clay Jarrett abstained) **PRD#18-07** as written.
Item 4:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ de Leo (LB) ▪ **PRD#18-124: Influenza virus H1N1 swine origin** ▪ Becky Anderson presented the risk assessment. The proposed studies are to determine potential mechanisms by which Influenza virus alters neutrophil function and viability, thereby contributing to the ability of bacteria to evade killing by these cells. Influenza virus infection symptoms usually include the sudden appearance of: high fever, cough, and muscle ache. Other common symptoms include: headache, chills, loss of appetite, fatigue, sore throat, diarrhea, nausea/vomiting, runny or stuffy nose. Treatment includes neuraminidase inhibitors such as oseltamivir, zanamivir, amantadine, and rimantadine. The natural route of transmission is through contact with aerosols or contaminated surfaces. The primary lab hazards include: accidental needle stick, generation of aerosols, and contact with contaminated surfaces. ▪ The biosafety level for work with Influenza virus H1N1 swine origin is BSL-2 according to the attached SOP with the following additional precautions: a. Access to the laboratory will be restricted (by posting a sign) when experiments are in progress. b. All work with infectious materials will be performed in a BSC. c. Sealed centrifuge cups and/or rotors will be used d. Samples to be removed from the lab will be sealed in primary and secondary containers e. All personnel will be enrolled in the influenza surveillance program and receive the seasonal influenza vaccination. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Scott Kobayashi abstained) **PRD#18-124** as written.
Item 5:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals

	(Renewal) ▪ Feldmann (LV) ▪ **PRD#18-90: Filoviridae (Ebola and Marburg virus)** ▪ Becky Anderson presented the risk assessment. Sudden onset of fever, malaise, abdominal pain, vomiting, diarrhea, renal and hepatic involvement and hemorrhagic diathesis. Involvement of liver, pancreas, kidney and to a much lesser degree the central nervous system and heart. Leukopenia, thrombocytopenia, and toxicity often lead to shock and death. The case fatality rate of Marburg is 83-90% and Ebola is 50-90%. The natural route of transmission is: contact with infectious secretions and materials and intimate person to person contact. There are no treatments for infection with Ebola or Marburg viruses. The primary lab hazards include: accidental parenteral inoculation, direct contact with broken skin or mucous membranes, and exposure to infectious aerosols and droplets. ▪ The biosafety level for work with Ebola and Marburg viruses is BSL-4/ABSL-4. ▪ Animal studies with mice, hamsters, guinea pigs, pigs, and non-human primates were proposed. ▪ The committee discussed the dual-use potential of these experiments. Question A1 is marked yes since the Feldmann lab adapted strains to animals. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#18-90** as written.
Item 6:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Feldmann (LV) ▪ **PRD#18-92: Bunyaviridae (Crimean-Congo Hemorrhagic Fever virus and Rift Valley Fever virus)** ▪ Becky Anderson presented the risk assessment. Crimean-Congo Hemorrhagic Fever virus (CCHFV) presents with sudden onset of fever, malaise, weakness, irritability, headache, and severe pain in the limbs and loin. Vomiting, abdominal pains and diarrhea may occur. Bleeding from the gums, nose, lungs uterus, intestine can occur in some cases and is associated with liver damage and death due to loss of blood. The case fatality rate ranges from 2-50%. Rift Valley Fever virus (RVF) infection can be either mild or severe in humans. Mild disease is characterized by a feverish syndrome with a sudden onset of flu-like fever, muscle pain, joint pain, and headache. Mild disease lasts 4 to 7 days. Severe disease affects only a small percentage of patients and can be either ocular, meningoencephalitis, or hemorrhagic fever. The fatality rate for hemorrhagic fever being the highest with a rate of approximately 50%. For both CCHFV and RVF, no specific treatment is available, supportive care is given. However, CCHFV is sensitive to ribavirin and it has been used in some patients

	with benefit. The natural route of transmission for CCHFV is through the bite of an infected tick. For RVF, virus is predominantly transmitted by mosquitoes. The primary lab hazards include: droplet exposure of the mucous membrane to infective blood, generation of aerosols, and accidental parenteral inoculation. ▪ The biosafety level for work with CCHFV and RVF is BSL-4/ABSL-4. RFV is a BSL-3 agent where vaccination is required, or additional respiratory protection is required. The PRD is requesting to work with RVF at BSL-4. ▪ Animal studies for mice, hamsters, and NHP, were proposed for work with CCHFV. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#18-92** as written.
Item 7:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Feldmann (LV) ▪ **RD#16-450 Amend**: Lloviu virus reverse genetics ▪ Reviewers: Chris Bosio, Sue Priola ▪ **Summary:** The RD describes a reverse genetics system for Lloviu virus. The amendment is to add animal work with mice. ▪ Chris Bosio summarized the RD. The amendment is to add animal work with mice. ▪ Sue Priola questioned why the ASP was written on an older version of the ASP form. (b)(6) stated that she had already converted it to the updated form. The ACUC will review the updated form at the next meeting. ▪ The NIH Guidelines were appropriate and there were no dual use concerns. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#16-450 Amend** as written. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-4 under III-D-1-a, III-D-1-c, and III-D-3-c of the NIH Guidelines.
Item 8:	**Methanol inactivation of *F. tularensis*** ▪ Sue Priola informed the committee that the data for the methanol inactivation of *F. tularensis* was submitted too late to convene a working group, so the IBC would review the data as a committee.

	▪ Sue Priola summarized the experimental parameters and the results of the testing to the committee. ▪ The committee had no additional comments or concerns with the presented data.
Item 9:	**Standard Operating Procedures: ABSL-3 *F. tularensis* SOP (Update)** ▪ Sue Priola informed the committee that the inactivation procedures described in the working group summary were accurately listed in the SOP update. ▪ Becky Anderson stated that the SOP should be updated to list 100% methanol. ▪ Scott Kobayashi questioned where/when the 20-minute incubation with methanol started. (b)(6) stated that it starts in the ABSL-3 when the samples are added to the tubes. The committee agreed the wording in the SOP should be clarified to state that the 20-minute incubation starts in the ABSL-3. Action: The committee unanimously approved **ABSL-3 *F. tularensis* SOP** with minor modifications: 1. Add that the methanol is 100%. 2. Indicate that the 20-minute incubation starts in the ABSL-3 when the samples are added to the tubes containing 100% methanol.
Item 10:	**Standard Operating Procedures: (b)(6) SOP BSL3-C-8 (Update)** ▪ Sue Priola informed the committee that the inactivation procedures described in the working group summary were accurately listed in the SOP update. ▪ Scott Kobayashi stated that to make it clear about the 20-minute incubation, the sentence in 9.1.1, (b)(6) eads to . . .” should be deleted. Instead a sentence stating that the organs will be incubated for 20 minutes should be added in its place. ▪ There were no additional comments or concerns with the SOP. Action: The committee unanimously approved (b)(6) **SOP BSL3-C-8** with minor modifications: 1. Delete the sentence in 9.1.1, (b)(6) leads to . . .”. Instead a sentence stating that the organs will be incubated for 20 minutes should be added in its place
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Reviewed the BSO report. ▪ Nancy Hoe informed the committee that Select Agent PRD and RD registrations are now approved to be added to PI Dashboard. Biosafety will populate the

	agents and lab fields and will then upload currently approved registrations for each PI. The IBC approval date will remain the same, although PI Dashboard will likely list the date that the document is uploaded. A comment will probably be added to the registration to clarify the approval date. Soon, PI's will be notified as to when everything will need to be included and updated in PI Dashboard. ▪ Nancy Hoe updated the committee on the recent CDC Permit Inspection that occurred in May. The inspections went well, the reports have been received and the PI's are working on responding to the minor findings.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ Not present.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ (b)(6) annual shutdown of (b)(6) is complete for this year. ▪ In June BSL-4 Medical Extraction training occurred for the BSL-4 employees. ▪ (b)(6) in the (b)(6) is currently shutdown to complete an autoclave replacement project. During that shutdown, the flooring will be replaced to meet the Arthropod Containment Laboratory Guidelines. Once the flooring is replaced in (b)(6) the flooring will also be replaced in (b)(6) for their flea room.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ None.

Other issues	▪ The IBC discussed the change of PI from Don Gardner to Dana Scott for PRD#15-176 (human/non-human primate blood and body fluid). Dana Scott is taking over as Chief of RMVB since (b)(6).

Next Meeting:

- Date: 7/19/18
- Place: Library conference room
- Time: 1:00 PM

RML Biosafety Committee Meeting
June 21, 2018
Biosafety Officer/Responsible Official Report

1) Requests approved by BSO since last meeting:

a) DeLeo (LB)

*i) **PRD-16-180**: Klebsiella pneumonia*

(1) add intranasal route of inoculation: approved 6/12/18

2) ***New requests approved by committee via electronic review:***

a) *None*

3) ***New requests***

a) *Pathogen Registration Documents*

i) ***New***

(a) *Bloom (LV)*

(a) *PRD-18-204: Kunjin virus*

ii) ***Renew***

(a) *Hinnebusch (LB)*

(a) ***PRD-18-86:** Human blood and body fluids*

(b) ***PRD-18-07**: Yersinia pseudotuberculosis*

(b) *DeLeo (LB)*

(a) ***PRD-18-124**: Influenza (exempt)*

(c) *Hasenkrug (LPVD)*

(a) ***PRD-18-55**: HIV*

(b) ***PRD-18-104**: Human blood and body fluids*

(d) *Feldmann (LV)*

(a) ***PRD-18-90**: Filoviridae*

(b) ***PRD-18-92**: Bunyaviridae*

b) *Registration Documents for Recombinant Nucleic Acid Experiments*

i) ***Amend***

(a) *Feldmann (LV)*

(a) ***RD-16-450**: Lloviu virus reverse genetics*

(i) add mice as an animal model

c) *Review of Validation of Inactivation Procedures*

i) *Bosio*

(a) *inactivation of Francisella tularensis in murine tissues by 100% methanol*

d) *Standard Operating Procedures*

i) *Update*

(a) ***BSL3-2**: Removal and manipulation of mouse organs following infection with F.tularensis*

(a) *add procedure for harvesting tissues that will be fixed with 100% methanol*

(b) ***BSL3-C-8**: Inactivation of Francisella spp.*

(a) *add procedure for fixation of murine tissues with 100% methanol*

2) ***Animal Study Protocols Review (since 4/15/18)***

Title	***Associated PRD***	***Associated RD***	***Reviewer***
Evaluation of Host Cell Recruitment to the Skin-draining Lymph Nodes of Y. pestis Infected Mice by Intravital Microscopy and Histocytometry	*14-66 (Yersinia pestis (exempt)) 13-04 (Yersinia pestis)*	*15-320 13-303*	*R. Anderson*
Production of rabbit antibody against K. pneumoniae capsular polysaccharide glycoconjugate	*N/A*	*N/A*	*M. Brose*
Establishment of a mouse model for Kyasanur forest disease virus infection	*18-135 (Kyasanur Forest Disease virus)*	*N/A*	*R. Anderson*
Production of Antibodies Against Filovirus Glycoproteins in Rousettus aegyptiacus Bats	*18-82 (VSV exempt)*	*15-404*	*M. Brose*
Analyzing the role of MAVS dependent signaling on spatial organization of the mouse lymph node following infection at a single cell resolution	*18-82 (VSV exempt)*	*15-404*	*M. Brose*
Immunotherapeutic in situ vaccination treatment with Toll-like receptor and co-stimiulation agonists to restore immune cell function in a model of murine retrovirus infection	*16-187 (Friend virus)*	*N/A*	*R. Anderson*
Effects of injection volume and infusion rate on Y. pestis LN dissemination	*14-66 (Yersinia pestis (exempt))*	*N/A*	*N. Hoe*
Generation of Prion Infected Brain Material from Various Mouse and Prion Strains for Experimental Use	*18-51 (CJD) 16-191 (rodent-adapted scrapie)*	*12-211*	*N. Hoe*
Confirmation of Inactivation of Prions, in Samples Prepared for Mass Spectrometry, in mic	*18-51 (CJD) 16-191 (rodent-adapted scrapie)*	*N/A*	*M. Brose*
Klebsiella pneumoniae infection in non-human primates	*16-180 (Klebsiella pneumoniae)*	*N/A*	*N. Hoe*
Efficacy of two VSV-NiV vaccines against homologous and heterologous challenge in African green monkeys	*18-82 (VSV exempt) 13-91 (Nipah virus)*	*15-404*	*R. Anderson*
Mechanisms of monocyte egress and trafficking during Orthobunyavirus infection in mice	*18-103 (Lacrosse virus and Orthobunyaviruses)*	*N/A*	*R. Anderson*
Imaging host metabolism in vivo in mice using the IVIS Illumina XR	*N/A*	*N/A*	*R. Anderson*
Determining the role of plasmacytoid dendritic cells and macrophages in interferon-mediated control of EBOV infection in mice.	*13-90 (Ebola virus)*	*N/A*	*M. Brose*

Title	*Associated PRD*	*Associated RD*	*Reviewer*
Evaluation of a recombinant attenuated Salmonella delivery system against metastatic breast cancer in mice.	*18-44 (Salmonella enterica serovar Typhimurium)*	*14-126*	*R. Anderson*
Contribution of bacterial membrane lipids in virulence of Francisella tularensis in mice	*13-71 (Francesella tularensis subsp. tularensis)*	*13-125*	*N. Hoe*
Preclinical testing of a DNA Vaccine for Middle East Respiratory Syndrome coronavirus (MERS-CoV) in rhesus macaques	*17-143 (MERS-CoV)*	*N/A*	*N. Hoe*
Protective efficacy of the immunotherapeuytic IMT504 against Ebola virus infection in mice	*13-90 (Ebola virus)*	*N/A*	*R. Anderson*
Cross-protection of ChAdOx1-NiV-B vaccination against Nipah virus Malaysia and Hendra virus in Syrian hamsters	*13-91 (Nipah and Hendra viruses)*	*17-410*	*M. Brose*
Experimental Nipah Virus Infection in Rousettus aegyptiacus Bats	*13-91 (Nipah virus)*	*N/A*	*N. Hoe*
Efficacy of active and passive immunization against Klebsiella pneumoniae infection in immunocompromised mouse model.	*16-180 (Klebsiella pneumoniae)*	*N/A*	*R. Anderson*
Rabbit model of recurring Staphylococcus aureus skin and soft infections	*18-1 (Staphylococcus aureus)*	*15-313*	*M. Brose*
Role of the Yersinia pestis F1 capsule in promoting mammal-to-flea transmission	*13-04 (Yersinia pestis)*	*15-320*	*R. Anderson*
Assessment of Lluvio virus pathogenicity in a murine infection model	*13-90 (Llovio virus)*	*16-450 14-407*	*N. Hoe*

3) ***Biosafety Training Performed – Rebecca Anderson, Megan Brose***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
Annual Refresher Training (General)	*2*	*60*
Select Agent Initial	*2*	*4*
BSL-3 Laboratory Biosafety	*3*	*3*
BSL-4 Laboratory Biosafety	*10*	*3*
BSL-4 Refresher	*3*	*43*
BSL-4 Medical Emergency	*4*	*32*
Support Personnel (BSL-3/BSL-4)	*2*	*2*
Visitor (BSL-3, BSL-4)	*7*	*21*

4) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
a) *Biological Incident Report:*
i) *None*

5) ***Select Agent Issues***
a) *Select Agent registrations on PI-Dashboard*

6) ***Other Issues –***
a) *CDC Import Permit Inspection*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 07/19/2018
Meeting Time: 1:06 PM **Adjourned:** 2:22 PM
Building A Seminar Room

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Karin Peterson	☒	☐
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Greg Saturday	☐	☒
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☒	☐	Alexandra Scranton	☐	☒
Alan Applebury	☐	☒	Nancy Hoe	☒	☐	Brian Vickrey	☐	☒
Chris Bosio	☐	☒	Chris Hoffman	☐	☒			
Marshall Bloom (EO)	☒	☐	Clay Jarrett	☒	☐			
Megan Brose	☒	☐	Josh Kellar (EO)	☐	☒			
Larry Brouwer	☐	☒	Scott Kobayashi	☐	☒			
Carol Calderwood	☐	☒	Jamie Lovaglio	☐	☒			
Marcie Caldwell (EO)	☐	☒	Andrea Marzi	☒	☐			
Paul Carlson	☒	☐	Alida Merritt	☒	☐			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 6/21/18 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 6/21/18** ▪ Nancy Hoe pointed out that the biosafety level for Kunjin virus was missing in Item one. It was BSL-2 and should be added. ▪ Nancy Hoe noted that Item 10 was not approved as written, but with minor modifications, this should be corrected. Action: Meeting minutes for 5/17/18 were unanimously approved with the minor corrections.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment)

- Feldmann (LV)
- **PRD#18-92: Bunyaviridae (Crimean Congo Hemorrhagic Fever Virus, Rift Valley Fever Virus)**
- Becky Anderson presented the risk assessment. The amendment is to create a non-human primate adapted CCHFV strain by passaging it through non-human primates. Currently, infection with the strain Hoti results in a spectrum of disease outcomes that range from asymptomatic to severe, lethal disease. The intent of the Feldmann lab is to be able to generate a variant of CCHFV that more consistently causes severe disease in non-human primates. Attached to the PRD is the animal study protocol describing the procedures that they will perform. The dual use questionnaire does have question A1 marked yes due to the proposed creation of the non-human primate adapted strain.
- Sue Priola stated that they would clearly be enhancing the virulence with the generation of this strain so question A1 is marked yes. The committee must decide if this is dual use research of concern. Sue Priola asked what the mortality rate of CCHF in humans is. Heinz Feldmann stated that it is about 30-50% depending on the outbreak, in some cases up to 80%. These numbers can be skewed however, depending on the extent of epidemiological studies. The current animal model results in 20 to 80% lethal and the problem is that it is so variable. Heinz Feldmann stated that if they have a study with 6 non-human primates, one will have severe disease, one mild, one no disease and the remaining a spectrum in between. Heinz Feldmann stated that this is the only human isolate so far that has been tested that can cause disease in non-human primates and they are trying to make a better model. In fact, reviewers of a recent publication from the Feldmann lab suggested that the lab do this experiment to try to enhance the consistency of the model. Nancy Hoe stated that we need to weigh the risks vs. benefits of the proposed study. The benefits are that they will use fewer animals and will be able to develop a better model to study potential vaccines and therapeutics. The risks are to potentially increase the mortality rate for humans and potentially lose drug sensitivity to ribavirin. (b)(6) stated that ribavirin is already not consistently effective for CCHF and that there is no indication that adaptation in non-human primates would make the strain become resistant to the drug. Heinz Feldmann stated that the adaptation typically affects genes that respond to innate immune response and glycoproteins and is not likely to affect sensitivity to ribavirin. He also stated that there currently is no recommended treatment for infection with CCHFV.
- Karin Peterson questioned whether the Feldmann lab will have trouble publishing the work if it is considered dual use. The group agreed that the study results could not be readily used to do harm and the group further agreed that the publication aspect was not a concern of the IBC. Nancy Hoe questioned if the transmissibility of the virus would be altered in this study. Heinz Feldmann stated that it is always a possibility, but that the study is not

	designed to select for transmissibility to create this variant. He further stated that it is likely that the passaging in non-human primates will make the variant unfit for ticks (the natural route of infection to humans) (b)(6) stated that generally when you adapt to another species, you typically attenuate for other species. Nancy Hoe stated that from a biosafety perspective, performing the study at BSL-4 will mitigating the risks, even if the variant caused 100% lethality in the non-human primates. The committee discussed this topic extensively and agreed that there was no dual use research of concern. ▪ Animal studies with non-human primates were proposed. ▪ The biosafety level for work with Bunyaviridae is BSL-4/ABSL-4. ▪ The committee extensively discussed the dual-use potential of these experiments, see discussion above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Andrea Marzi abstained) **PRD#18-92** as written.
Item 2:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Feldmann (LV) ▪ **PRD#18-91: Paramyxoviridae (Hendra, Nipah, and Cedar virus)** ▪ Becky Anderson presented the risk assessment. o Nipah Virus—many cases are mild or sub-clinical. Symptomatic cases present with high fever, severe headache and muscle pain. The disease can progress to inflammation of the brain with drowsiness, disorientation, convulsions and coma. Approximately 40% of clinically apparent diseases are fatal. o Hendra—only 3 cases have been recognized and 2 of the 3 were fatal. Symptoms include flu-like symptoms, fever, headache, shortness of breath, dizziness, drowsiness and confusion. Death can occur by either severe encephalitis or septic pneumonia. o Cedar virus is a recently discovered virus that was identified by isolation from flying fox urine in Australia during a field study for Hendra virus. Preliminary animal studies have indicated that Cedar virus is less pathogenic than Hendra or Nipah. To date, no known cases of human infection have been identified. ▪ Natural transmission occurs through contact with infected hosts: Nipah-pigs, humans, and bats, Hendra—horses and humans, and Cedar Virus—bats, unknown. Ribavirin has been shown to be effective *in vitro*, but the *in vivo* effect is not clear. ▪ The primary lab hazards include: direct contact with broken skin or mucous membranes, accidental parenteral inoculation, exposure to infectious aerosols, animal bites and scratches.

	▪ The biosafety level for work with Paramyxoviridae is BSL-4/ABSL-4. ▪ Animal studies with mice, hamsters, non-human primates, and bats were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Andrea Marzi abstained) **PRD#18-91** as written.
Item 3:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Feldmann (LV) ▪ **PRD#18-94: Arenaviridae (Chapare, Guanarito, Junin, Lassa, Lujo, Machupo, and Sabia virus)** ▪ Becky Anderson presented the risk assessment. o Lassa Fever Virus: acute viral illness of 1 to 4 weeks duration. Disease may be asymptomatic to mild (80 % of cases), severe, or fatal. Early symptoms include gradual onset of fever, nausea, abdominal pain, severe sore throat, cough, conjunctivitis, ulceration of buccal mucosa, exudative pharyngitis, and cervical lymphadenopathy. Late symptoms include severe swelling of head and neck, pleural and pericardial effusions. The disease is severe in pregnancy, resulting in fetal loss in 80 % of cases. Death because of infection with Lassa virus is usually due to cardiac arrest. o Pathogenicity of other viruses includes: fever, malaise, headache, and muscular pains. Bleeding may occur from nose, gums, stomach and intestine. Severe cases present with hypotensive shock and neurologic crisis. Fatality rate ranges from 5 to 80% depending on the specific virus listed. ▪ The natural route of transmission is through aerosols, contact with infected rodents, excretions, etc. The primary lab hazards include parenteral inoculation, generation of aerosols, and accidental sharps injuries. For treatment, ribavirin is known to be effective for some of the viruses. ▪ The biosafety level for work with Arenaviridae is BSL-4/ABSL-4. ▪ Animal studies with mice, rats, hamsters, guinea pigs, and non-human primates were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Andrea Marzi abstained) **PRD#18-94** as written.
Item 4:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals

	(Renewal) ▪ Feldmann (LV) ▪ **PRD#18-147: Coltivirus** ▪ Becky Anderson presented the risk assessment. The proposed studies are to understand the molecular basis of Colorado Tick fever virus life cycle, pathogenesis, mechanisms of virulence acquisition, ecology, and evolution. ▪ Infection of humans with Coltiviruses is characterized by abrupt onset of fever, chills, headache, retroorbital pain, photophobia, myalgia, abdominal pain, and generalized malaise. Half of patients have a biphasic fever, usually lasting for 5 to 10 days. Severity is sufficient to result in hospitalization of approximately 20% of patients. Virus can be detected in blood for up to 12 days. Death from Coltivirus infections is rare. There are no treatments or vaccines, treatment of the symptoms is offered. The natural route of transmission is from the bite of an infected tick and from blood transfusions. ▪ The primary lab hazards include: accidental parenteral inoculation, generation of aerosols, tick bites, and accidental needle sticks. ▪ Nancy Hoe pointed out that mammalian cells will be worked with on this PRD so the human blood and body fluid language should be added to the recommendations section. ▪ Nancy Hoe noted that the BSL-2 lab that will be used for this work no longer has restricted access, this should be removed from the Eukaryote Cell section in the PRD. ▪ Sue Priola pointed out that in the Eukaryote cell section and the Pathogen section, rodent field isolates should be added where tick field isolates are listed. ▪ Sue Priola also stated that the language about identification of a BSL-3 pathogen should be added to the new section on isolation of Coltiviruses from rodent samples. ▪ The biosafety level for work with Coltiviruses is BSL-2. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Andrea Marzi abstained) **PRD#18-147** with minor modifications: 1. Add the human blood and body fluid language to the recommendation section of the PRD. 2. Remove language from the Eukaryote cell section that states the lab has restricted access. 3. Add rodent field isolates to the Eukaryote cell section and the Pathogen section where the tick field isolates are listed.

	4. Add language to the Eukaryote cell section, rodent sample section that describes what to do if there is identification of a BSL-3 pathogen.
Item 5:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Bosio (LB) ▪ **PRD#18-73: *Francisella tularensis* (exempt, non-Select Agent)** ▪ Becky Anderson presented the risk assessment. The proposed study is to determine the bacterial and host components associated with the suppression of protective inflammatory responses during infection with *F. tularensis*. The Live Vaccine strain (LVS) is an attenuated experimental vaccine strain that was attenuated by repeated passaging of the bacteria. It was used in the 1950s and 1960s as an experimental vaccine at Fort Detrick, but use was later discontinued. It is not an FDA approved vaccine because the mechanism of attenuation is not well characterized, it can cause disease in immunocompromised persons, and is not protective against higher challenge doses. *Francisella novicida* is considered non- or low pathogenicity in humans. Only a few cases of human infections have been identified. The natural route of inoculation occurs through contact of skin or mucosa with blood or tissue while handling infected animals, ingestion of contaminated food and drinking water, and inhalation of contaminated dust. It is not known to be transmitted human to human. *F. tularensis* is susceptible to aminoglycosides, streptomycin, gentamycin, tobramycin, kanamycin, tetracyclines, chloramphenicol, and streptomycin; gentamycin is drug of choice. ▪ The primary lab hazards include: ingestion and exposure to aerosols and infectious droplets. ▪ The biosafety level for work with *F. tularensis* exempt, non-Select Agent is BSL-2/ABSL-2. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#18-73** as written.
Item 6:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Feldmann (LV) ▪ **RD#17-452 Amend**: Use of an Alphavirus replicon system to produce vaccines ▪ Reviewers: Karin Peterson, Sue Priola ▪ **Summary:** The amendment describes adding additional methods for generating the replicon system. ▪ Karin Peterson summarized the RD. The amendment is to add two new

	methods of generating a replicon system. They will create a stable transfection. The diagrams are attached depicting how the replicon system works. Basically, one round of infection occurs to produce antigen, but there is no replication. Karin Peterson stated that the RD does not list how much of the virus will be used. Andrea Marzi stated that it cannot be more than 3 kb because they are limited by what can be added in the replicon system. Sue Priola stated that the information is included in the original RD and that it will not be more than 66%. Karin Peterson asked that it be added to the amendment as well. ▪ Sue Priola asked if there was a reference for the statement that the production cell line will lack untranslated regions of the alphavirus genome that are necessary for replication. Andrea Marzi stated that some of these are kits and that language probably came from the manual. ▪ The NIH Guidelines were appropriate and there were no dual use concerns. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **RD#17-452 Amend** with minor modifications: 1. Add to the amendment description that less than 66% of the source genome will be used. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a and III-E-1 of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a and III-D-3-a of the NIH Guidelines.
Item 7:	<u>Registration Documents for Recombinant DNA Experiments (Amendment)</u> ▪ Heinzen (LB) ▪ **RD#14-106 Amend**: Genetic transformation of *C. burnetii* ▪ Reviewers: Scott Kobayashi, Andrea Marzi ▪ **Summary:** The RD describes utilizing CRISPR technology for gene silencing. ▪ Scott Kobayashi was not present, but provided comments to Sue Priola by email stating that he had no concerns with the RD amendment. Andrea Marzi summarized the RD. The amendment is to utilize modified CRISPR systems to silence genes in *C. burnetii*. This method is a commonly used system and Andrea Marzi had no concerns with the proposed work. Andrea Marzi stated that there was a typo at the bottom, CRISPR was misspelled. Bob Heinzen stated that the last sentence should be changed from mutagenesis to silencing to be clearer.

	▪ The NIH Guidelines were appropriate and there were no dual use concerns. ▪ The committee had no additional comments or concerns. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Bob Heinzen abstained) **RD#14-106 Amend** with minor modifications: 1. Correct the CRISPR misspelling on the bottom of the first page. 2. Change the last sentence from "mutagenesis" to "silencing". Research using prokaryotic hosts is approved at BSL-2 and BSL-3 under section III-D-1-a, III-D-1-b, and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 and BSL-3 under III-D-1-a, and Appendix G-II-C of the NIH Guidelines.
Item 8:	**Exposure Control Plan (Annual Review)** ▪ Sue Priola informed the committee that the Exposure Control Plan was due for annual review. The proposed changes are tracked in the document. ▪ Alida Merritt suggested that any reference to St. Patrick Hospital should be changed to Providence St. Patrick Hospital throughout the document to be more accurate with the hospital's name change. ▪ Alex Scranton submitted questions to Sue Priola via email. Alex Scranton questioned why the RML Infectious Disease Advisor (IDA) is not listed in the section on Roles and Responsibilities. Becky Anderson stated that the title IDA was more recently changed to ID Specialist and apparently that was not updated throughout the document. Alex also asked if the IDA should be included in the BEAP. The committee discussed that the ID Specialist is not a part of the BEAP because the NIH OMS Physicians are part of the BEAP and they consult with the ID Specialist whose role is providing medical care to the patient. ▪ Nancy Hoe stated that an ID Specialist role was listed under the OMS Physician role on page 8 and should be moved to under the ID Specialists list of roles. ▪ Under responsibilities, it should be added that the ID Specialist will notify Missoula County Public Health. ▪ Bob Heinzen stated on page 9 the sentence, "if the *injury* involves a potential . . ." should be changed to "if the *exposure* involves a potential…..". Action: The committee unanimously approved the **Exposure Control Plan (Annual Review)** with minor modifications:

	1. Replace St. Patrick Hospital with Providence St. Patrick Hospital. 2. Remove the ID Specialist line on page 8 under the OMS Physician role. 3. Ensure that ID Specialist is throughout the document and remove reference to the IDA. 4. Under responsibilities for the ID Specialist, add that they will notify Missoula County Public Health. 5. On page 9 change the following: "if the *injury* involves a potential . . ." should be changed to "if the *exposure* involves a potential".
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Reviewed the BSO report. ▪ Nancy Hoe informed the committee that Biosafety performed an escaped flea drill. The drill was coordinated with (b) (6) and lab staff and went very well. From that drill, there will be some updates to the Flea Biosafety Plan.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ There has been one minor injury since the last meeting. An employee sustained a finger laceration on a BSC used for TSE. ▪ BSL-2 lab safety surveys are in progress for all of campus. ▪ Paul Carlson is working on scheduling another drill with Providence St. Patrick Hospital. ▪ Fire drills will be performed next week on campus. ▪ The week of August 6, the NIH Fire Marshall will be onsite.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ The (b)(6) BSL-3 lab is currently shutdown for an autoclave replacement project. ▪ We are in the beginning stages of planning an effluent decon system upgrade and tank inspections. This will be planned to coincide with one of the BSL-4 annual lab shutdowns.
Report	**Associate Director Report/Marshall Bloom** ▪ The next High Containment Task Force meeting will be September 13. (b)(6) (b)(6) from UTMB will be onsite at RML to present at this meeting.
Around the room	▪ None

Other issues	▪ None

Next Meeting:

- Date: 8/16/18
- Place: Library conference room
- Time: 1:00 PM

RML Biosafety Committee Meeting
July 19, 2018
Biosafety Officer/Responsible Official Report

1) Requests approved by BSO since last meeting:

a) Hackstadt (LB)

*i) **PRD-14-38**: Rickettsia spp. (exempt)*

(1) add intraperitoneal route of inoculation for guinea pigs: approved 7/9/18

2) ***New requests approved by committee via electronic review:***

a) *None*

3) ***New requests***

a) *Pathogen Registration Documents*

i) ***Amend***

(a) *Feldmann (LV)*

(a) *PRD-18-92: Bunyaviridae (Crimean Congo hemorrhagic fever virus, Rift Valley Fever virus)*

(i) add experiments to passage CCHFV in non-human primates

ii) ***Renew***

(a) *Feldmann (LV)*

(a) ***PRD-18-91**: Paramyxoviridae, Genus Henipavirus (Nipah, Hendra, Cedar virus)*

(b) ***PRD-18-94**: Arenaviridae (Chapare, Guanarito, Junin, Lassa, Lujo, Machupo, Sabia viruses)*

(c) ***PRD-18-147**: Molecular biology, evolution, and ecology of Colorado tick fever viruses*

(b) *Bosio (LB)*

(a) ***PRD-18-73**: Francisella tularensis (exempt)*

b) *Registration Documents for Recombinant Nucleic Acid Experiments*

i) ***Amend***

(a) *Feldmann (LV)*

(a) ***RD-17-452**: Use of an Alphavirus replicon system to produce vaccines*

(i) add two Alphavirus replicon production methods

(b) *Heinzen (LB)*

(a) ***RD-14-106**: Genetic transformation of Coxiella burnetii*

(i) Use of CRISPR-Cas as a gene silencing system in C. burnetii

c) *Review of Exposure Control Plan*

(a) *Safer Sharps Evaluation*

RML Biosafety Committee Meeting
July 19, 2018
Biosafety Officer/Responsible Official Report

2) ***Animal Study Protocols Review***

Title	*Associated PRD*	*Associated RD*	*Reviewer*
Analysis of blood brain barrier breakdown in LACV-infected mice	*18-103 (La Crosse virus and orthobunyaviruses)*	*N/A*	*R. Anderson*
Influence of mosquito salivary gland proteins on CSG viral pathogenesis in mice	*18-103 (La Crosse virus and orthobunyaviruses)*	*N/A*	*M. Brose*
Efficacy of an alphavirus replicon vaccine for Crimean Congo Hemorrhagic fever virus	*18-92 (CCHFV)*	*17-452*	*M. Brose*
Assessment of oral dosing of LHF-535 as a post-exposure countermeasure to Lassa virus infection in Cynomolgus macaques	*18-94 (Lassa virus)*	*N/A*	*R. Anderson*
Protective efficacy of the immunotherapeuytic IMT504 against MERS-CoV infection in mice	*17-143 (MERS-CoV)*	*N/A*	*M. Brose*
Role of normal prion protein in white matter degeneration	*N/A*	*12-211*	*R. Anderson*
Contribution of itaconate in IFN-γ mediated control of Francisella tularensis strain LVS in mice	*13-73 (F. tularensis subsp. holartica/LVS (exempt))*	*N/A*	*R. Anderson*
Isolation of R. rickettsii from ticks by passage through Guinea pigs	*14-34 (R. rickettsia)*	*N/A*	*M. Brose*

3) ***Biosafety Training Performed – Rebecca Anderson, Megan Brose, Nancy Hoe***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
Annual Refresher Training (General)	*3*	*Many*
Select Agent Initial	*1*	*5*
BSL-3 Laboratory Biosafety	*2*	*4*
BSL-4 Laboratory Biosafety	*2*	*2*
BSL-4 Medical Emergency	*1*	*1*
Visitor (BSL-3, BSL-4)	*2*	*7*
Biosafety Briefs	*1*	*WIP*

4) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
a) *Biological Incident Report:*
   i) *None*

5) ***Select Agent Issues***
a) *Escaped Flea Drill*

6) ***Other Issues –***
a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 08/16/2018
Meeting Time: 1:04 PM **Adjourned:** 1:40 PM
Building A Library, (b)(6)

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Karin Peterson	☒	☐
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Greg Saturday	☐	☒
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Alexandra Scranton	☐	☒
Alan Applebury	☐	☒	Nancy Hoe	☒	☐	Brian Vickrey	☐	☒
Chris Bosio	☐	☒	Chris Hoffman	☐	☒			
Marshall Bloom (EO)	☐	☒	Clay Jarrett	☒	☐			
Megan Brose	☒	☐	Josh Kellar (EO)	☐	☒			
Larry Brouwer	☒	☐	Scott Kobayashi	☒	☐			
Carol Calderwood	☐	☒	Jamie Lovaglio	☐	☒			
Marcie Caldwell (EO)	☐	☒	Andrea Marzi	☒	☐			
Paul Carlson	☒	☐	Alida Merritt	☒	☐			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 7/19/18 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 7/19/18** ▪ Sue Priola pointed out in Item 7 that Scott Kobayashi was absent but provided comments to her by email. This should be clarified. Action: Meeting minutes for 7/19/18 were unanimously approved with the minor corrections.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment) ▪ Best (LV)

	▪ **PRD#17-140 Amend: Dengue virus** ▪ Becky Anderson presented the risk assessment. The amendment is to add animal work with non-human primates. The primary lab hazards include bites or scratches from infected non-human primates. To mitigate these hazards all lab personnel on the ASP are trained on non-human primate handling procedures. PPE includes: lab coat or disposable gown, surgical mask, eye protection, and two pair of gloves. ▪ Animal studies with non-human primates were proposed. ▪ The biosafety level for work with Dengue virus is BSL-2/ABSL-2. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#17-140 Amend** as written.
Item 2:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New) ▪ Bloom (LV) ▪ **PRD#18-205: Dengue virus** ▪ Becky Anderson presented the risk assessment. The proposed studies are to examine and characterize changes caused by acute or persistent Dengue virus infection in mammalian or arthropod cells. The Bloom lab will use Dengue virus as a positive control for assays looking at cellular responses to flavivirus infection. Dengue virus infection results in an acute febrile disease characterized by the sudden onset of fever for 3 to 5 days, with an intense headache, myalgia, arthralgia, retro-orbital pain, anorexia and rash, symptoms are usually self-limiting. In the case of Dengue hemorrhagic fever, a more severe manifestation on the second exposure is characterized by abnormal vascular permeability, decreased blood volume and abnormal clotting mechanisms. The fatality rate can be as high as 40-50%. Infection with one serotype does not offer cross protection to another serotype. There are no vaccines or specific treatments for Dengue virus infection, treatment typically includes maintaining hydration. The natural route of transmission occurs through the bite of an infected mosquito. The primary lab hazards include: accidental parenteral inoculation, contact with broken skin or mucous membranes, accidental needle stick and generation of aerosols. ▪ Additional precautions for working with Dengue virus include: all work is to be done within a BSC, everything should be sealed prior to removal from the BSC, this includes sealed/gasketed safety cups for centrifuges, parafilming of microtiter plates, etc. Additionally, employees should be informed of the following risks of working with Dengue virus: there is an increased severity of disease upon second exposure to Dengue virus, as well as working with multiple serotypes increases your risk of disease.

	▪ The biosafety level for work with Dengue virus is BSL-2/ABSL-2. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#18-205** as written.
Item 3:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Feldmann (LV) ▪ **RD#16-440 Amend**: Development of a reverse genetics system for Coronaviruses ▪ Reviewers: Sue Priola, Karin Peterson ▪ **Summary:** The amendment describes adding procedures for gene replacement. ▪ Sue Priola summarized the RD. The amendment is to the reverse genetics RD for Coronaviruses. The current RD covers mutating WT virus with substitutions or gene deletions. The amendment is to add work that includes replacing the entire spike gene that differs from WT by 1 or 2 mutations. Sue Priola stated that it is not clear the way the amendment is written that the new work is the gene replacement, this needs to be clarified. Additionally, it is not clear that the strains listed from S. Korea are MERS Co-V isolates/strains. This should also be clarified. ▪ Karin Peterson stated that she thought everything was already covered by the original RD. Karin Peterson clarified with the PI that the are just working with the spike protein for the gene replacement work. (b)(6) stated that was correct. ▪ The NIH Guidelines were appropriate and there were no dual use concerns. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Andrea Marzi abstained) **RD#16-440 Amend** with minor modifications: 1. Clarify that the new work is gene replacement. 2. Specify that the new strains from S. Korea are MERS-CoV. Research using prokaryotic hosts is approved at BSL-2 to -4 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 to -4 (depending on virus used) under III-D-3-a, III-D-3-b, and III-D-1-a of the NIH

	Guidelines.
Item 4:	**Working Group Summary** ▪ Sue Priola reviewed the Working Group summary with the committee. Karin Peterson, Scott Kobayashi, and Bob Heinzen were the working group members that reviewed the inactivation methods from Joe Hinnebusch's lab. ▪ The Hinnebusch lab tested the ability of 1% paraformaldehyde to inactivate *Y. pestis* infected animal tissues. They showed that all the bacteria were inactivated. ▪ The associated SOPs were updated to reflect the addition of 1% paraformaldehyde to inactivate *Y. pestis*. Action: The committee unanimously approved the Working Group recommendation that 1% paraformaldehyde completely inactivated *Y. pestis* and approved the validation studies as written.
Item 5:	**Standard Operating Procedures: (b)(6) SOP BSL3-B-4 (Update)** ▪ Sue Priola informed the committee that the inactivation procedures described in the working group summary were accurately listed in the SOP update. ▪ There were no additional comments or concerns with the SOP. Action: The committee unanimously approved (b)(6) SOP BSL3-B-4 as written.
Item 6:	**Standard Operating Procedures: ABSL-3 Plague animal SOP (Update)** ▪ Sue Priola informed the committee that the inactivation procedures described in the working group summary were accurately listed in the SOP update. ▪ There were no additional comments or concerns with the SOP. Action: The committee unanimously approved ABSL-3 Plague animal SOP as written.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Reviewed the BSO report. ▪ Nancy Hoe asked Becky Anderson to brief the IBC on a recent issue that has been brought to light by new policy statements from the Select Agent Program. Becky Anderson informed the IBC that Heinz Feldmann and (b) (6) are the registered Select Agent PI's at RML. According to Select Agent regulations, when an inactivated sample is removed from the BSL-4 (registered space) in this case, the PI needs to sign prior to removal. (b) (6) currently is the only PI approved for Flaviviruses while Heinz Feldmann is registered for all the other BSL-4 Select Agents. Technically (b) (6) s the PI that should sign for Flaviviruses that are inactivated and removed from the lab. However, the IBC

	has reviewed inactivation procedures that were all listed under Heinz Feldmann, not(b) (6) Becky Anderson wanted to clarify with the group that ALL inactivated samples that are removed from the BSL-4 are performed the exact same way according to the BSL-4 approved SOPs regardless of the PI the employee works for. Because of this, we want to put a memo with the inactivation procedure binder that states the IBC approved procedures are approved for all BSL-4 PI's. The committee discussed extensively and agreed that the approved procedures could be applied to all BSL-4 PI's as long as they all followed the same SOP.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ The NIH Fire Marshal was onsite not long ago. Some items that were noted during the inspection included: materials were blocking a few pull stations, and that corridors and hallways should be kept clean. Some areas will have upgrades put in place in response to the fire marshal's report. ▪ The St. Patrick Hospital Drill will take place September 27th. The drill will be a full transfer drill from RML to St. Patrick Hospital.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ The (b)(6) autoclave and flooring replacement project is ongoing. ▪ When the (b)(6) flooring is replaced, they will move on to replace flooring in (b)(6) This will occur September 4-13th.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ None

Other issues	▪ None

Next Meeting:

- Date: 9/20/18
- Place: Library conference room
- Time: 1:00 PM

RML Biosafety Committee Meeting
August 16, 2018
Biosafety Officer/Responsible Official Report

1) Requests approved by BSO since last meeting:

a) None

2) ***New requests approved by committee via electronic review:***

a) *None*

3) ***New requests***

a) *Pathogen Registration Documents*

i) ***Amend***

(a) *Best (LV)*

(a) *PRD-17-140: Dengue virus serotype 1-4*

(i) add experiments in non-human primates

ii) ***New***

(a) *Bloom (LV)*

(a) ***PRD-18-205**: Dengue virus serotype 1-4*

b) *Registration Documents for Recombinant Nucleic Acid Experiments*

i) ***Amend***

(a) *Feldmann (LV)*

(a) ***RD-16-440**: Reverse genetics of coronaviruses*

(i) add BAC system to generate coronavirus variants

4) ***Working Group Summary***

i) *Hinnebusch*

(a) *inactivation of Y. pestis with 1% PFA*

5) ***Standard Operating Procedures***

i) *Update*

(a) *ABSL-3 Plague Animal SOP: add inactivation of Y. pestis with 1% PFA*

(b) *BSL-3-B-4: in vitro cell culture assays – add inactivation of Y. pestis with 1% PFA*

6) ***Animal Study Protocols Review***

Title	***Associated PRD***	***Associated RD***	***Reviewer***
Second Passage and Clearance Kinetics of Chronic Wasting Disease in Mice	*16-90 (Chronic Wasting Disease)*	*RD-12-211*	*R. Anderson*
Shedding and pathogenesis of MERS-CoV receptor-binding mutants	*17-143 (MERS-CoV)*	*RD-16-440*	*N. Hoe*

Title	*Associated PRD*	*Associated RD*	*Reviewer*
Investigating the effect of aging (immune senescence) and the efficacy of checkpoint immune therapy on acute and chronic immune responses and viral load in a model of murine retrovirus infection.	*16-187 (Friend virus)*	*N/A*	*M. Brose*
Investigating the tissue distribution and functional significance of SIRPα, a newly discovered receptor expressed on virus-activated CD8+ T cells during acute and chronic infection in a model of murine retrovirus infection	*16-187 (Friend virus)*	*N/A*	*M. Brose*
Determining Effects of Corticosteroid Treatment in Collaborative Cross Mice with Lethal Ebola Virus Disease	*18-90 (Ebola virus)*	*N/A*	*N. Hoe*
Isolation of monocytes from pigtail macaques	*N/A*	*N/A*	*R. Anderson*

7) ***Biosafety Training Performed – Rebecca Anderson, Megan Brose***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
BSL-4 Refresher	*2*	*3*
BSL-4 Laboratory Biosafety	*3*	*4*
Visitor (BSL-3, BSL-4)	*7*	*14*
Biosafety Briefs	*2*	*WIP*

8) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
a) *Biological Incident Report:*
   i) *None*

9) ***Select Agent Issues***
a) *Scope of reviewed and approved inactivation procedures.*

10) ***Other Issues –***
a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 08/20/2018
Meeting Time: 1:01 PM **Adjourned:** 2:22 PM
Building A Library, (b)(6)

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Karin Peterson	☒	☐
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Greg Saturday	☒	☐
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Alexandra Scranton	☐	☒
Alan Applebury	☐	☒	Nancy Hoe	☒	☐	Brian Vickrey	☐	☒
Chris Bosio	☒	☐	Chris Hoffman	☐	☒			
Marshall Bloom (EO)	☐	☒	Clay Jarrett	☐	☒			
Megan Brose	☒	☐	Josh Kellar (EO)	☐	☒			
Larry Brouwer	☐	☒	Scott Kobayashi	☒	☐			
Carol Calderwood	☐	☒	Jamie Lovaglio	☒	☐			
Marcie Caldwell (EO)	☒	☐	Andrea Marzi	☐	☒			
Paul Carlson	☐	☒	Alida Merritt	☒	☐			

(P=present; A=absent)

Guests (b)(6)

Minutes: Meeting minutes from 8/16/18 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 8/16/18** ▪ No changes. Action: Meeting minutes for 8/16/18 were unanimously approved.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment) ▪ Best (LV) ▪ **PRD#18-135 Amend: Tick-borne encephalitis viruses** ▪ Becky Anderson presented the risk assessment. The amendment is to add

	Alkhurma virus that is a variant of Kyasanur Forest Disease virus. The virus was initially isolated in 1995 from a patient in Saudi Arabia. Subsequent cases of Alkhurma virus have been documented in tourists in Egypt, extending the geographic range of the virus and suggesting that geographic distribution of the virus is wide and that infections due to Alkhurma virus are underreported. Based on limited information, after an incubation period that could be as short as 2-4 days, the disease presents initially with non-specific flu-like symptoms, including fever, anorexia, general malaise, diarrhea, and vomiting; a second phase has appeared in some patients, and includes neurologic and hemorrhagic symptoms in severe form. Multi-organ failure precedes fatal outcomes. There is some evidence that suggests a milder form of disease may develop that does not require hospitalization. The natural route of transmission is through the bite of an infected tick. There is no known human to human transmission. Contact with domestic animals or livestock may increase the risk of infection. The primary lab hazards include: accidental parenteral inoculation, generation of aerosols, and droplet exposure to the mucous membranes. There are no treatments or vaccines available for Alkhurma virus. ▪ Sue Priola asked if the approved animal species and routes will apply to Alkhurma virus. Becky Anderson stated that all the previously approved animal studies will apply to Alkhurma virus as well. The Best lab does not need a separate approval for each of the viruses on the pathogen registration. ▪ Alkhurma virus is a Select Agent ▪ No new animal studies were submitted, reviewed, or approved. ▪ The biosafety level for work with Alkhurma virus is BSL-4/ABSL-4. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **PRD#18-135 Amend** as written.
Item 2:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New)</u> ▪ Feldmann (LV) ▪ **PRD#18-206: Alphaviruses (Chikungunya virus, Chikungunya virus vaccine strain, and Ross River virus)** ▪ Becky Anderson presented the risk assessment. The new PRD is for Alphaviruses, but specifically the following three viruses are being added: Chikungunya virus, Chikungunya virus vaccine strain, and Ross River virus. The purposes of these studies are to investigate the host and viral determinants of viral pathogenesis by infection of cell culture or established animal models with either WT or mutant alphaviruses. o The most common symptoms of chikungunya virus infection are fever and

joint pain and occur within 3-7 days of being bitten by a mosquito. Other symptoms may include headache, muscle pain, joint swelling, or rash. Chikungunya disease does not often result in death, but the symptoms can be severe and disabling. Most patients recover within a week. People at risk for more severe disease include newborns and adults over 65 years of age, and people with medical conditions such as high blood pressure, diabetes, or heart disease. Once a person has been infected, they are likely to be protected from future infections.

- Ross river virus: many people that become infected with the virus never develop the symptoms. Some people have flu-like symptoms that include fever, chills, headache and aches and pains in the muscles and joints. This is termed, Ross River fever. Sometimes a rash occurs on the body, arms, or legs. The rash usually disappears within 7 to 10 days.
- Chikungunya virus vaccine strain- has been tested in humans as a vaccine, the virus proved highly immunogenic. However, 5 out of 59 vacinees developed mild, transient arthralgia. This suggests insufficient or unstable attenuation. To develop the vaccine strain, it was passaged 18 times thru cell culture from a WT strain.

- The natural route of transmission is through the bite of an infected mosquito, there is no known human to human transmission. The primary lab hazards include: accidental needle stick, parenteral inoculation and generation of aerosols.
- Nancy Hoe stated that the IBC should recommend to the PI that they get assurances from the collaborator that is providing the Chikungunya virus vaccine strain that it is appropriate for work at BSL-2. They could provide sequencing data or state that the BSL-2 strain is worked with physically separate from the WT BSL-3 strain of Chikungunya. The IBC agreed that this would be an appropriate recommendation.
- Sue Priola pointed out in the ASP that the scientific description section makes it sound like RML has worked with or is already working with Chikungunya virus. Becky Anderson stated that the work described did not occur at RML, the Feldmann lab does not currently possess any of these Alphaviruses. Sue Priola agreed, but stated that the language should be changed so there is no confusion to others.
- The biosafety level for work with Ross River virus and the vaccine strain of Chikungunya virus is BSL-2/ABSL-2. The biosafety level for work with Chikungunya virus is BSL-3/ABSL-3.
- Animal studies with non-human primates were proposed.
- The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.

Action: The committee unanimously approved **PRD#18-206** with the following minor modifications:

	1. The IBC recommends that the PI get assurances from the collaborator that is providing the Chikungunya virus vaccine strain that it is appropriate for work at BSL-2. They could provide sequencing data or state that the BSL-2 strain is worked with physically separate from the WT BSL-3 strain of Chikungunya. 2. Update the attached ASP to state in the scientific description section that work was done by collaborators, not at RML.
Item 3:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal)</u> ▪ Caughey (LPVD) ▪ **PRD#18-47: Human TSE agents** ▪ Becky Anderson presented the risk assessment. The PRD is for human TSE agents. The purposes of the studies are the following: 1. further develop and use the RTQ assay for clinical and research applications for the various human TSEs, Parkinson's, Alzheimer's, and other protein misfolding diseases; 2. analyze various human tissues from normal and TSE, Parkinson's, or Alzheimer's affected patients in the RTQ assay; 3. test potential therapeutic drugs *in vitro* using biochemical and cell culture models followed by *in vivo* testing of promising candidates in human TSE transgenic mice. After exposure, human TSE diseases incubate for long periods of time (up to decades) without observable signs of disease until late in the disease course. Once signs develop, the disease is typically fatal within 6-12 months. Initial signs and symptoms typically include: personality changes, anxiety, depression, memory loss, Impaired thinking, blurred vision or blindness, insomnia, difficulty speaking, difficulty swallowing, sudden and jerky movements. As the disease progresses, mental symptoms worsen. Most people eventually lapse into a coma. Heart failure, respiratory failure, pneumonia or other infections are generally the cause of death. In some cases, CJD has spread to other people from grafts of dura mater (a tissue that covers the brain), transplanted corneas, implantation of inadequately sterilized electrodes in the brain, and injections of contaminated pituitary growth hormone derived from human pituitary glands taken from cadavers. However, since 1985, all human growth hormone used in the United States has been synthesized by recombinant DNA procedures, which eliminates the risk of transmitting CJD by this route. Accidental exposure to brain tissue and spinal cord fluid from infected individuals should be avoided to prevent transmission of the disease through these materials. ▪ Sue Priola informed the committee that there is also a liquid nitrogen freezer in (b)(6) that should be added to the Refrigerator/Freezer section. ▪ Animal studies with mice were proposed. ▪ The biosafety level for work with human TSE agents is BSL-2/ABSL-2. The lab is a restricted access lab with the following PPE: gown, face mask, and gloves.

	▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#18-47** with the following minor modifications: 1. Add liquid nitrogen freezer to the refrigerator/freezer section in Room (b) (6)
Item 4:	**Operations and Safety Procedures:** (b) (6) **(Annual Review)** ▪ Becky Anderson informed the committee that the document is due for annual review. The updates to the document are summarized in the table at the beginning of the document. Most of the updates are to the requirement for an inactivation certificate for removal of Select Agent samples from the BSL-3 labs. She informed the committee that in August the Division of Select Agents sent out notice that the certificate needs to be signed by the PI prior to removal of the inactivated sample. The updated procedures in the OSP describe the methods for generating the certificate. ▪ Bob Heinzen asked why on page 35 "or not" is listed for the indication of PI approval. Nancy Hoe stated that the PI may not approve the removal. Bob Heinzen felt that the "or not" was confusing. The committee discussed and agreed it would be clearer to remove the "or not". ▪ Bob Heinzen also asked if it would be a good idea to include an example of the sample removal log. The committee agreed that it could be added in an appendix to the document. ▪ There were no additional comments or concerns with the SOP. Action: The committee unanimously approved **Operations and Safety Procedures:** (b)(6) with the following minor modifications: 1. Remove "or not" from page 35 in the updated section. 2. Add an example of the sample removal log in an appendix.
Item 5:	**Operations and Safety Procedures:** (b)(6) **(Annual Review)** ▪ Becky Anderson informed the committee that the document is due for annual review. She stated that the updates for the ABSL-3 OSP are the same as for the lab BSL-3 OSP. ▪ The committee agreed that the IBC changes for the BSL-3 OSP should be the same for the ABSL-3 OSP. ▪ Jamie Lovaglio stated that the Attending Veterinarian should be changed to Attending/Clinical Veterinarian as the Attending Veterinarian may not always perform some of the listed duties. The committee agreed to update that section.

	▪ There were no additional comments or concerns with the SOP. Action: The committee unanimously approved **Operations and Safety Procedures:** (b)(6) with the following minor modifications: 1. Remove "or not" from page 35 in the updated section. 2. Add an example of the sample removal log in an appendix. 3. Throughout the document, change Attending Veterinarian to Attending/Clinical Veterinarian.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Reviewed the BSO report. ▪ Nancy Hoe reviewed two incident reports with the IBC. The two incidents occurred in August in the BSL-4. In both incidents the positive pressure suits had a 1-2 inch tear in the suit bootie. Nancy Hoe described the incidents and discussed the risk assessment that biosafety and OMS performed and deemed the incidents neglible risk to the individuals involved. The follow-up actions from these two incidents included: 1. LV contacted the manufacturer, Honeywell, to inform them of the incidents and ask for corrective actions , 2. Staff were reminded to not over-inflate suits during suit integrity tests, the SOP for suit integrity testing will be updated to remind staff not to over-inflate the suits, 3. Reminded staff to pay close attention to foot seams when donning laboratory shoes (Crocs). ▪ Nancy Hoe provided annual IBC training.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ Not present.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ The (b)(6) autoclave and flooring replacement projects are ongoing. Estimated completion date is October. ▪ The (b)(6) annual shutdown is scheduled for October. It will be the last one for the year.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ None

Other issues	▪ None

Next Meeting:

- Date: 10/18/18
- Place: Library conference room
- Time: 1:00 PM

RML Biosafety Committee Meeting
September 20, 2018
Biosafety Officer/Responsible Official Report

1) ***Requests approved by BSO since last meeting:***
   a) *None*
2) ***New requests approved by committee via electronic review:***
   a) *None*
3) ***New requests***
   a) *Pathogen Registration Documents*
      i) ***New***
         (a) *Feldmann (LV)*
            (a) ***PRD-18-206**: Alphaviruses*
      ii) ***Amend***
         (a) *Best (LV)*
            (a) ***PRD-18-135**: Flaviviruses*
               (i) add Alkhurma virus
      iii) ***Renew***
         (a) *Caughey (LPVD)*
            (a) *PRD-18-47: Sporadic CJD, variant CJD, GSS, FFI, and other human TSE diseases*
4) ***Standard Operating Procedures***
   i) *Annual Review*
      (a) *BSL-3 Operations and Safety Procedures*
      (b) *ABSL-3 Operations and Safety Procedures*
   ii) *Update*
      (a) *DRAFT BSL-3-Cb-5: Inactivation of C. burnetiid*
         (a) *remove sentence in 1.6*

5) ***Animal Study Protocols Review***

Title	***Associated PRD***	***Associated RD***	***Reviewer***
Ornithodoros tick colony feeding and maintenance on mice	*N/A*	*N/A*	*R. Anderson*
Infectious cycle of Relapsing Fever Spirochetes in mice	*14-03 (Borrelia hermsii)*	*14-319*	*R. Anderson*
Virus-induced regulatory T cells (Tregs) in HIV infection	*18-55 (HIV)*	*N/A*	*M. Brose*
The effect of anti-CCL2 antibody on latent reservoir of HIV-1 in TKO-BLT mice	*18-55 (HIV)*	*18-104*	*N. Hoe*

Title	*Associated PRD*	*Associated RD*	*Reviewer*
Pilot study of tick-borne encephalitis virus and Kyasanur forest disease virus pathogenesis in Pigtail macaques	*18-135 (TBEV, Kyasenur forest disease virus)*	*N/A*	*M. Brose*
Preclinical Efficacy Assessment of Electroporation Devices for Delivery of DNA Vaccines Against Marburg Virus in Cynomolgus Macaques	*18-90 (Marburg virus)*	*N/A*	*N. Hoe*
Determine the contribution of circulating T cells during virulent Francisella infection using mouse parabiosis	*18-73 (F. tularensis (exempt)) 18-71 (F. tularensis)*	*N/A*	*N. Hoe*
Protective efficacy of a dual VSV-based vaccine against Lassa and Ebola virus infection in Guinea pigs	*18-90 (Ebola virus) 18-94 (Lassa virus)*	*15-404*	*R. Anderson*

6) ***Biosafety Training Performed – Rebecca Anderson, Megan Brose, Nancy Hoe***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
Select Agent Initial	*1*	*1*
Select Agent Annual Refresher	*5*	*~110*
BSL-4 Refresher	*2*	*35*
BSL-4 Laboratory Biosafety	*5*	*3*
Visitor (BSL-3, BSL-4)	*5*	*7*

7) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
   a) *Biological Incident Report:*
      i) *8/21/18 and 8/29/18: hole in foot of positive pressure suit*

8) ***Select Agent Issues***
   a) *None*

9) ***Other Issues –***
   a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 10/18/2018
Meeting Time: 1:08 PM **Adjourned:** 1:50 PM
Building A Library, (b)(6)

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Karin Peterson	☐	☒
Bob Heinzen, Vice Chair	☐	☒	Frank DeLeo (EO)	☐	☒	Greg Saturday	☒	☐
Becky Anderson (EO)	☐	☒	Heinz Feldmann (EO)	☐	☒	Alexandra Scranton	☐	☒
Alan Applebury	☐	☒	Nancy Hoe	☒	☐	Brian Vickrey	☐	☒
Chris Bosio	☒	☐	Chris Hoffman	☐	☒			
Marshall Bloom (EO)	☐	☒	Clay Jarrett	☒	☐			
Megan Brose	☐	☒	Josh Kellar (EO)	☐	☒			
Larry Brouwer	☐	☒	Scott Kobayashi	☐	☒			
Carol Calderwood	☒	☐	Jamie Lovaglio	☒	☐			
Marcie Caldwell (EO)	☐	☒	Andrea Marzi	☐	☒			
Paul Carlson	☒	☐	Alida Merritt	☐	☒			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 9/20/18 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 9/20/18** ▪ Under Item 1, specify that Alkhurma virus is a select agent. ▪ Fix minor typos. Action: Meeting minutes for 9/20/18 were unanimously approved with the changes listed above.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment) ▪ Haigh (LPVD)

	▪ **PRD#17-198 Amend: Investigation of prion disease using animal prion infections (Transmissible spongiform encephalopathies)** ▪ Nancy Hoe presented the risk assessment. The amendment is to add work with mice. The lab will be infecting WT and transgenic mice with prions. ▪ Primary hazards are rodent bites or scratches, and accidental sharps injuries. ▪ All work with mice will be performed in an ABSL-2 facility (b)(6). All manipulations will be performed according to the SOP: Rodent Experiments using BSL2 TSE Agents. ▪ PPE will consist of scrubs or lab coat over street clothes, shoe covers, gloves and mask. ▪ The biosafety level for work with mice and prions is ABSL-2. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#17-198 Amend** as written.
Item 2:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New) ▪ Feldmann (LV) ▪ **PRD#18-207: SEB stimulation of cells (Staphylococcal enterotoxin B)** ▪ Nancy Hoe presented the risk assessment. The new PRD is for exempt quantities (<100 mg) of Staphylococcal enterotoxin B. The investigator will use SEB as a positive control for in vitro stimulation experiments, specifically to activate dendritic cells for cytokine secretion analysis. ▪ SEB is a toxin produced by the *Staphylococcus aureus* bacterium. SEB is most commonly associated with food poisoning presenting with symptoms including a sudden onset of fever, chills, headache, myalgia, and a non-productive cough. Some patients can develop a shortness of breath and chest pain. The fever can last 2-5 days, and a cough may continue for up to a month. Patients may also present with nausea, vomiting, and diarrhea when the toxin is swallowed. High levels of aerosol exposure can lead to septic shock and death. Because SEB can easily be aerosolized it is therefore considered a potential biological warfare agent and regulated by the CDC Division of Select Agents and Toxins. ▪ The natural route of transmission is through consumption of contaminated food. It is not contagious and cannot be transmitted from person to person. The primary lab hazards include: accidental sharps injuries, ingestion, or generation of aerosols. ▪ The biosafety level for work with Staphylococcal enterotoxin B is BSL-2. PPE consists of lab coat, gloves and eye protection. Preparative work with the toxin

	should be done in a Class II B2 BSC or chemical fume hood with proper PPE being worn. Users should reference Appendix I of the BMBL for work with this toxin. ▪ SEB can be possessed and used without registering with the CDC Division of Select Agents and Toxins if amounts stored and used remain under Select Agent exempt quantities, which is less than 100 mg. A logbook must be kept documenting all purchases and acquisitions, including all usage and disposal of the registered toxin as they occur in mg quantities. This inventory will be inspected by the RML SAP on a regular basis. The SEB should be secured in a locked freezer or locked box within a freezer. ▪ Attached to this registration will be Toxin Exclusion Certification from the PI and all personnel on the PRD documenting that they will not possess more than 100 mg at any time. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **PRD#18-207**
Item 3:	**Working Group Summary** ▪ Sue Priola presented the Working Group summary and associated SOP (see Item 4 below). Karin Peterson, Chris Bosio, and Clay Jarrett were the working group members that reviewed the inactivation methods from Bob Heinzen's lab. ▪ The purpose of the validation was to be able to remove paraformaldehyde-fixed *Coxiella burnetii* samples from BSL-3 containment for use in vaccination experiments. As written originally, the SOP did not allow this in the absence of a validated study. ▪ See attached summary. The Heinzen lab tested the ability of 4% paraformaldehyde at 4°C to inactivate *C. burnetii* cells. They demonstrated in three different experiments that all the bacteria were inactivated. ▪ The Working Group recommended changes to SOP-BSL-3-Cb-5 that were incorporated in the draft document. ▪ Alex Scranton submitted 2 comments by email to Becky Anderson: o There was a discrepancy in the WG summary, in that the WG approved PFA inactivation of *C. burnetii* with a fixation period of 12 hrs, not 6 hrs as stated later in the document. The committee agreed that this should be changed. o It was not clear why or if the recommended change to SOP section 14.7 to match language in the rest of the SOP was done. Nancy Hoe

	explained that the change had been made to allow the inactivated samples to be removed from the BSL-3. As originally written section 14.7 specified that the samples could not be removed from the BSL-3. ▪ The committee agreed with the WG group recommendation that fixation of *C. burnetii* in 4% paraformaldehyde at 4°C for 12hrs was a validated method for inactivating *C. burnetii.* ▪ Action: The committee unanimously approved the Working Group recommendation that fixation in 4% paraformaldehyde at 4°C for 12hrs completely inactivated *C burnetii* and approved the validation studies as written.
Item 4:	**Standard Operating Procedure: SOP BSL3-Cb-5 (Update)** Sue Priola informed the committee that the inactivation procedures described in the working group summary were accurately listed in the SOP update. There were no additional comments or concerns with the SOP. Action: The committee unanimously approved SOP BSL3-Cb-5 as written.
Item 5:	**Standard Operating Procedure: SOP 4-28-6: BSL-4 Positive Pressure Protective Suit Integrity Testing** ▪ Nancy Hoe summarized the SOP. The changes in the SOP are being made due to issues with holes in the seams of the boots on the suit. One possible reason for the holes is that users are over-inflating the suits when performing suit integrity tests thus putting stress on the foot seams. ▪ Jamie Lovaglio suggested modifying the text on page 3, point #4 to read, "…gloves should be extended but not **over-**inflated,…" The committee agreed. ▪ In an email to Becky, Alex Scranton asked how the suit could stand for 5 minutes (point #5) when the instructions in point #4 specifically state that when inflated the suit should "not stand fully upright on the feet". The committee discussed this issue and Jamie Lovaglio suggested that "**In** standing the suit upright" should be changed to "**If** standing the suit upright". The committee agreed. ▪ Greg Saturday suggested that point #5 could be rephrased to state that the suit should remain inflated for 5 minutes but not to specify whether the suit is upright or on the floor. It was suggested to change the text to read, "Allow the suit to **remain inflated** for 5 minutes…". The committee agreed. ▪ Sue Priola asked why on page 1 under IRFBSM it states that suit integrity records should be kept "for the life of the suit plus one year". Paul Carlson explained that suit records are kept for the extra year just in case an individual who had worn the suit becomes sick. They can check the records to see if the illness is related to potential problems with suit integrity. Nancy Hoe added that since suits are purchased infrequently in batches, it helps to be able to look back at

	records in case there are batch issues. Action: The committee unanimously approved the SOP with the changes to the text described above.
Item 6:	**Standard Operating Procedure: SOP 4-28-12: Dunk Tank Operations** ▪ Nancy Hoe summarized the SOP and explained that it had been updated to specify that prior to removal of specimens from the BSL-4, written approval with a signature must be received from a select agent-registered PI or designee. ▪ Greg Saturday asked about the type of signature and Nancy Hoe said that it could be a digital signature via email. ▪ Sue Priola asked for further clarification of designee, i.e. did this also have to be a select agent-registered PI. Nancy said they needed to be an approved person on the PI's select agent registration ▪ Jamie Lovaglio suggested changing "designee" to "**approved** designee" and the committee agreed. Action: The committee unanimously approved the SOP with the change to the text described above.
Item 7:	**BSL-3 Operations and Safety Procedures –** (b)(6) • Sue Priola explained that the minor changes to the SOP were to add Alphaviruses. As discussed in the last IBC meeting, procedures validated to inactivate enveloped, positive sense ssRNA viruses can be applied to Alphaviruses (which are also enveloped, positive sense ssRNA viruses). • Nancy Hoe noted the exception to this in the OSP is irradiation (pg. 37) as this inactivation procedure can be dependent on virus size. Irradiated Alphaviruses cannot be removed from the BSL-3 until a validated protocol is reviewed and approved by the IBC. • In an email to Becky Anderson, Alex Scranton pointed out that the chart on pg.2 "For Revisions and Annual Review" needs to be updated to reflect the changes in this version (1.5) of the OSP. The committee agreed. Action: The committee unanimously approved the OSP with the following change a. update the Revisions section to document changes to OSP
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Reviewed the BSO report. ▪ Nancy Hoe reported that the CDC Division of Select Agents and Toxins had performed an unannounced inspection of the Effluent Decontamination System

	on October 4th. The inspection was brief and only 1 minor item was noted.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ RML participated in a medical transport exercise with Providence St. Patrick Hospital. The mock patient was supposed to have been exposed to MERS, a respiratory pathogen, so they were transported in an isopod. MESI ambulance service was used. One item noted during the exercise was difficulty in communicating with the Infectious Disease Advisor at the hospital. This will be fixed in an updated communication plan.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ Not present
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ Carol Calderwood stated that Ravalli County had not reported any cases of influenza, but Missoula County had. She reminded everyone to get their flu shot!

Other issues	▪ None

Next Meeting:

- Date: 11/15/18
- Place: Library conference room
- Time: 1:00 PM

RML Biosafety Committee Meeting
October 18, 2018
Biosafety Officer/Responsible Official Report

1) Requests approved by BSO since last meeting:

a) None

2) ***New requests approved by committee via electronic review:***

a) *None*

3) ***New requests***

a) *Pathogen Registration Documents*

i) ***Amend***

(a) *Haigh (LPVD)*

(a) ***PRD-17-198**: Investigation of prion disease using animal prion infections*

(i) add mice as an animal model

ii) ***New***

(a) *Feldmann (LV)*

(a) ***PRD-18-207**: Staphylococcal enterotoxin B (exempt quantities)*

4) ***Working Group Summary***

a) *Heinzen*

i) *inactivation of Coxiella burnetiid by fixation in 4% PFA at 4°C*

5) ***Standard Operating Procedures***

i) *Update*

(a) *BSL-3-Cb-5: Inactivation of C. burnetiid*

(a) *update section on preparation of paraformaldehyde-fixed Coxiella to reflect validated details and remove language indicating samples cannot be removed from the BSL-3*

(b) *SOP#4-28-6: BSL-4 Positive Pressure Protective Suit Integrity Testing*

(a) *update procedure for suit integrity test to eliminate requirement of standing suit up*

(c) *SOP#4-28-12: Dunk Tank Operations*

(a) *update procedures to indicate PI approval prior to removal of inactivated samples from containment*

(b) *BSL-3 Operations and Safety Procedures* (b) (6)

(i) add references to Alphaviruses throughout document

RML Biosafety Committee Meeting
October 18, 2018
Biosafety Officer/Responsible Official Report

6) ***Animal Study Protocols Review***

Title	*Associated PRD*	*Associated RD*	*Reviewer*
Understanding the relative role of RLR- and TLR-dependent innate signaling pathways in TBEV infection in the brain using the mouse model	*18-135 (Tick Borne Encephalitis Virus)*	*N/A*	*R. Anderson*
Determining the treatment window for GS-5734 (remdesivir) in the African green monkey model of Nipah virus infection	*18-91 (Nipah virus)*	*N/A*	*M. Brose*
Pathogenesis of a glycoprotein mutant chikungunya virus in rhesus macaques	*18-206 (Chikungunya virus)*	*N/A*	*M. Brose*
Analyzing the role of MAVS dependent signaling on organization and activation of immune cells in the lymph node following EBOV infection	*18-90 (Ebola virus)*	*N/A*	*N. Hoe*
Protective efficacy of a dual VSV-based vaccine against Lassa and Ebola virus infection in Guinea pigs	*18-90 (Ebola virus) 18-94 (Lassa fever virus)*	*15-404*	*R. Anderson*
Role of FAM134B in limiting Ebola virus (EBOV) replication in a mouse model (strain C57B6/N)	*18-90 (Ebola virus)*	*N/A*	*N. Hoe*

7) ***Biosafety Training Performed – Rebecca Anderson, Megan Brose***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
Select Agent Initial	*1*	*2*
BSL-4 Refresher	*2*	*6*
BSL-3 Laboratory Biosafety	*1*	*1*
BSL-4 Laboratory Biosafety	*NA*	*NA*
Biosafety for Support Personnel	*1*	*1*
Visitor (BSL-3, BSL-4)	*4*	*4*
Biosafety Briefs	*1*	*WIP*

8) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
a) *Biological Incident Report:*
   i) *None*

9) ***Select Agent Issues***
a) *CDC unannounced inspection of the Effluent Decontamination System (EDS), October 3, 2018*

10) ***Other Issues –***
a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 11/15/2018
Meeting Time: 1:01 PM **Adjourned:** 1:37 PM
Building A Library, (b)(6)

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☐	☒	Bruce Chesebro (EO)	☐	☒	Karin Peterson	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Greg Saturday	☒	☐
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Alexandra Scranton	☐	☒
Alan Applebury	☐	☒	Nancy Hoe	☒	☐	Brian Vickrey	☐	☒
Chris Bosio	☒	☐	Chris Hoffman	☐	☒			
Marshall Bloom (EO)	☐	☒	Clay Jarrett	☒	☐			
Megan Brose	☒	☐	Josh Kellar (EO)	☐	☒			
Larry Brouwer	☐	☒	Scott Kobayashi	☒	☐			
Carol Calderwood	☐	☒	Jamie Lovaglio	☒	☐			
Marcie Caldwell (EO)	☐	☒	Andrea Marzi	☒	☐			
Paul Carlson	☐	☒	Alida Merritt	☐	☒			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 10/18/18 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 10/18/18** Action: Meeting minutes for 10/18/18 were unanimously approved as written.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment) ▪ Haigh (LPVD) ▪ **PRD#17-197 Amend: Investigation of human prion infection in induced pluripotent stem cells derived cells and tissues** ▪ Becky Anderson presented the risk assessment. The amendment is to add work

	with mice. The lab will be infecting WT and transgenic mice with prion infected human organoid homogenates. ▪ Primary hazards are rodent bites or scratches, and accidental sharps injuries. ▪ All work with mice will be performed in an ABSL-2 facility (b)(6) All manipulations will be performed according to the SOP: Rodent Experiments using BSL2 TSE Agents. ▪ PPE consists of scrubs or lab coat over street clothes, shoe covers, gloves and mask. ▪ The biosafety level for work with mice and prions is ABSL-2. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#17-197 Amend** as written.
Item 2:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment) ▪ Haigh (LPVD) ▪ **PRD#17-199 Amend: Human blood and body fluids** ▪ Becky Anderson presented the risk assessment. The amendment is to add work with mice. The lab will be infecting WT and transgenic mice with prion infected human organoid homogenates. ▪ Primary hazards are rodent bites or scratches, and accidental sharps injuries. ▪ All work with mice will be performed in an ABSL-2 facility (b)(6). All manipulations will be performed according to the SOP: Rodent Experiments using BSL2 TSE Agents. ▪ PPE consists of scrubs or lab coat over street clothes, shoe covers, gloves and mask. ▪ The biosafety level for work with mice and human blood and body fluids is ABSL-2. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#17-199 Amend** as written.
Item 3:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment) ▪ Feldmann (LV) ▪ **PRD#18-90 Amend: Filoviruses** ▪ Becky Anderson presented the risk assessment. The amendment is to add a

	new strain of Ebolavirus, Bombali virus. Bombali virus (BOMV) is a new ebolavirus identified by a PCR-screen in free-tailed bats (*Chaerephon pumilus*) and Angolan free-tailed bats (*Mops condylurus*) in Sierra Leone. The sequence showed high identity to other Ebolaviruses, and phylogenetic analysis indicated a distinct species within the Ebolavirus genus. No virus has been isolated, so any sequences will be commercially synthesized, and virus will be generated by reverse genetics, similar to what the Feldmann lab did for Lloviu virus. Glycoproteins from from Bombali virus mediated entry into human osteosarcoma cells suggesting there may be potential for Bombali virus to infect humans. ▪ Primary hazards are accidental sharps injuries, parenteral inoculation, production of aerosols, and accidental sharps injuries. ▪ No new animal studies were submitted, reviewed, or approved. ▪ The biosafety level for work with Bombali virus is BSL-4/ABSL-4. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **PRD#18-90 Amend** as written.
Item 4:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New)</u> ▪ Feldmann (LV) ▪ **PRD#18-208: Bornaviruses** ▪ Becky Anderson presented the risk assessment. The purpose of these studies is to understand the reservoirs, epidemiology and (molecular) biology of Bornaviruses to provide a model for novel zoonotic infections, and to evaluate medical countermeasures. ○ Borna disease virus (BoDV) normally infects horses and sheep as well as a variety of other animal species. In those animals it causes a chronic, progressive meningoencephalomyelitis causing both neurological and behavioral signs in animals. Although mammalian BoDV infects numerous animal species, it is not very infectious within species, and BoDV cases in sheep and horses are mainly sporadic. There is much controversy about transmission from domestic animals to humans in the literature. However, there are countless studies that link BoDV with human behavioral disorders. ○ Variegated squirrel bornavirus: in 2011, three men in succession (63, 62, and 72 years of age) from the Germany, developed a progressive encephalitis or meningoencephalitis that led to death within 2 to 4 months after the onset of clinical symptoms. The clinical course was characterized by fever, shivers, or both; progressive psychomotor slowing; confusion; unsteady gait; myoclonus, ocular paresis, or both;

	and finally, coma. All three patients had preexisting medical conditions (hypertension, diabetes, or obesity). All three patients were treated in intensive care units, had to undergo mechanical ventilation, and died despite receiving treatment with broad anti-infective chemotherapy (anti-bac, anti-fungal, antihelminthic, antiprotozoal, antiviral). All three patients were breeders of variegated squirrels. They were friends and had exchanged their squirrel breeding pairs on multiple occasions. At least two of the patients had been scratched by their squirrels in the past, and one had been bitten. There are no vaccines or specific treatments, just treatment for the symptoms. Variegated squirrel bornavirus has a known transmission from bites/scratches of infected animals. Not known to be transmitted from human to human. ▪ Becky Anderson stated that the precautions for working with human blood and body fluid should be added to the recommendations section. ▪ Primary hazards are accidental sharps injuries, parenteral inoculation, production of aerosols, and accidental sharps injuries. ▪ Animal studies with non-human primates were proposed. ▪ The biosafety level for work with Borna disease virus is BSL-2/ABSL-2. The biosafety level for Variegated squirrel bornavirus is BSL-3/ABSL-3. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **PRD#18-208** with the following modifications: 1. Add to the recommendations section precautions for working with human blood and body fluids.
Item 5:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renew)</u> ▪ Bloom (LV) ▪ **PRD#18-95: Tick-borne encephalitis viruses (TBEV), Far Eastern subtype, Omsk hemorrhagic fever virus, Kyasanur Forest disease virus** ▪ Becky Anderson presented the risk assessment. This registration is a renewal for continued storage of the listed TBEV viruses. These viruses will continue to be stored in the BSL-4 with the Feldmann & Best inventory. ▪ No animal studies were submitted, reviewed, or approved. ▪ The biosafety level for storage of TBEV is BSL-4. ▪ The committee discussed the dual-use potential of these experiments. The

	committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#18-95** as written.
Item 6:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renew) ▪ Bosio (LB) ▪ **PRD#18-71: *Francisella tularensis* subsp. *tularensis* & subsp. *holartica*** ▪ The committee agreed that Becky Anderson did not need to present a risk assessment for the renewal as they as familiar with the information. Becky Anderson informed the committee that there was a minor update to the PRD. The Bosio lab would like to include 3 new routes of inoculation, IM, IP, and IV. These new routes of inoculation require CDC DSAT approval. The IBC can approve the renewal of this registration; however, the new routes of inoculation will be pending DSAT approval. ▪ Animal studies with mice were proposed. ▪ The biosafety level for work with *F. tularensis* subsp. *tularensis* & *holartica* is BSL-3/ABSL-3. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Chris Bosio abstained) the renewal of **PRD#18-71** as written, the new routes of inoculation are PENDING DSAT approval.
Item 7:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renew) ▪ Hinnebusch (LB) ▪ **PRD#18-04: *Yersinia pestis*** ▪ The committee agreed that Becky Anderson did not need to present a risk assessment for the renewal as they as familiar with the information. Becky Anderson informed the committee that there was a minor update to the PRD. The Hinnebusch lab would like to include 2 new routes of inoculation, IP and IV. These new routes of inoculation require CDC DSAT approval. The IBC can approve the renewal of this registration; however, the new routes of inoculation will be pending DSAT approval. ▪ Animal studies with mice and rats were proposed. ▪ The biosafety level for work with *Yersinia pestis* is BSL-3/ABSL-3. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Chris Bosio and Clay Jarrett abstained) the

	renewal of **PRD#18-04** as written, the new routes of inoculation are PENDING DSAT approval.
Item 8:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renew) ▪ Heinzen (LB) ▪ **PRD#18-43: *Coxiella burnetii*** ▪ The committee agreed that Becky Anderson did not need to present a risk assessment for the renewal as they as familiar with the information. Becky Anderson informed the committee that there were no updates to the PRD. ▪ Animal studies with guinea pigs were proposed. ▪ The biosafety level for work with *Coxiella burnetii* is BSL-3/ABSL-3. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Bob Heinzen abstained) the renewal of **PRD#18-43** as written.
Item 9:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Feldmann (LV) ▪ **RD#17-431 Amend**: Molecular characterization of viral proteins of pathogenic RNA viruses ▪ Reviewers: Sue Priola, Bob Heinzen ▪ **Summary:** The amendment describes the addition of a new virus and vector map. ▪ Sue Priola was not present for the meeting but submitted by email to Bob Heinzen that she had no concerns with the amendment. Bob Heinzen summarized the RD amendment and stated that the Feldmann lab is adding Bombali virus to the RD, a new plasmid map, and is updating the language in the attached file. The new language describes procedures for generating transcripts as part of a detection assay for use in the field to detect viruses including Bombali virus. This is a straightforward amendment with no DURC concerns. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Andrea Marzi abstained) **RD#17-431 Amend** as

	written. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-2-a and III-E-1 of the NIH Guidelines.
Item 10:	<u>Registration Documents for Recombinant DNA Experiments (Amendment)</u> ▪ Feldmann (LV) ▪ **RD#14-407 Amend**: Ebola virus ▪ Reviewers: Bob Heinzen, Scott Kobayashi ▪ **Summary:** The amendment describes the addition of a new virus and vector map. ▪ Bob Heinzen summarized the RD amendment and stated that the Feldmann lab is adding Bombali virus to the RD, a new plasmid map, and is updating the language in Section B. The Feldmann lab will use the new vector map to encode all the open reading frames, synthesize the sequences, then try to make virus in the BSL-4. The new language changes from a list of Ebola viruses to a reference to the Feldmann PRD 18-90 for Filoviruses so all the viruses do not need to be listed anymore. Bob Heinzen pointed out that III-E-1 should be removed from the RD because it does not relate to this amendment. ▪ Scott Kobayashi had no additional comments or concerns. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved (Andrea Marzi abstained) **RD#14-407 Amend** with the following minor modifications: 1. Remove III-E-1 from the NIH Guidelines section. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-4 under III-D-3-a, III-D-1-a, and III-D-1-c of the NIH Guidelines.
Item 11:	<u>Registration Documents for Recombinant DNA Experiments (Amendment)</u> ▪ Feldmann (LV) ▪ **RD#14-427 Amend**: Ebola virus ▪ Reviewers: Chris Bosio, Clay Jarrett ▪ **Summary:** The amendment describes the addition of a new virus. ▪ Chris Bosio summarized the RD amendment and stated that they are adding

	Bombali virus to the RD. No other changes are proposed in the amendment. ▪ Clay Jarrett had no additional comments or concerns. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Andrea Marzi abstained) **RD#14-427 Amend** as written. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 or BSL-4 under III-D-3-c, III-D-1-a, and III-E-1 of the NIH Guidelines.
Item 12:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Heinzen (LB) ▪ **RD#14-106 Amend**: Genetic transformation of *Coxiella burnetii* ▪ Reviewers: Scott Kobayashi, Chris Bosio ▪ **Summary:** The amendment describes gene replacement and complementation. ▪ Scott Kobayashi summarized the RD amendment. The amendment is to add a strain for gene deletion and complementation in the avirulent Dugway strain. There are no other changes to the protocol. They want to do this method in the avirulent strain but will be conducting the experiments at BSL-3. They do not expect anything to be more virulent than the 9-mile strain. The NIH Guidelines are the same as the original RD. ▪ Chris Bosio noted that "frameshifted" is spelled wrong. ▪ Bob Heinzen pointed out that there are a few employee initials that still need to be obtained. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Bob Heinzen abstained) **RD#14-106 Amend** with minor modifications: 1. Correct spelling for "frameshifted". 2. Obtain the additional initials from employees listed on the RD. Research using prokaryotic hosts is approved at BSL-2 or BSL-3 under section III-D-1-

	a, III-D-1-b, and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 or BSL-3 III-D-1-a and Appendix G-II-C of the NIH Guidelines.
Item 13:	**Standard Operating Procedure: SOP#4-28-59: Use of BD BACTEC FX40 Blood Culturing System** ▪ Bob Heinzen summarized the changes to the committee. He informed the committee that the changes to procedures are to reduce the use of sharps in the BSL-4. ▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved the SOP with the change to the text described above.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Reviewed the BSO report. ▪ Nancy Hoe informed the IBC that on October 23, 2018 the CDC inspection for 2018 was closed out. ▪ Nancy Hoe also informed the committee that PI Dashboard has been upgraded.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson** ▪ Not present
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ Construction on (b)(6) is almost complete. ▪ SEA will be at RML on December 3rd to test (b)(6). Users will be notified of this scheduled work. ▪ (b)(6) flooring replacement is complete. ▪ The BSL-4 (b)(6) annual shutdown is complete.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ None

Other issues	▪ None

Next Meeting:

- Date: 12/20/18

- Place: Library conference room
- Time: 1:00 PM

RML Biosafety Committee Meeting
November 15, 2018
Biosafety Officer/Responsible Official Report

1) Requests approved by BSO since last meeting:

a) Bosio (LB)

i) ***PRD-17-73****: Francisella tularensis (exempt)*

(1) add IV route of inoculation – approved 11/5/18

2) ***New requests approved by committee via electronic review:***

a) *None*

3) ***New requests***

a) *Pathogen Registration Documents*

i) ***Amend***

(a) *Haigh (LPVD)*

(a) ***PRD-17-197****: Investigation of human prion infection in induced pluripotent stem cell derived cells and tissues.*

(i) add mice as an animal model

(b) *Haigh (LPVD)*

(a) ***PRD-17-199****: Human blood and body fluids*

(i) add mice as an animal model

(c) *Feldmann (LV)*

(a) ***PRD-18-90****: Filoviridae*

(i) add Bombali virus

ii) ***New***

(a) *Feldmann (LV)*

(a) ***PRD-18-208****: Bornavirus*

iii) ***Renewal***

(a) *Bloom (LV)*

(a) ***PRD-18-95****: Flaviviruses (storage only)*

(b) *Bosio (LB)*

(a) ***PRD-18-71****: Francisella tularensis*

(i) add routes of inoculation

(c) *Heinzen (LB)*

(a) ***PRD-18-43****: Coxiella burnetii*

(d) *Hinnebusch (LB)*

(a) ***PRD-18-04****: Yersinia pestis*

b) *Registration Documents for Recombinant Nucleic Acid Experiments*

i) ***Amend***

(a) *Feldmann (LV)*

(a) ***RD-17-431****: Molecular characterization of viral proteins of pathogenic RNA viruses*

(i) add Bombali virus, subcloning plasmid pUC57

(b) ***RD-14-407****: Full-length clones of Ebola virus*

(i) add Bombali virus, subcloning plasmid pTM T7-Bombali-Ribo

(c) ***RD-14-427****: Ebola and Marburg virus minigenome and transcription/replication competent virus-like particle systems*

(i) add Bombali virus

4) ***Standard Operating Procedures***

i) *Update*

(a) *SOP#4-28-59: Use of BD BACTEC FX40 Blood Culturing System*

(a) *update procedure for disposal of Peds Plus bottles*

5) ***Animal Study Protocols Review***

Title	***Associated PRD***	***Associated RD***	***Reviewer***
Influence of SOD2 expression on prion disease pathogenesis	*17-198 (Prions)*	*N/A*	*N. Hoe*
Understanding the relative role of RLR- and TLR-dependent innate signaling pathways in TBEV infection in the brain using the mouse model	*18-135 (Tickborne encephalitis virus)*	*N/A*	*R. Anderson*
The effect of depletion of CD4 T cells on latent reservoir of HIV-1 in TKO-BLT mice	*12-55 (HIV) 18-104 (HBBF)*	*15-404*	*M. Brose*
Bioassay of cerebral organoids for confirmation of prion infection	*17-197, 198, 199 (Prions)*	*N/A*	*R. Anderson*
Protective efficacy of truncated VSV-EBOV vaccines against Ebola virus infection in mice	*18-90 (Ebola virus) 18-82 (VSV)*	*15-404*	*N. Hoe*

6) ***Biosafety Training Performed – Rebecca Anderson, Megan Brose, Nancy Hoe***

RML Biosafety Committee Meeting
November 15, 2018
Biosafety Officer/Responsible Official Report

Type of Training	*Number of Sessions*	*Number of Employees Trained*
Select Agent Initial	*1*	*1*
BSL-4 Laboratory Biosafety	*8*	*1*
Biosafety for Support Personnel	*1*	*1*

7) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
   a) *Biological Incident Report:*
      i) *None*

8) ***Select Agent Issues***
   a) *Closeout of CDC DSAT Inspection of February/March 2018*

9) ***Other Issues –***
   a) *PI-Dashboard upgrade*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 12/18/2018
Meeting Time: 1:00 PM **Adjourned:** 1:47 PM
Building A Library, (b)(6)

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☐	☒	Bruce Chesebro (EO)	☐	☒	Karin Peterson	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Greg Saturday	☒	☐
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Alexandra Scranton	☐	☒
Alan Applebury	☐	☒	Nancy Hoe	☒	☐	Brian Vickrey	☐	☒
Chris Bosio	☒	☐	Chris Hoffman	☐	☒			
Marshall Bloom (EO)	☒	☐	Clay Jarrett	☒	☐			
Megan Brose	☐	☒	Josh Kellar (EO)	☐	☒			
Larry Brouwer	☐	☒	Scott Kobayashi	☒	☐			
Carol Calderwood	☐	☒	Jamie Lovaglio	☒	☐			
Marcie Caldwell (EO)	☐	☒	Andrea Marzi	☒	☐			
Paul Carlson	☐	☒	Alida Merritt	☒	☐			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 11/15/18 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 11/15/18** Action: Meeting minutes for 11/15/18 were unanimously approved as written.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New) ▪ Haigh (LPVD) ▪ **PRD#18-209: Tetrodotoxin** ▪ Becky Anderson presented the risk assessment. The Haigh lab proposes to use tetrodotoxin to block synaptic activity in brain slices and in human

	cell culture derived from induced pluripotent stem cells. Tetrodotoxin is an extremely potent toxin found mainly in the liver and gonads of some fish, such as puffer fish, globefish, and toadfish and in some amphibian, octopus, and shellfish species. Human poisonings typically occur when the flesh and/or organs of the fish are improperly prepared and eaten. Tetrodotoxin interferes with the transmission of signals from nerves to muscles and causes an increasing paralysis of the muscles of the body including the respiratory tract which can lead to respiratory arrest and death. The toxin is produced by *Vibrio* and *Pseudomonas* bacterial species (such as *Vibrio alginolyticus*, *Pseudoalteromonas tetraodonis*). Tetrodotoxin poisoning may either have a rapid onset (10 to 45 minutes) or delayed onset (generally within 3 to 6 hours but rarely longer). Death may occur as early as 20 minutes, or as late as 24 hours, after exposure; however, death usually occurs within the first 4 to 8 hours. Patients who live through the acute intoxication in the first 24 hours usually recover without residual deficits. There is no known antidote, the main treatment is respiratory support and supportive care until the tetrodotoxin is excreted in the urine. The natural route of transmission is typically from eating improperly prepared or contaminated food. The primary lab hazards include inhalation from aerosols, accidental ingestion, or mucous membrane contact. ▪ The biosafety level for work with tetrodotoxin is BSL-2. Additional precautions and procedures include: Work with concentrated or solid lyophilized toxin must be performed in a CFH or BSC wearing appropriate PPE (gloves, lab coat, eye protection) and all toxin containing waste should be inactivated and sent to the MPW stream. Avoid contact with skin or eyes and avoid aerosolization of this agent. Fresh 0.5% NaOCl treatment for 30 minutes is effective and preferred for inactivation of TTX containing solutions as autoclaving is ineffective, please See BMBL 5th edition, Appendix I regarding work with biological toxins. Work with this agent is exempt from Select Agent registrations provided aggregate amounts in the laboratory do NOT exceed 500mg at any one time. Therefore, a toxin usage logbook must be kept accurate at all times and the toxin stored in a secure, locked location accessible only to registered users. The completed Toxin Exclusion Form (TEF, uploaded in this document) must be kept within the toxin usage logbook in a secure location. This TEF indicates the amount of material the laboratory will keep on hand once the agent is acquired. Over time, new personnel should sign the original document and be added to this registration in the linked records/personnel section, and the registration amended electronically to request to update it with the updated and signed toxin exclusion form and new work description if necessary. ▪ Nancy Hoe stated that the precautions listed in the recommendations

	section should state the BSC must be ducted. Also, if working with larger quantities, the chemical fume hood must have a HEPA and charcoal filter. Nancy Hoe added that the recommendations section should include a description that the use of liners on work surfaces is required. ▪ Nancy Hoe also pointed out that the training for animal handling and animal care and use should be deleted since there is no animal work associated with this registration. ▪ Bob Heinzen stated that the abbreviations in the recommendations section should be spelled out. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **PRD#18-209** with minor modifications: 1. Add to the recommendations section: a. BSC must be ducted. b. If working with larger quantities, the chemical fume hood must have a HEPA and charcoal filter. c. Use of liners on work surfaces is required. 2. Delete training for animal handling and animal care. 3. Spell out abbreviations in the recommendations section.
Item 2:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New)</u> ▪ Hinnebusch (LB) ▪ **PRD#18-210: Various bacteria (*Salmonella enteritidis, Staphylococcus epidermidis, Streptococcus mutans, Pseudomonas fluorescens, Enterococcus faecalis, Enterobacter cloaca, Bacillus cereus*)** ▪ Becky Anderson presented the risk assessment. The goal of the proposed work is to approximate the limits of the diversity of bacteria that can infect the flea and colonize the proventriculus, a valve between the esophagus and the midgut of the flea. The listed bacteria range from non-pathogenic species to pathogenic species causing fever, vomiting, diarrhea, headache, and/or lower respiratory tract infection. Most of these infections resolve on their own and do not require treatment. However, in severe cases, or those in immunocompromised persons, antibiotic treatment may be required. The natural route of transmission for these bacteria range from consumption of

	contaminated foods to opportunistic infections in immunocompromised persons. The primary lab hazards include ingestion, generation of aerosols, and sharps injuries. ▪ Nancy Hoe questioned if trying to transmit these bacteria by a flea bite should be considered dual use. She stated that this should be addressed in the DURC questionnaire. She said that there are mitigation procedures in place that reduce the risk of exposure. She also stated that there are likely other factors that *Y. pestis* has that allows it to be transmitted by the flea that other bacteria may not have. The registration states that *Ymt* is critical for flea transmission and is critical for *Y. pestis* to transmit from a flea. Bob Heinzen questioned the justification for these experiments. Clay Jarrett stated that *Ymt* is critical in the flea but does not have anything to do with mammalian infection. He informed the committee that adding *Ymt* to any of the bacteria should not affect the virulence or course of infection of those bacteria. Long term studies of the Hinnebusch lab do not include any work attempting to transmit to mice. When they test transmission, they will only do it on a glass feeder into sterile blood. Clay Jarrett stated that the Hinnebusch lab tried to pick bacteria that had little to no pathogenicity for these studies. In addition, fleas are likely already naturally exposed to the bacteria proposed in this registration. Clay Jarrett described historical studies that tested the ability of some bacteria to survive in the flea. With the proposed work Joe Hinnebusch wants to confirm what is published in the literature. Scott Kobayashi stated that if *Ymt* is the key in the flea, what do you gain by adding *Ymt* to other bacteria that survive in the flea. Clay Jarrett stated that their focus is on trying to determine what bacteria need to survive in the flea. He stated the Joe Hinnebusch previously did this work in *E. coli* and *Y. pseudotuberculosis*. They want to go back and replicate those early experiments and ask whether all of these bacteria can survive in the flea. Both *Enterobacter* and *Enterococcus* have been isolated from insects, Salmonella has been found in a flea previously and fleas probably naturally get exposed to these bacteria. Bob Heinzen stated that this is likely a dead-end cycle in nature with most of the bacteria, unlike what happens with plague. Bob Heinzen stated that he does not see any DURC. Scott Kobayashi and the IBC agreed that there were no dual use concerns. ▪ The biosafety level for work with the listed bacteria strains is BSL-1 and BSL-2. The lab is registered at BSL-2 so all work will be performed at that level. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved (Chris Bosio and Clay Jarrett abstained) **PRD#18-**

	210 as written.
Item 3:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment) ▪ Hinnebusch (LB) ▪ **PRD#14-66 Amend: *Yersinia pestis* (exempt)** ▪ Becky Anderson presented the risk assessment. The amendment is to add work with lice. The lice will be worked with in the same room as the fleas, but the lice will be stored in a different incubator. Most handling precautions will be the same as that used for fleas. These procedures include: 1) lice will be worked with in a smooth sided, high walled container. 2) they will live on strips of cloth (like corduroy). 3) strips of cloth containing lice will be stored in a petri dish in secondary containers in an incubator. The lice are different from fleas in that they do not jump so they are easier to work with than fleas. ▪ The biosafety level for work with *Y. pestis* exempt strain and lice is BSL-2. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Chris Bosio and Clay Jarrett abstained) **PRD#14-66 Amend** as written.
Item 4:	Registration Documents for Recombinant DNA Experiments (NEW) ▪ Hinnebusch (LB) ▪ **RD#18-323**: Diversity of flea pathogens ▪ Reviewers: Bob Heinzen, Scott Kobayashi ▪ **Summary:** The RD describes testing the ability of bacteria to survive in fleas. ▪ Bob Heinzen summarized the RD. The registration describes genetically modifying various bacteria for flea infection as was discussed extensively in the PRD#18-210 review earlier in the meeting. These studies will use both gram positive and gram negative bacteria. The gram negative strains will be modified to express GFP and the *Ymt* gene. They will use antibiotics that are approved for *Y. pestis*. They will also test the strains to see what they are sensitive to and will make sure they are sensitive to at least two antibiotics on the list. There is a statement that ampicillin and kanamycin are only approved for *Y. pestis*, this refers to the Select Agent strain only, not the exempt strain. Scott Kobayashi asked about the use of gentamycin because it can be used to treat infections in people. Bob Heinzen added that a kanamycin cassette can also confer resistance to gentamycin, you must make sure you use the gene that does not give cross resistance. Clay Jarrett stated that the Hinnebusch lab already uses

	the gene that is specific for kanamycin. ▪ The group discussed that the following should be added to the RD to make sure antibiotic usage is clear: 1) Make sure the discussion on antibiotics states that the kanamycin cassette does not confer cross resistance to gentamycin, 2) Testing will only be done for those antibiotics that will be used as selectable markers. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Chris Bosio and Clay Jarrett abstained) **RD#18-323** with the following minor modifications: 1. Make sure the discussion on antibiotics states that the kanamycin cassette does not confer cross resistance to gentamycin 2. Testing will only be done for those antibiotics that will be used as selectable markers Research using prokaryotic hosts is approved at BSL-2 under section III-D-1-a and III-D-2-a of the NIH Guidelines.
Item 5:	**Standard Operating Procedure: Maximum Containment Lab Operations and Safety Procedures (MCL OSP)** ▪ Bob Heinzen summarized the changes to the committee. Becky Anderson pointed out that the only changes are to the sample removal procedures and these changes outline what is currently done. ▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved the **MCL OSP** as written.
Item 6:	**Standard Operating Procedure: BSL-3 (b)(6) Powassan Virus** ▪ Bob Heinzen summarized the changes to the committee. He informed the committee that the changes are the result of a new pass-through autoclave in the lab. ▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved the **BSL-3 (b)(6) Powassan Virus SOP** as written.
Report:	**BSO/Responsible Official Report/Nancy Hoe**

	▪ Reviewed the BSO report. ▪ Nancy Hoe informed the committee that the proposed dates for the 2019 BSL-4 DSAT inspection will be the first week of April
Report:	**Occupational Safety and Health Manager Report/Paul Carlson/Shanda Sarchette** ▪ Nothing to report.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ Not present.
Report	**Associate Director Report/Marshall Bloom** ▪ Marshall Bloom announced that one of the IBC committee members is a pending principal investigator. Andrea Marzi will be a new tenure track investigator for LV. ▪ Nancy Hoe is the new contract representative for the Regional Referral Hospital contract.
Around the room	▪ None

Other issues	▪ None

Next Meeting:

- Date: 1/17/19
- Place: Library conference room
- Time: 1:00 PM

RML Biosafety Committee Meeting
December 20, 2018
Biosafety Officer/Responsible Official Report

1) Requests approved by BSO since last meeting:

a) None

2) ***New requests approved by committee via electronic review:***

a) *None*

3) ***New requests***

a) *Pathogen Registration Documents*

i) ***New***

(a) *Haigh (LPVD)*

(a) ***PRD-18-209****: Tetrodotoxin (exempt)*

(b) *Hinnebusch (LB)*

(a) ***PRD-18-210****: various bacteria (E. coli, Enterobacter cloacae, Pseudomonas fluorescens, Salmonella enteritidis)*

ii) ***Amend***

(a) *Hinnebusch (LB)*

(a) ***PRD-14-66****: Yersinia pestis (exempt)*

(i) add lice as an arthropod model

b) *Registration Documents for Recombinant Nucleic Acid Experiments*

i) ***New***

(a) *Hinnebusch (LB)*

(a) ***RD-18-323****: Diversity of Flea Pathogens*

4) ***Standard Operating Procedures***

i) *Annual Review*

(a) *Maximum Containment Laboratory Operations and Safety Procedures (MCL OSP)*

ii) *Update*

(a) (b)(6) *BSL-3 SOP*

(i) update procedures for new autoclave

RML Biosafety Committee Meeting
December 20, 2018
Biosafety Officer/Responsible Official Report

5) ***Animal Study Protocols Review***

Title	*Associated PRD*	*Associated RD*	*Reviewer*
Protective Efficacy of a VSV-Based Vaccine Against Reston Ebolavirus Infection in Young Pigs	*18-90 (Ebola virus) 18-82 (VSV)*	*15-404*	*R. Anderson*
Efficacy of DNA-Based Vaccines in Nonhuman Primates Against Infection with Crimean-Congo Hemorrhagic Fever Virus	*18-92 (CCHFV)*	*17-431*	*N. Hoe*
Evaluation of chimp adenovirus vaccines against Crimean-Congo hemorrhagic fever virus infection in mice	*18-92 (CCHFV)*	*17-410*	*M. Brose*
Protective efficacy of a novel subunit vaccine against lethal EBOV challenge in mice.	*18-90 (Ebola virus)*	*N/A*	*R. Anderson*
Role of Ajuba in limiting Interferon and Inflammatory signaling in a mouse model (strain C57B6/N)	*18-82 (VSV)*	*N/A*	*R. Anderson*
Control of bacterial driven inflammation with Francisella lipids and Francisella inspired liposomes	*17-195 (Bordetella pertussis) 14-157 (Listeria monocytogenes) 18-202 (Yersinia pestis (exempt))*	*N/A*	*N. Hoe*
The effect of experimental Bcl-2 antagonists Venetoclax and 25-43 on HIV load in TKO-BLT mice	*18-55 (HIV) 18-104 (HBBF)*	*N/A*	*R. Anderson*
Analysis of the protective efficacy of a VSV- based vaccine against Kyasanur forest disease virus infection in mice.	*18-135 (Kyasenur forest disease virus) 18-82 (VSV)*	*15-404*	*M. Brose*
Evaluation of a glucagon-like peptide-receptor (GLP1R) agonist, exendin-4, in protecting against West Nile virus-induced neurological disease in a mouse model.	*17-108 (West Nile Virus)*	*N/A*	*M. Brose*

6) ***Biosafety Training Performed – Rebecca Anderson, Megan Brose***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
Select Agent Initial	*1*	*1*
BSL-3 Laboratory Biosafety	*2*	*2*
BSL-4 Laboratory Biosafety	*1*	*1*
Biosafety for Support Personnel: Refresher	*3*	*35*
ABSL-3 Refresher (with RMVB)	*3*	*36*
Visitor (for BSL-3/BSL-4)	*3*	*6*

7) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
a) *Biological Incident Report:*
   i) *None*

8) ***Select Agent Issues***
a) *Proposed dates for 2019 CDC DSAT Inspection*

9) ***Other Issues –***
a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 1/17/2019
Meeting Time: 1:05 PM **Adjourned:** 1:35 PM
Building A Library, (b)(6)

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Karin Peterson	☒	☐
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Greg Saturday	☒	☐
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Alexandra Scranton	☐	☒
Alan Applebury	☐	☒	Nancy Hoe	☐	☒	Brian Vickrey	☐	☒
Chris Bosio	☒	☐	Erik Hoover	☐	☒			
Marshall Bloom (EO)	☐	☒	Clay Jarrett	☐	☒			
Megan Brose	☒	☐	Josh Kellar (EO)	☐	☒			
Larry Brouwer	☒	☐	Scott Kobayashi	☒	☐			
Carol Calderwood	☐	☒	Jamie Lovaglio	☒	☐			
Marcie Caldwell (EO)	☐	☒	Andrea Marzi	☒	☐			
Paul Carlson	☐	☒	Alida Merritt	☒	☐			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 12/20/18 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 12/20/18** Action: Meeting minutes for 12/20/18 were unanimously approved as written.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renew) ▪ Steele-Mortimer (LB) ▪ **ST-PRD#19-155: *Shigella flexneri*** ▪ Becky Anderson presented the risk assessment. There is no proposed work at this time. The renewal for this registration is storage only and

	the PI will renew the registration at the time they want to begin work with Shigella. ▪ *Shigella flexneri* will be stored in the Steele-Mortimer BSL-2 lab. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **ST-PRD#19-155** as written.
Item 2:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renew) ▪ Hackstadt (LB) ▪ **PRD#19-150: *Coxiella burnetii Phase II (exempt)*** ▪ Becky Anderson presented the risk assessment. The proposed studies are to use *C. burnetii* as a control for studies with Chlamydia. The purpose of these studies is to define the mechanisms by which Chlamydia survive within mammalian host cells. There are two phase variants of *C. burnetii*, Phase I is a highly virulent variant and phase II is an attenuated variant. Attenuation was achieved by a ~26 kb chromosomal deletion that eliminates multiple genes involved in LPS biosynthesis. The deletion results in a strain that is avirulent for immunocompetent mice and guinea pigs. Pathogenesis in humans is unknown and to date there have been no known infections of humans with avirulent *C. burnetii*. ▪ Becky Anderson stated that the precautions for work with human blood and body fluids should be added to the recommendations section. ▪ The biosafety level for work with *C. burnetii* exempt strain is BSL-2. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#19-150** with minor modifications: 1. Add precautions for human blood and body fluids to the recommendations section.
Item 3:	**Standard Operating Procedure: 2/3-28-01 Handling Field Collected Fluid Blood and Tissue Samples** ▪ Becky Anderson summarized the changes to the committee. Becky Anderson

	pointed out that the only changes are to the RLT and AVL inactivation procedures. The SOP was updated to state that samples can either be in vials OR 96 well plates for these procedures. Allowing the use of 96 well plates does not change the validated inactivation procedure, just the containers the samples are placed it. ▪ Alex Scranton submitted questions to Sue Priola by email. Megan Brose stated that Alex Scranton may not have been present orcalled in when the IBC reviewed the field sample SOP when it was initially approved. At that time, the biosafety staff conducted a risk assessment for the work with field samples and it was reviewed and approved by the IBC. It provides a lot of background for what was evaluated and why the BSL-2 lab with BSL-3 practices was deemed sufficient to mitigate the risks of working with these types of field samples. ▪ Alex Scranton stated in her email that the SOP appears to be written for the scenario in which RML would not find BSL-3 or BSL-4 agents and in that situation, she felt the SOP may be lacking details on how to handle the situation if BSL-3 or BSL-4 agents were identified. She stated that this is exactly what we would want to be best prepared for. Alex Scranton questioned why samples are not taken into the BSL-4 lab, tested, and then removed to lower containment levels. Megan Brose informed the group that we cannot take the samples into the BSL-4 lab first because if you discover there are no risk group 4 agents present, you can never remove the sample from the BSL-4 lab and take it to lower containment levels. Once you have opened the tube(s) inside the BSL-4 lab, the live sample has to stay there due to the risk of becoming contaminated with any other risk group 4 agent that may be present. So, what they do instead is split the samples in BSL-2 with 3 practices. They can either take one sample into the BSL-4 to test for live agents or, what is most commonly done, inactivate one sample to bring out to a different BSL-2 lab to run PCR testing to see what agents might be present in the sample. Then the other tubes from this sample can be taken to the appropriate biosafety level after the agent(s) is/are identified. These remaining live samples are stored in the freezer in the secure, BSL-2 with 3 practices lab in sealed vials in a locked freezer inside a secured access lab and therefore do not pose a risk. It should also be noted that identifying an agent in a sample by PCR only tells you that there is genetic material (e.g. DNA, RNA fragments) present in that sample. It does not mean there is live virus present in the sample. The researchers working in the BSL-4 noted that in their experience it can be very difficult, and sometimes impossible, to isolate and grow live virus from these PCR-positive samples. ▪ Alex Scranton also questioned that statement in Section 6.8, “field samples are not considered Select Agents unless demonstrated otherwise.” Is this a precautionary approach that RML usually takes toward biosafety only after the need for them has been demonstrated? Megan Brose responded no, this is

	referring to what are considered "select agents" from a regulatory standpoint. This is taken straight from the select agent regulations. The CDC/USDA Federal Select Agent Program does not consider a sample taken from its natural environment to be a select agent until you have identified that the select agent is present. This is how the entire research community handles this type of situation, including hospitals across the country who frequently identify risk group 3 agents. ▪ Alex Scranton stated the 6.1.C needs a lot more clarity on what happens if a BSL-4 agent is identified. She felt that the statements in 6.1.C were contradictory because initially it states that agents will be moved immediately to high containment and moving of that agent will depend on appropriate PRD for the agent. The SOP allows for a possible situation where a BSL-4 agent will be in the hands of staff that won't have donned BSL-4 PPE protections, in a room without the necessary pressure containment, etc. Megan Brose stated that they do wear BSL-3 PPE when processing samples, this includes a Tyvek, double gloves, shoe covers, and respiratory protection. LV processes quite a lot of field samples in this lab, however, it is important to note that to date they have not had a single instance of identifying a risk group 3 or 4 agent in any of these samples. So, the likelihood or frequency of identifying these higher risk agents is extremely low, as Alex Scranton mentioned. It is also very important to note that they are not conducting experiments or analyzing these samples in this lab. All they are doing is splitting the samples (opening one tube containing the specimen and transferring small amounts into two or three other tubes and sealing them back up again). They then inactivate one of the samples to remove and test for genetic material using PCR in a different BSL-2 lab to determine if there could be any agents present. The other live samples are sealed, secured and locked in the freezer where they wait to be taken into the BSL-3 or BSL-4 lab if they identify any agents that require that corresponding level of containment. ▪ The Entry/Exit procedures in Section 6.2 were questioned by Alex Scranton. She was concerned that if a sample was identified unexpectedly during the analysis of the sample, the exit procedures would have to be changed. The current section does not cover that. Megan Brose stated, since they are not actually analyzing any samples in this room and all they are doing is pipetting and adding inactivation chemicals to one tube and sealing the others (all within a biosafety cabinet), there is no added risk no matter what agent is identified. The samples that are taken out are either inactivated or sealed in leak-proof tubes and secured in a locked freezer. So, this lab and the BSL-2 lab (elsewhere in the building) where the PCR testing is done are never exposed to the live agent that is subsequently identified. Once they identify a risk group 3 or 4

	agent, those sealed/secured tubes in the freezers are taken into the appropriate biosafety level and kept there for subsequent testing/analysis. Therefore, the exit procedures from this field samples lab are appropriate. The PPE that they are wearing would adequately protect them regardless of what is identified. ▪ Alex Scranton also asked if there are ever cases where samples come from an area with outbreaks of Ebola or CCHFV where the field samples would be sent to RML where the likelihood or expectation of finding something is quite high. In those cases, this SOP seems inadequate. Do we need a separate SOP for that? Megan Brose stated that human samples from outbreaks are handled differently and they are not considered field samples. Those samples are taken directly into the BSL-4 and stay there for processing. They are only removed if they are inactivated by a validated method. ▪ The committee discussed these questions extensively and decided that the scope of the SOP could be clarified to state that the SOP is used for initial processing of the samples, not experimental work. The group also decided that the Chief Scientist should be added to reporting in Section 6.1.D and 6.8.D. Sue Priola also noted that "HPRD" should be updated to "PRD". ▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved the **2/3-28-01 Handling Field Collected Fluid Blood and Tissue Samples** with the following minor modifications: 1. Update scope section to clarify that this SOP is for initial processing of samples, not experimental work. 2. Add Chief Scientist to reporting in 6.1.D and 6.8.D. 3. Change "HPRD" to "PRD".
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Not present.
Report:	**Occupational Safety and Health Manager Report/Paul Carlson/**(b)(6) ▪ Not present
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ Megan Brose reviewed the Full Length Clone Lab annual report. ▪ There will be a BSL-3 users meeting on January 28th to schedule the BSL-3 annual shutdowns. ▪ The BSL-3 (b)(6) shutdown started today.

	▪ The BSL-4 (b)(6); (b)(3):42 s currently shutdown and should be reactivated on January 25th. ▪ The Effluent Decon System (EDS) controls are being updated this week. The project is almost wrapped up. This work included completing a 10 year mandatory tank inspection. Everything looked good on the tanks after inspection.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ None

Other issues	▪ None

Next Meeting:

- Date: 2/21/19
- Place: Library conference room
- Time: 1:00 PM

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 2/21/2019
Meeting Time: 1:02 PM **Adjourned:** 1:53 PM
Building A Library, (b)(6)

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Karin Peterson	☒	☐
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Greg Saturday	☒	☐
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Alexandra Scranton	☐	☒
Alan Applebury	☐	☒	Nancy Hoe	☒	☐	Brian Vickrey	☐	☒
Chris Bosio	☐	☒	Erik Hoover	☐	☒			
Marshall Bloom (EO)	☒	☐	Clay Jarrett	☒	☐			
Megan Brose	☒	☐	Josh Kellar (EO)	☐	☒			
Larry Brouwer	☐	☒	Scott Kobayashi	☒	☐			
Carol Calderwood	☐	☒	Jamie Lovaglio	☐	☒			
Marcie Caldwell (EO)	☐	☒	Andrea Marzi	☒	☐			
Paul Carlson	☐	☒	Alida Merritt	☐	☒			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 1/17/19 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 1/17/19** Action: Meeting minutes for 1/17/19 were unanimously approved with the following minor modification: 1. Add to page 4, the first full bullet, a description that proper PPE is worn when handling field samples.
Item 2:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Clarification) ▪ Bosio (LB) ▪ **PRD#17-194: *Mycobacterium tuberculosis*** ▪ Becky Anderson informed the committee that the registration covers virulent and attenuated strains of *M. tuberculosis*. The Bosio lab has obtained the attenuated strains of *M. tuberculosis*, but not the virulent

	strains. The recommendations section of the PRD states that, "Personnel must be enrolled in the TB surveillance program." Currently, the Bosio staff listed on the registration are required to perform annual TB testing in order remain in compliance with the PRD. We consulted with OMS and they determined that enrollment in the TB surveillance program is only necessary if staff are working with the virulent strains. We would like to change the wording in the recommendations section to the following, "Personnel must be enrolled in the TB surveillance program if working with virulent strains of *M. tuberculosis*." ▪ The committee discussed the language change and agreed with the proposed changes. Action: The committee unanimously approved the changes to the recommendation section of **PRD#17-194.**

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New) ▪ Martens (RTB) ▪ **PRD#19-211: *Roseomonas mucosa*** ▪ Becky Anderson presented the risk assessment. The Marten lab will determine genes/proteins in *R. mucosa* that are involved in treating and protecting patients with atopic dermatitis. Associated with this PRD is an RD that will be reviewed this meeting. *R. mucosa* can be found in water and soil, some recent reports indicate that it can also be found on skin. Human cases of infection have mainly been associated with patients with underlying diseases or indwelling devices. Symptoms include fever, malaise, nausea, vomiting, and inflammation at the sight of the indwelling device. Infections with *R. mucosa* can be treated with antibiotics. Primary lab hazards include aerosolization, droplet or inhalation exposure. ▪ Nancy Hoe stated that (b) (6) are missing from the PRD, their names need to be added back. ▪ Bob Heinzen stated that they need to define the HyHK gene in the PRD. ▪ *Roseomonas mucosa* is approved at BSL-2. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the

	proposal. Action: The committee unanimously approved **PRD#19-211** with minor modifications: 1. Add (b) (6) to the associated researcher's section. 2. Define HyHK gene in the Prokaryote host section.
Item 2:	Registration Documents for Recombinant DNA Experiments (NEW) ▪ Martens (RTB) ▪ **RD#19-550**: *Roseomonas mucosa* RNA-Seq of strains carrying WT or KO Hybrid Histidine Kinase Gene ▪ Reviewers: Bob Heinzen, Scott Kobayashi ▪ **Summary:** The RD describes knocking out a single gene in *Roseomonas mucosa* ▪ Bob Heinzen summarized the RD. It is a straightforward RD and Bob Heinzen had no issues with the rDNA part. He stated that there are a few sentences that are not complete sentences in the Recombinant DNA section. The following changes should be made: define HyHK gene in the Prokaryote Host section, fix the incomplete sentences in the Recombinant DNA section, delete the wording in the "What proteins and/or siRNA targeting proteins are being expressed" section and change the answer to "No", clarify that all of the antibiotics that will be used will be used on the same vector backbone, and better describe that they will test the resistance profile of the bacteria and will then choose the antibiotic used for selection. ▪ Nancy Hoe stated that they need to change NIH Guidelines to III-E. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#19-550** with the following minor modifications: 1. Define HyHK gene in the Prokaryote Host section. 2. Fix the incomplete sentences in the Recombinant DNA section. 3. Delete the wording in the "What proteins and/or siRNA targeting proteins are being expressed" section and change the answer to "No". 4. Change NIH Guidelines to III-E. 5. Clarify that all of the antibiotics that will be used will be used on the same vector backbone. 6. Better describe that they will test the resistance profile of the bacteria and will then choose the antibiotic used for selection.

	Research using prokaryotic hosts is approved at BSL-2 under section III-E of the NIH Guidelines.
	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Heinzen (LB) ▪ **RD#14-106 Amend**: Genetic transformation of *Coxiella burnetii* ▪ Reviewers: Andrea Marzi, Clay Jarrett ▪ **Summary:** The RD amendment describes adding an inducible gene expression system and expanding the approved nutritional selection system. ▪ Andrea Marzi summarized the RD. The amendment for the Heinzen lab is to add an inducible gene expression system. The system is very straightforward, once genetically modified, the addition of arabinose will then result in gene expression of selected genes. In section 2 of the amendment, they want to add tyrosine and proline for the auxotrophs. Work with *E. coli* and *Legionella* were already added in a previous amendment. Andrea Marzi stated that her only concern was that the statement at the bottom of the amendment did not make it clear that the same plasmids that are already approved will be used in both parts of the amendment. The committee agreed that this could be added to make it clearer. ▪ Clay Jarrett had no comments or concerns. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Bob Heinzen abstained) **RD#14-106 Amend** with the following minor modifications: 1. Clarify that the same plasmids will be used in all experiments. Research using prokaryotic hosts is approved at BSL-2 under section III-D-1-a, III-D-1-b, and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 and BSL-3 under Appendix G-II-C and III-D-1-a of the NIH Guidelines.
	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Feldmann (LV) ▪ **RD#15-406 Amend**: Replication deficient VSV ▪ Reviewers: Chris Bosio, Sue Priola ▪ **Summary:** The RD amendment is to add a new vector and update wording in the Eukaryotic cell section.

	▪ Sue Priola summarized the amendment. The amendment to the RD is to add a new vector backbone pcDNA3.1. They also updated the text in the Eukaryotic cell section. Sue Priola had no concerns with the amendment and no dual use concerns. ▪ Alex Scranton submitted a question by email to Sue Priola. She asked why the amendment number is listed as 0001 when it looks like there have been previous amendments. Becky Anderson stated that the system was updated last fall and the amendment number is a new feature that is generated in PI Dashboard. Amendments created since the update will start at 0001 regardless of the amendment history. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved (Andrea Marzi abstained) **RD#15-406 Amend** as written. Research using prokaryotic hosts is approved at BSL-2 under section III-D-1-a and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-3-a of the NIH Guidelines.
	<u>Registration Documents for Recombinant DNA Experiments (Amendment)</u> ▪ Feldmann (LV) ▪ **RD#17-431 Amend**: Molecular characterization of viral proteins of pathogenic RNA viruses ▪ Reviewers: Sue Priola, Karin Peterson ▪ **Summary:** The RD amendment is to add new viruses. ▪ Sue Priola summarized the RD amendment. Sue Priola informed the committee that the amendment is to add Coronaviruses to the table. The RD describes expressing viral proteins to characterize viral protein functions and viral/host protein interactions. Sue Priola stated that everything that is being expressed is less than 2/3 of the viral genome. ▪ Alex Scranton submitted questions by email. She questioned what can be done with these viruses once they are added to the RD table. The committee discussed that the Feldmann lab can do anything that is described in the original RD which is basically protein expression of genes from the listed viruses. ▪ Alex Scranton also asked about a note at the bottom of the table which states, "We will add other viruses in the species/genus dependent on the experiment, following consultation/approval with the IBC." The IBC asked for this wording

	to be added to indicate that any new virus addition requires IBC approval. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Andrea Marzi abstained) **RD#17-431 Amend** as written. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-2-a and III-E-a of the NIH Guidelines.
Item 3:	**Standard Operating Procedure: (b)(6) BSL-3 OSP: BSL-3-28-13 Concentration of viral stocks by centrifugation (New SOP)** ▪ Becky Anderson summarized the new SOP to the committee. ▪ Alex Scranton submitted questions by email to Sue Priola. She stated that the SOP was not consistent using ethanol vs EtOH. Alex Scranton also noted that it would seem ideal to disinfect the tissue culture flasks immediately after they were emptied, not at the end of the entire procedure. The committee agreed that is appropriate and realistically what is done. Alex Scranton also pointed out that transferring of the box to the freezer was listed twice, that needs to be corrected. ▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved the (b)(6) **BSL-3 OSP: BSL-3-28-13 Concentration of viral stocks by centrifugation (New SOP)** with the following minor modifications: 1. Make language about ethanol consistent throughout SOP. 2. Move disinfection of tissue culture flasks to the beginning of the SOP. 3. Remove redundant statement about transferring the box to the freezer.
	Standard Operating Procedure: *Francisella tularemia* animal SOP BSL3-4 Real Time monitoring of bacterial infection and metabolism *in vivo* (New SOP) ▪ Becky Anderson summarized the new SOP to the committee. ▪ Bob Heinzen asked if we should list what the strains are expressing that the IVIS is imaging? (b)(6) stated that they are using a metabolic tracer so they are not using a bacteria expressing fluorescence. They use probes in the far red so they can transcend through the tissue. The committee discussed and

	decided that was not necessary to add greater detail to the SOP. ▪ Alex Scranton submitted questions by email that the ethanol language is not consistent. She questioned the steps that state turning on the equipment but at the end it lists that the equipment must be left on. The committee agreed to include in 1.2, "if not already on, . . ." ▪ Alex Scranton questioned disinfection of the secondary container as well as the black construction paper from the imaging platform in section 1.4. The committee agreed that additional detail about disinfecting the secondary container and disposal of the black paper needs to be described. ▪ There was confusion with the statement in Section 2.0, where the SOP describes infections with BSL-3 agents. The committee discussed that the language should be removed as nothing in that section is infected with BSL-3 agents. Delete the last two sentences in 2.0. ▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved the ***Francisella tularemia*** **animal SOP BSL3-4 Real Time monitoring of bacterial infection and metabolism in vivo (New SOP)** with the following minor modifications: 1. Update Section 1.2 to state, "If not already on . . . " 2. Add additional detail to section 1.4 regarding disinfection of secondary container and black construction paper. 3. Remove the last two sentences of Section 2.0.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Reviewed the BSO Report
Report:	**Occupational Safety and Health Manager Report/Paul Carlson/**(b)(6) ▪ Not present
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ The (b)(6) shutdown has begun. ▪ (b)(6) shutdown starts next week. ▪ We are looking into purchasing an ionized VHP system that would be an alternative method to formaldehyde for the decon of the BSL-4. We are going to obtain this equipment and then begin our own testing and validation studies.

Report	**Associate Director Report/Marshall Bloom** ▪ Nothing to report.
Around the room	▪ None

Other issues	▪ None

Next Meeting:

- Date: 3/21/19
- Place: Library conference room
- Time: 1:00 PM

RML Biosafety Committee Meeting
February 21, 2019
Biosafety Officer/Responsible Official Report

1) ***Requests approved by BSO since last meeting:***
   a) *None*
2) ***New requests approved by committee via electronic review:***
   a) *None*
3) ***New requests***
   a) *Pathogen Registration Documents*
      i) ***New***
         (a) *Martens (RTB)*
            (a) ***PRD-19-211****: Roseomonas mucose*

   b) *Registration Documents for Recombinant Nucleic Acid Experiments*
      i) ***New***
         (a) *Martens (RTB)*
            (a) ***RD-19-550****: Roseomonas mucosa RNA-Seq of strains carrying wild-type or knockout Hybrid Histidine Kinase Gene*
      ii) ***Amend***
         (a) *Heinzen (LB)*
            (a) ***RD 14-106****: Genetic transformation of Coxiella burnetiid*
               (i) Add arabinose-inducible expression system
               (ii) Add selection based on complementation of tyrosine and proline auxotrophies
         (b) *Feldmann (LV)*
            (a) ***RD 15-406****: Replication deficient VSV*
               (i) Add a new vector backbone for use as a foreign GP expression plasmid, pcDNA3.1
            (b) ***RD 17-431****: Molecular characterization of viral proteins of pathogenic RNA viruses*
               (i) Add additional Coronaviruses

4) ***Standard Operating Procedures***
   i) *Update*
      (a) (b)(6) *BSL-3 SOP*
         (a) *Add procedures for concentration of viral stocks by centrifugation*
      (b) *Standard Operating Procedures for Animal Biosafety Level 3 (ABSL-3): Francisella tularensis*

(a) *Add SOP BSL3-4: Real time monitoring of bacterial infection and metabolism in vivo*

5) *Animal Study Protocols Review*

Title	*Associated PRD*	*Associated RD*	*Reviewer*
Determining the effectiveness of a ChAdOx1-Lassa vaccine in a heterologous challenge of Strain 13 Guinea pigs	*18-94 (Lassa virus)*	*17-410*	*N. Hoe*
Defining the Effect of Unique Host Genetic Backgrounds and Sex in Ebola Virus Pathogenicity in Mice and Linking Genetic Loci to Phenotype	*18-90 (Ebola virus)*	*N/A*	*N. Hoe*
Evaluation of a nanoparticle delivered vaccine for Crimean-Congo hemorrhagic fever virus	*18-92 (CCHFV)*	*17-452*	*R. Anderson*
Prion disease pathogenesis and microglial involvement in mice	*16-190 (TSE)*	*N/A*	*N. Hoe*
Efficacy testing of mouse antibodies against Andes virus in the hamster HCPS model	*17-81 (Hantavirus)*	*N/A*	*N. Hoe*
Virulence of fluorescent protein-labeled strains of Yersinia pestis in a mouse model and the effect of different intradermal sites of infection on disease progression	*18-04 (Y. pestis)*	*15-303*	*R. Anderson*
Efficacy of DNA-Based Vaccines in Cynomolgus Macaques Against Lethal Lassa Virus Challenge	*13-94 (Lassa virus)*	*N/A*	*M. Brose*
Maintenance of Experimental Flea Colonies Using Mice 2019-2021	*14-66 (Y. pestis exempt) 18-07 (Y. pseudotuberculosis) 18-04 (Y. pestis)*	*15-320 15-321*	*M. Brose*
Cellular and humoral immune responses to Lassa virus infection in Mastomys natalensis, the natural reservoir	*18-94 (Lassa virus)*	*N/A*	*R. Anderson*
Influence of the Prion Protein and Sarm1 on Herpes Simplex Virus pathogenesis in mice	*14-162 (Herpes Simplex Virus)*	*N/A*	*N. Hoe*

6) *Biosafety Training Performed – Rebecca Anderson, Megan Brose*

Type of Training	*Number of Sessions*	*Number of Employees Trained*
Select Agent Initial	*1*	*3*
BSL-3 Laboratory Biosafety	*2*	*6*
BSL-4 Laboratory Biosafety	*7*	*3*
Biosafety for Support Personnel: Refresher	*1*	*6*
BSL-4 Refresher	*2*	*1*
Biosafety Brief	*1*	*LB WIP*
Visitor (for BSL-3/BSL-4)	*4*	*9*
Full length clone lab Refresher	*2*	*8*

7) *Safety Audits and Inspections*

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

a) *Biological Incident Report:*
   i) *None*

8) *Select Agent Issues*

a) *None*

9) ***Other Issues –***
a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 3/21/2019
Meeting Time: 1:02 PM **Adjourned:** 1:53 PM
Building A Library, (b)(6)

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Bruce Chesebro (EO)	☐	☒	Karin Peterson	☒	☐
Bob Heinzen, Vice Chair	☐	☒	Frank DeLeo (EO)	☐	☒	Greg Saturday	☒	☐
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Alexandra Scranton	☐	☒
Alan Applebury	☐	☒	Nancy Hoe	☒	☐	Brian Vickrey	☐	☒
Chris Bosio	☒	☐	Erik Hoover	☒	☐			
Marshall Bloom (EO)	☒	☐	Clay Jarrett	☐	☒			
Megan Brose	☒	☐	Josh Kellar (EO)	☐	☒			
Larry Brouwer	☒	☐	Scott Kobayashi	☒	☐			
Carol Calderwood	☐	☒	Jamie Lovaglio	☒	☐			
Marcie Caldwell (EO)	☐	☒	Andrea Marzi	☐	☒			
Paul Carlson	☐	☒	Alida Merritt	☐	☒			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 2/21/19 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 1/17/19** Action: Meeting minutes for 1/17/19 were unanimously approved with the following minor modification: 1. At the bottom of page 4, in the last sentence, change "working" to "wording". 2. At the top of page 7 change the sentence from, "… not necessary to list that. . ." to "…not necessary to add that".

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New)

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- Best (LV)
- **PRD#19-212: Yellow Fever virus**
- Becky Anderson presented the risk assessment. The Best lab is interested in understanding how different flaviviruses escape recognition by the innate immune response. This PRD adds Yellow fever virus to their flavivirus collection, so that they can compare interferon evasion strategies by the different viruses. It is estimated that 15 to 50 % of people infected with Yellow Fever develop illness, beginning abruptly about 3-6 days post exposure with fever, chills and headache, body aches, fatigue, and vomiting. Of the individuals that develop illness, about 57 to 85 % abort infection and recover without developing classic yellow fever. Severe cases result in high fever, jaundice, bleeding, shock and organ failure. Those that develop severe disease have a mortality rate of 30-60%. Treatment is supportive care; however, it can vary depending on each case. The natural route of transmission is through the bite of an infected mosquito. The primary lab hazards include direct or indirect exposure to aerosols, infected animals and animal tissues.
- Becky Anderson informed the committee that the recommendations section should be updated to state, "All personnel who work with this agent, infected animals, and those entering rooms where agent is actively being worked with must be offered the Yellow Fever vaccine." This ensures that we are consistent with the BMBL.
- Nancy Hoe suggested that we add to the recommendations section: (b)(6) (b)(6) will post a sign on the door when Yellow Fever virus is actively being worked with. Incubators with yellow fever virus will be posted." This will communicate to the users when Yellow fever virus studies are in progress. She also informed the committee that the (b)(6) BSL-3 OSP will need to be updated to include these procedures as well as spill procedures, but this statement does not need to be added to the recommendations section of the registration.
- Sue Priola stated that the vector map should be deleted.
- Sue Priola asked if specific strains should be listed for Yellow Fever virus. (b)(6) (b)(6) clarified that there are hundreds of named strains. Nancy Hoe informed the committee that the only additions that would be necessary is if the Best lab wanted to add one that was known to have a higher virulence.
- Larry Brouwer added that the Hepatitis B vaccination is a series that takes several months so planning should be made to ensure staff have it in place before working with human blood and body fluids. Becky Anderson stated that the RML staff gets assessed by OMS on the need for vaccination at the start of employment and when their work objectives change, so most staff in the Best lab should already be current on their vaccinations. (b)(6) acknowledged that her staff is current with those vaccinations.
- No animal studies were submitted, reviewed, or approved.

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	▪ Yellow Fever virus is approved at BSL-3/ABSL-3. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#19-212** with minor modifications: 1. Delete the attached vector map. 2. Update recommendations section to match wording with BMBL, "All personnel who work with this agent, infected animals, and those entering rooms where agent is actively being worked with must be offered the yellow fever vaccine." 3. Add to the recommendations section: (b)(6) will post a sign on the door when Yellow Fever virus is actively being worked with. Incubators with yellow fever virus will be posted. 4. The (b)(6) BSL-3 OSP will be updated to include these procedures as well as spill procedures, but this statement does not need to be added to the recommendations section.
Item 2:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New) ▪ Bloom (LV) ▪ **PRD#19-213: *Borrelia burgdorferi*** ▪ Becky Anderson presented the risk assessment. The proposed studies are to determine if *Borrelia burgdorferi* and Powassan virus can positively or negatively impact the other for infection of the tick. *B. burgdorferi* causes Lyme disease. It is a tickborne zoonotic disease characterized by distinctive skin lesions and can present with fever, chills, headache, fatigue, muscle and joint aches, and swollen lymph nodes. An erythema migrans rash occurs in approximately 70 to 80% of infected people and begins at the site of a tick bite after approximately 3 to 30 days. This rash can expand over a period of days reaching up to 12 inches and can be warm to the touch. The rash can also appear like a "bull's-eye" and appear on any part of the body. Approximately 10 to 20% of patients treated for Lyme disease with a recommended 2 to 4 week course of antibiotics will have lingering symptoms of fatigue, pain, or joint and muscle aches. In some cases, these can last for more than 6 months. Antibiotics commonly used are doxycycline and amoxicillin, erythromycin is used for those with allergies to penicillins or tetracyclines. The natural route of transmission is through the bite of an infected tick. The primary lab hazards include accidental needle stick and generation of aerosols. ▪ Nancy Hoe stated that the Bloom lab will need an approved biosafety plan for working with ticks at BSL-3. Marshall Bloom informed the committee that his lab is currently working on developing a biosafety plan for their proposed tick work.

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	▪ *Borrelia burgdorferi* is approved at BSL-2. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#19-213** as written.
Item 3:	Registration Documents for Recombinant DNA Experiments (New) ▪ Best (LV) ▪ **RD#19-454**: Flavivirus interactions with host innate immune responses ▪ Reviewers: Karin Peterson, Sue Priola ▪ **Summary:** The RD describes understanding how different flaviviruses escape recognition from the innate immune response. ▪ Karin Peterson summarized the RD. Karin Peterson commented that the details of the RD project are not clearly stated, this should be added to the Synopsis section, details of your study subsection. Karin Peterson stated that this RD is very similar to the other RD for the Best lab. The Best lab should consider combining the RDs since the methods for both RDs are the same. The RD describes generating infectious clones of Yellow Fever virus. They will do individual cloning for specific genes and then express them in different cell lines with lots of different types of cells. Karin Peterson stated that the current RD is very specific and suggested that the Best lab consider changing the language to make it more flexible. As written the RD covers one experiment. The committee agreed that (b)(6) could amend the RD to make it broader if the experiments do not result in strains that are any more virulent than wild type Yellow Fever virus. ▪ Karin Peterson stated that the biosafety level for the Eukaryote cells section should be BSL-2 for expression of specific genes, however BSL-3 is appropriate for PCR ligation and any infectious work with Yellow fever virus. The committee agreed that this should be added to the comments section of the biosafety level question in the Eukaryote Cell section. ▪ Sue Priola stated the NIH Guidelines for the Research Product section should have III-E-1 and III-D-1-b added to the NIH Guidelines section. For the Eukaryote Cell section: add III-D-3-b to the NIH Guidelines section ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#19-454** with the following

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	minor modifications: 1. Add details of RD project 2. Research Product section: add III-E-1 and III-D-1-b to the NIH Guidelines section 3. Eukaryote Cell section: add III-D-3-b to the NIH Guidelines section 4. Eukaryote Cell section: specify in the comments that BSL-3 is for infectious virus work. PCR for ligation of fragments must be done in the BSL-3. Research using prokaryotic hosts is approved at BSL-2 under section III-D-1-b, III-D-2-a, and III-E-1 of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 and BSL-3 under III-D-1-a and III-D-3-b of the NIH Guidelines.
Item 4:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Best (LV) ▪ **RD#14-420 Amend**: Langat virus evasion of host immunity ▪ Reviewers: Sue Priola, Karin Peterson ▪ **Summary:** The RD amendment is to add a new method for generating an infectious molecular clone. ▪ Sue Priola summarized the amendment. The methods for generating the infectious clone are being updated with this amendment. The procedures are the same as described for the Yellow Fever RD that was just reviewed. The same guidelines and biosafety level are already included in the original RD and are still appropriate. ▪ Karin Peterson had no additional comments or concerns. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#14-420 Amend** as written. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a, III-D-3-a, and III-E-1 of the NIH Guidelines.
Item 5:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Feldmann (LV) ▪ **RD#15-404 Amend**: VSV Replication Competent ▪ Reviewers: Scott Kobayashi, Clay Jarrett ▪ **Summary:** The RD amendment is to add Plasmodium ORFs to the list of agents being studied.

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	▪ Scott Kobayashi summarized the RD amendment. The amendment is to add Plasmodium to the replication competent RD. To know the sequences that they will add, the RD instructs the reader to look at a different document. Scott Kobayashi recommended that the sequences that are being added should be included in this RD amendment. Clay Jarrett submitted his questions by email to Scott Kobayashi. Clay Jarrett asked for the Feldmann lab to add a sentence to state why they are adding Plasmodium. The committee agreed that both the sequences and a statement clarifying why Plasmodium is being added to the amendment should be included in the amendment summary. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#15-404 Amend** with the following modifications: 1. Add the ORFs to the amendment description so that you do not have to look in a different document. 2. Add a short description of why they are doing the proposed work. Research using prokaryotic hosts is approved at BSL-2 under section III-D-1-a and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a and III-D-3-a of the NIH Guidelines.
Item 6:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Feldmann (LV) ▪ **RD#17-431 Amend**: Molecular characterization of viral proteins of pathogenic RNA viruses ▪ Reviewers: Chris Bosio, Bob Heinzen ▪ **Summary:** The RD amendment is to add Plasmodium ORFs to the list of agents being studied. ▪ Chris Bosio summarized the amendment. The amendment is to add Plasmodium ORFs to the RD. There is no detail on what the Feldmann lab plans to do with the addition of Plasmodium, but the table has been updated to include the Plasmodium ORFs. The committee agreed that a sentence describing why they want to add Plasmodium needs to be included. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal.

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	Action: The committee unanimously approved **RD#17-431 Amend** with the following modifications: 1. Add a short description of why they are doing the proposed work. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-2-a and III-E-a of the NIH Guidelines.
Item 7:	**Standard Operating Procedure: (b)(6) BSL-3 SOP: BSL3-C-3 Equipment Operation (Update)** ▪ Sue Priola summarized the changes to the SOP to the committee. The Priola lab will be handing off samples for analysis that contain BSL-2 prions in them. The decontamination process for those samples is different than that for *Francisella tularensis* so the process for decontaminating these plates has been added to the (b)(6) SOP. ▪ The committee discussed that the layout of the added text is not clear for which steps are being done when. Becky Anderson will change the format of the added text to make it clearer. ▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved the (b)(6) **BSL-3 SOP: BSL3-C-3 Equipment Operation (Update)** with the following minor modifications: 1. Change format of text to make the process clearer.
Item 8:	**Standard Operating Procedure: SOP#4-28-32 Removal of Specimens for Nucleic Acid Extraction (Update)** ▪ Becky Anderson summarized the changes to the SOP to the committee. The changes are minimal and expand the procedures from just MERS-CoV to non-select agent positive strand RNA viruses. ▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved the **SOP#4-28-32 Removal of Specimens for Nucleic Acid Extraction (Update)** as written.
Item 9:	**Standard Operating Procedure: SOP#4-28-51 Intratracheal and Intrabronchial Inoculation Procedures for Non-Human Primates (Update)** ▪ Becky Anderson summarized the changes to the SOP to the committee. The only change to the SOP is the addition of procedures to perform ocular inoculations. ▪ Nancy Hoe was concerned that the word "dropping" sounds like there would be

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	splashes. Is there a better word for this process? Marshall Bloom stated that "instilling" would be more appropriate. ▪ Greg Saturday stated that all sharps are not disinfected before disposal as the sixth bullet in the general precautions section states. There are some sharps that go directly to disposal. The committee discussed and agreed to separate the single sentence into two separate sentences for clarity, "All sharps and inoculation material will be handled with extreme care. Inoculation material will be disinfected before appropriate disposal." ▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved the **SOP#4-28-51 Intratracheal and Intrabronchial Inoculation Procedures for Non-Human Primates (Update)** with the following modifications: 1. For the ocular inoculation, change "dropping" to "instilling" throughout the document. 2. Update the sixth sentence in the General Precautions section to, "All sharps and inoculation material will be handled with extreme care. Inoculation material will be disinfected before appropriate disposal."
Item 10:	**Standard Operating Procedure: SOP#4-28-48 Inoculation/Infection and blood collection Procedures for Rodents in Level 4 Biocontainment (Update)** ▪ Becky Anderson summarized the changes to the SOP to the committee. She informed the committee that the changes are the same as for SOP#4-28-51. ▪ The committee agreed that the changes to SOP#4-28-51 should be applied to SOP#4-28-48. ▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved the **SOP#4-28-48 Inoculation/Infection and blood collection Procedures for Rodents in Level 4 Biocontainment (Update)** with the following modifications: 1. For the ocular inoculation, change "dropping" to "instilling" throughout the document. 2. Update the fifth sentence in the General Precautions section to, "All sharps and inoculation material will be handled with extreme care. Inoculation material will be disinfected before appropriate disposal."
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Reviewed the BSO Report

DRAFT

Report:	**Occupational Safety and Health Manager Report/Paul Carlson/** (b)(6) ▪ Not present
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ The (b)(6) is shutdown now for the annual shutdown. ▪ All BSL-3 annual shutdowns are complete until (b)(6) in November. ▪ Next week the (b)(6) annual shutdown will begin.
Report	**Associate Director Report/Marshall Bloom** ▪ Nothing to report.
Around the room	▪ None

Other issues	▪ None

Next Meeting:

- Date: 4/18/19
- Place: Library conference room
- Time: 1:00 PM

DRAFT

RML Biosafety Committee Meeting
March 21, 2019
Biosafety Officer/Responsible Official Report

1) Requests approved by BSO since last meeting:

a) Pathogen Registration Document

i) Bosio (LB)

*(1) **PRD-17-194- Amend 0001**: Mycobacterium tuberculosis*

(a) Add handling of NHP fluids including bronchoalveolar lavage (BAL) fluid

2) ***New requests approved by committee via electronic review:***

a) *None*

3) ***New requests***

a) *Pathogen Registration Documents*

i) ***New***

(a) *Best (LV)*

(a) ***PRD-19-212**: Yellow Fever virus*

(b) *Bloom (LV)*

(a) ***PRD-19-213**: Borrelia burgdorferi*

b) *Registration Documents for Recombinant Nucleic Acid Experiments*

i) ***New***

(a) *Best (LV)*

(a) ***RD-19-454**: Flavivirus interactions with host innate immune responses*

ii) ***Amend***

(a) *Feldmann (LV)*

(a) ***RD 15-404**: VSV replication competent*

(i) Add Plasmodium to list of agents being studies

(b) *Feldmann (LV)*

(a) ***RD 17-431**: Molecular characterization of viral proteins of pathogenic RNA viruses*

(i) Add Plasmodium ORFS

(c) *Best (LV)*

(a) ***RD-14-420**: Pathogenesis of Langat virus*

(i) add a new infectious molecular clone of LGTV called the CPER (circular polymerase extension cloning) method

RML Biosafety Committee Meeting
March 21, 2019
Biosafety Officer/Responsible Official Report

4) ***Standard Operating Procedures***

i) ***Update***

(a) *Standard Operating Procedures for Biosafety Level 3 (BSL-3): Francisella tularensis*

(a) *Update SOP BSL-C-3: Equipment Operation*

(i) Add procedures for use of Seahorse with prion samples

(b) *SOP#4-28-32: Removal of specimens for nucleic acid extraction*

(a) *Update procedures for positive-sense viruses to indicate all, not just MERS*

(c) *SOP#4-28-51: Inoculation procedures for NHPs*

(a) *Add procedures for ocular route of infection*

(d) *SOP#4-28-48: Inoculation of rodents*

(a) *Add procedures for ocular route of infection*

5) ***Animal Study Protocols Review***

Title	***Associated PRD***	***Associated RD***	***Reviewer***
Determining the effectiveness of a ChAdOx1-Lassa vaccine in a heterologous challenge of Strain 13 Guinea pigs	*18-94 (Lassa virus)*	*17-410*	*N. Hoe*
Defining the Effect of Unique Host Genetic Backgrounds and Sex in Ebola Virus Pathogenicity in Mice and Linking Genetic Loci to Phenotype	*18-90 (Ebola virus)*	*N/A*	*N. Hoe*
Production and titration of rat-passaged prion stocks #2	*16-190 (rodent TSE)*	*N/A*	*N. Hoe*
Role of BDL regulatory B cells in the control of regulatory T cells in Friend virus infection.	*16-187 (Friend virus)*	*N/A*	*N. Hoe*
Testing of Recombinant Attenuated Salmonella Vaccines against Lassa virus infection in Mastomys natalensis	*18-44 (Salmonella enterica serovar Typhimurium) 13-94 (Lassa virus)*	*14-126*	*N. Hoe*
Treatment of viral encephalitis with Rottlerin and other small molecule compounds in mice	*18-103 (California Serogroup of Orthobunyaviruses)*	*N/A*	*N. Hoe*
Investigating the significance of SIRP a newly discovered receptor expressed on virus-activated CD8+ T cells, by microscopy in a model of murine Friend Virus Infection	*16-187 (Friend virus)*	*N/A*	*N. Hoe*

6) ***Biosafety Training Performed – Rebecca Anderson, Megan Brose***

Type of Training	***Number of Sessions***	***Number of Employees Trained***
Select Agent Initial	*1*	*3*
BSL-4 Laboratory Biosafety	*7*	*1*
BSL-3/BSL-4 PPE Donning/Doffing for HazMat	*1*	*15*

7) ***Safety Audits and Inspections***

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer

or designee (list under each item, a-b, indicates audit or inspection submitted)

a) *Biological Incident Report:*
   i) *None*

8) ***Select Agent Issues***
   a) *None*

9) ***Other Issues –***
   a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 4/18/2019
Meeting Time: 1:02 PM **Adjourned:** 1:53 PM
Building A Library, (b)(6)

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Greg Saturday	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Heinz Feldmann (EO)	☐	☒	Alexandra Scranton	☐	☒
Becky Anderson (EO)	☒	☐	Nancy Hoe	☐	☒	Brian Vickrey	☐	☒
Alan Applebury	☐	☒	Erik Hoover	☐	☒			
Chris Bosio	☒	☐	Clay Jarrett	☐	☒			
Marshall Bloom (EO)	☐	☒	Josh Kellar (EO)	☐	☒			
Megan Brose	☒	☐	Scott Kobayashi	☒	☐			
Larry Brouwer	☐	☒	Jamie Lovaglio	☐	☒			
Carol Calderwood	☐	☒	Andrea Marzi	☒	☐			
Marcie Caldwell (EO)	☐	☒	Alida Merritt	☒	☒			
Bruce Chesebro (EO)	☐	☒	Karin Peterson	☐	☒			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 3/21/19 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 3/21/19** Action: Meeting minutes for 3/21/19 were unanimously approved with the following minor modification: 1. Typos submitted by Sue Priola.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New) ▪ Bloom (LV) ▪ **PRD#19-214: Leptospira spp.**

	▪ Becky Anderson presented the risk assessment. The Bloom lab will take over the long-term maintenance of stocks from the Rosa lab and potentially grow up for distribution if requested. (b) (6) from the Rosa lab has recently joined the Bloom lab and he would like to maintain these stocks as the Rosa lab is discontinuing this line of work. ▪ In humans, Leptospirosis can cause a wide range of symptoms including high fever, headache, chills, muscle aches, vomiting, jaundice, red eyes, abdominal pain, diarrhea and rash. Some individuals can also remain asymptomatic. The time from exposure to onset of disease is approximately 2 to 4 days. Illness lasts from a few days to 3 weeks or longer. If left untreated, recovery may take several months. Antibiotic treatment is effective with penicillin, streptomycin, erythromycin, and/or doxycycline. The natural route of transmission is from person to person. The primary lab hazards include: accidental needle stick, direct exposure to skin or mucous membranes and generation of aerosols. ▪ No animal studies were submitted, reviewed, or approved. ▪ Leptospira spp. are approved at BSL-2. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#19-214** with minor modifications: 1. Remove the first-person language. 2. Specify in the Pathogen/Toxin Section, that the antibiotic strains are not resistant to clinically relevant antibiotics.
Item 2:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Heinzen (LB) ▪ **RD#14-106 Amend**: Genetic transformation of *Coxiella burnetii* ▪ Reviewers: Andrea Marzi, Chris Bosio ▪ **Summary:** The RD amendment describes adding an inducible gene expression system and expanding the approved nutritional selection system. ▪ Andrea Marzi summarized the RD. The amendment for the Heinzen lab is straightforward. They have already amended the RD to add Cas9, now they want to add Cas9 from two bacterial strains. They will use the same methods as previously proposed for this work. In addition, they are proposing to treat Coxiella with LPS inhibitors because LPS is a virulence factor. Andrea Marzi stated that it is not clear if the Heinzen lab is making or obtaining these small molecules. Also, it is not clear what LPC is an abbreviation for. Bob Heinzen stated that they will not be making these inhibitors, instead they will be obtaining them from a collaborator. The committee agreed that more detail

	about the LPC inhibitors should be included in the RD amendment. ▪ Chris Bosio had no comments or concerns. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved (Bob Heinzen abstained) **RD#14-106 Amend** with the following minor modifications: 1. Add a description about the LPS inhibitors and references if applicable. Research using prokaryotic hosts is approved at BSL-2 under section III-D-1-a, III-D-1-b, and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 and BSL-3 under Appendix G-II-C and III-D-1-a of the NIH Guidelines.
Item 3:	**Working Group Summary** ▪ Becky Anderson informed the committee that the inactivation data was submitted because of the recent CDC DSAT BSL-4 Inspection that occurred on April 1-5. The IBC has previously reviewed and approved inactivation data from the BSL-4 using the Filovirus, Ebola virus, as a surrogate for all enveloped viruses worked with in the BSL-4. The Select Agent regulations were updated in 2017 to include regulations for inactivation requirements. In April of 2017 a regulatory interpretation of "surrogates" was published. Everyone thought that the IBC approved procedures were in compliance with these regulations, including the regulatory interpretation. The CDC DSAT BSL-4 Inspection in 2018 went well and there were no concerns with the inactivation methods that were established. This year at the inspection, the CDC DSAT inspectors stated that the regulatory interpretation from April 2017 requires that entities use surrogates from the same viral family. The language in that regulatory interpretation states that, "Viruses from the same family can be suitable surrogates for select agent viruses". The committee discussed that the language is not clear and that there is no good justification for testing every viral family for all inactivation procedures. Becky Anderson informed the committee that the Laboratory of Virology (LV) is in the process of testing every viral family for their currently approved inactivation methods. As of now, Nancy Hoe as the Responsible Official has stopped LV from removing any samples out of the BSL-4 that have not had IBC approved validation of inactivation methods at the viral family level. LV is anxious to get the testing complete and will be submitting data as soon as they get it over the next several months. ▪ Sue Priola stated that she would like this process to be as smooth as possible for the committee knowing that there will a lot of data to review. The committee discussed that, if the validation experiment followed SOPs that had

	previously been approved as validated by the IBC, the validation study could be reviewed electronically as long as there were no changes to the approved SOP. ▪ Sue Priola presented the Working Group summary and associated SOP. Bob Heinzen, Scott Kobayashi, and Karin Peterson were the working group members that reviewed the inactivation methods for the BSL-4 lab. ▪ The purpose of the validation was to use AVL/ethanol and RLT/ethanol to inactivate Arena, Bunya, and Paramyxo infected samples from BSL-4 containment. ▪ See attached summary. ▪ The Working Group recommended changes to SOP#4-28-32 that were incorporated in the draft document. ▪ The committee agreed with the WG group recommendation that AVL/ethanol and RLT/ethanol treatment of infected samples was a validated method for inactivating Arena, Bunya, and Paramyxo viral families. ▪ Action: The committee unanimously approved the Working Group recommendation that AVL/ethanol and RLT/ethanol completely inactivated Arena, Bunya, and Paramyxo viral families and approved the validation studies as written.
Item 4:	**Standard Operating Procedure: SOP#4-28-32 Removal of Specimens for Nucleic Acid Extraction (Update)** ▪ Becky Anderson summarized the changes to the SOP to the committee. The update is to add a table listing the inactivation methods and viral families that have been tested and IBC approved. The table will continue to be completed as LV works on testing more viral families. ▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved the **SOP#4-28-32 Removal of Specimens for Nucleic Acid Extraction (Update)** as written.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Not Present
Report:	**Occupational Safety and Health Manager Report/**(b)(6) ▪ Not present
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ All BSL-4 annual shutdowns are complete until May. ▪ Biosafety held BSL-4 medical extraction training, it went very well, another

	session will be held again in May. At the end of April/beginning of May, sessions will take place for NIH Police and RML First Responders.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ Alida Merritt informed the committee that Marcus Daly Memorial Hospital (MDMH) is working to prepare for a potential measles case/outbreak. The Director of Public Health in Montana is receiving suspected cases on a weekly basis now. The likelihood of measles spreading to Montana is expected to be likely. There is now a confirmed case of Mumps in Ravalli County. There will be a HEAT meeting on Monday to discuss the mumps case.

Other issues	▪ None

Next Meeting:

- Date: 5/16/19
- Place: Library conference room
- Time: 1:00 PM

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 5/16/2019
Meeting Time: 1:04 PM **Adjourned:** 2:20 PM
Building A Library, (b)(6)

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Greg Saturday	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Heinz Feldmann (EO)	☐	☒	Alexandra Scranton	☐	☒
Becky Anderson (EO)	☒	☐	Nancy Hoe	☒	☐	Brian Vickrey	☐	☒
Alan Applebury	☐	☒	Erik Hoover	☒	☐			
Chris Bosio	☐	☒	Clay Jarrett	☒	☐			
Marshall Bloom (EO)	☐	☒	Josh Kellar (EO)	☐	☒			
Megan Brose	☐	☒	Scott Kobayashi	☒	☐			
Larry Brouwer	☐	☒	Jamie Lovaglio	☐	☒			
Carol Calderwood	☐	☒	Andrea Marzi	☒	☐			
Marcie Caldwell (EO)	☐	☒	Alida Merritt	☒	☐			
Bruce Chesebro (EO)	☐	☒	Karin Peterson	☐	☒			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 4/18/19 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 4/18/19** Action: Meeting minutes for 4/18/19 were unanimously approved with the following minor modification: 1. Typos submitted by Sue Priola.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New) ▪ Bloom (LV) ▪ **PRD#19-215: Lymphocytic choriomeningitis (LCMV)**

	▪ Becky Anderson presented the risk assessment. The Bloom lab will use LCMV to confirm the absence of dystroglycan (DAG1) in DAG1 knock out cells. DAG1 is the receptor for LCMV virus infection. These knockout cells are important for the Bloom lab's work involving tick-borne flaviviruses. ▪ Infection with LCMV may result in some individuals remaining asymptomatic, for infected persons who do become ill, onset of symptoms usually occurs 8-13 days after exposure to the virus as part of a biphasic febrile illness. This initial phase, which may last a week, typically begins with any or all of the following symptoms: fever, malaise, lack of appetite, muscle aches, headache, nausea, and vomiting. Following a few days of recovery, a second phase of illness may occur. Symptoms may consist of meningitis, encephalitis, or meningoencephalitis. LCMV is usually not fatal. In general, mortality is less than 1%. Women who become infected with LCMV during pregnancy may pass the infection on to the fetus. Infections occurring during the first trimester may result in fetal death and pregnancy termination, while in the second and third trimesters, birth defects can develop. The natural route of transmission occurs through handling mice infected with LCMV where the virus can be shed in urine, feces, saliva, etc. Transmission also occurs through organ transplants and vertically from an infected mother to her fetus. The primary lab hazards include: accidental needle stick, generation of aerosols, and contact with contaminated animal materials. ▪ No animal studies were submitted, reviewed, or approved. ▪ LCMV work is approved at BSL-2 with additional precautions: all work with infectious material is conducted in a biosafety cabinet, centrifugation of infectious materials must be carried out in sealed safety cups or removable rotors that can be loaded and unloaded in a biosafety cabinet. Minimum PPE requirement when handling LCMV include: mucous membrane protection (surgical mask and eye protection), back closing gown and double gloves. Any significant aerosol generating procedures will required the use of N95 respirator. ▪ Alex Scranton submitted questions to Sue Priola by email. Alex Scranton questioned why work will not be performed at BSL-3 and referenced the material attached to the PRD. Nancy Hoe stated that the Bloom lab is not performing any aerosol generating procedures, the strains that are listed are commonly worked with at BSL-2. The committee discussed the statement in the recommendations section for how to handle any significant aerosol producing procedures and determined that it would be best to reword to the following, "Prior to performing any significant aerosol producing procedures, consult biosafety." ▪ Alex Scranton also questioned by email why the NIH Guidelines are not included in the PRD. Nancy Hoe stated that this is a PRD and not an RD. Unfortunately, the form now includes that question regardless of the type of work. NIH

	recombinant DNA Guidelines only apply to recombinant work. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#19-215** with minor modifications: 1. Update the recommendations section to state, "Prior to performing any significant aerosol producing procedures, consult biosafety."
Item 2:	Full Committee Review of BSL-4 Inactivation Data ▪ Sue Priola informed the committee that there are two sets of inactivation data that were included in this month's packet. She explained to the committee that so may PI's were out last week at the PI retreat that there were not enough people to set up a working group review of the inactivation data. The entire committee can review the data and corresponding SOPs. ▪ Nancy Hoe summarized for the committee the inactivation issues that arose from the April CDC DSAT inspection in April. From that inspection, RML received an immediate action letter regarding RML's inactivation procedures and the requirement to test every inactivation method at the viral family level. Nancy Hoe also reviewed with the committee a policy statement from CDC DSAT on tissue inactivation, tissue size, and tissue types that can be used as surrogate material. ▪ Sue Priola informed the committed that the first set of data is from the BSL-4, this is a continuation of their effort to verify inactivation by viral families with the previously tested inactivation methods which used Ebola virus as a surrogate for enveloped viruses. ▪ The inactivation data for this review includes: ▪ Orthomyxoviridae inactivated by AVL + Ethanol, 10% formalin and 2% PFA fixation of cells ▪ Bunyaviridae inactivated by 2% PFA fixation of cells, RLT + Ethanol of tissue, 10% formalin and 2% PFA fixation of tissues ▪ Arenaviridae inactivated by RLT + Ethanol in tissues, 10% formalin and 2% PFA fixation of tissues ▪ Paramyxoviridae inactivated by RLT + Ethanol in tissues, 10% formalin and 2% PFA fixation of tissues ▪ Sue Priola confirmed with the committee that the surrogates were appropriate, the samples and titers tested were appropriate, all necessary controls were included and that the procedures matched what is listed in the SOP. ▪ Nancy Hoe noted a couple of minor typos in the document that need to be

	corrected. ▪ Nancy Hoe also stated that the SOP#4-28-33 should have section 6.a updated to state 1cm^3 or less. This ensures that the tissue size is restricted to what was tested. The SOP infers that this is the size requirement, but we need to make sure it is clearly stated. ▪ (b)(6) questioned the committee if they would have any issues with using the same testing results for cells that are an attached monolayer or in suspension. (b)(6) stated that this would apply to 2% PFA and 10% formalin. The committee discussed extensively and agreed there is no scientific or logical reason that suspended cells would be different than attached cells in a monolayer. The IBC agreed that the data submitted can be applied to both suspended and monolayer attached cells. Action: The committee approved (Andrea Marzi abstained) BSL-4 inactivation data as presented with the following minor modifications: 1. Correct minor typos. 2. Update Section 6.a in SOP#4-28-33 to state tissue samples cannot be larger than 1cm^3.
	Standard Operating Procedure: SOP#4-28-32 Removal of Specimens for Nucleic Acid Extraction (Update) ▪ Sue Priola summarized the changes to the SOP to the committee. The table was updated with the inactivation methods that the committee reviewed. ▪ There were no comments or concerns with the updated procedures. Action: The committee approved (Andrea Marzi abstained) the **SOP#4-28-32 Removal of Specimens for Nucleic Acid Extraction (Update)** as written.
	Standard Operating Procedure: SOP#4-28-33 Removal of Specimens for Fluorescence, Immunofluorescence, Histopathology, Immunohistochemistry, and Flow Cytometry (Update) ▪ Sue Priola summarized the changes to the SOP to the committee. The update to the SOP was the addition of a table listing the inactivation methods and viral families that have been tested and IBC approved. ▪ As discussed with the inactivation data, Section 6.a needs to be updated to restrict tissue sizes to 1cm^3 or less. ▪ There were no comments or concerns with the updated procedures. Action: The committee approved (Andrea Marzi abstained) the **SOP#4-28-33 Removal of Specimens for Fluorescence, Immunofluorescence, Histopathology,**

	Immunohistochemistry, and Flow Cytometry (Update) With the following minor modifications: 1. Update section 6.a to restrict tissue size to 1cm^3.
Item 3:	Full Committee Review of Hinnebusch Lab Inactivation Data ▪ Sue Priola summarized the 10% formalin inactivation of *Y. pestis* tissue data that was provided by the Hinnebusch lab. Nancy Hoe and Sue Priola both stated that the size of the spleen and liver need to be specified for this testing. There needs to be size listed so that specific constraints can be included in the SOP to ensure that tissues larger than those tested are not removed from the lab. Clay Jarrett informed the committee that the acute spleen infected with *Y. pestis* is typically less than 1 cm^3. The committee discussed the type of information that they wanted from Hinnebusch lab. The IBC decided that they want to know the size or weight of the spleen and liver samples to determine the limits to set in the SOP. The committee also discussed that a safety margin needs to be included in the SOP. The testing was performed with a 24-hour incubation, so the IBC suggested that the samples be incubated for 48 hours prior to removal from the lab. ▪ The committee discussed that the testing with virulent *Y. pestis* was appropriate, the samples and titers tested were suitable, all necessary controls were included and that the procedures matched what is listed in the SOP. Once tissue size information is incorporated to the SOP and a safety margin added, the IBC could review the associated SOP electronically. Action: The committee approved (Clay Jarrett abstained) 10% formalin inactivation data as presented with the following minor modifications: 1. Have the Hinnebusch lab include spleen and liver sizes/weights in the testing data. This information will then be used to set limits on tissue size in the SOP. 2. Update the SOP to state 48 hours prior to removal.
Item 4:	**Standard Operating Procedure: ABSL3-YP-5 Inactivation of *Y. pestis* in tissues using 10% formalin (NEW)** ▪ Sue Priola informed the committee that the SOP could not be approved until there was more information obtained regarding the tissue sizes. Once this information is obtained, size limitations can be added to the SOP and it can be emailed to the committee for electronic review. ▪ The committee discussed that a safety margin should be added, the SOP should be updated from 24 to 48 hours for inactivation with 10% formalin. ▪ There were no comments or concerns with the updated procedures.

	Action: The committee unanimously tabled **ABSL3-YP-5 Inactivation of *Y. pestis* in tissues using 10% formalin (NEW)** pending more information. This information can be added and the SOP sent out for electronic review. 1. Contact (b) (6) in the Hinnebusch lab to determine the spleen and liver weights/sizes of tissues that were tested. If those weights/sizes are not available, determine the averages of similarly infected animals. 2. Update the SOP to list weight or size restrictions that match the inactivation data. 3. Update the time for inactivation from 24 to 48 hours to ensure that there is a safety margin.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Nancy Hoe reviewed the BSO report ▪ Nancy Hoe summarized the CDC DSAT inspection preliminary findings. ▪ A recent NBL/RBL Network meeting in Galveston, Texas was useful for RML staff that attended. Nancy Hoe reviewed the agenda and discussed relevant topics with the IBC. ▪ Providence St. Patrick Hospital recently participated in a National Ebola Training and Education Center Readiness Consultation that Nancy Hoe attended. The training was very informative and further helped to prepare Providence St. Patrick Hospital for a potential Ebola patient.
Report:	**Occupational Safety and Health Manager Report/S** (b)(6) ▪ Nothing to report.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ Not present.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ Alida Merritt informed the committee that Marcus Daly Memorial Hospital (MDMH) is working on measles preparedness preparation. Approximately 160 employees need their titers tested. The hospital requires definitive proof, serological proof, or documentation of vaccination. So far, in Ravalli County, there is 1 case of pertussis and 1 case of mumps.

Other issues	▪ None

Next Meeting:

- Date: 6/20/19
- Place: Library conference room
- Time: 1:00 PM

RML Biosafety Committee Meeting
May 16, 2019
Biosafety Officer/Responsible Official Report

1) Requests approved by BSO since last meeting:

a) None

2) ***New requests approved by committee via electronic review:***

a) *Standard Operating Procedures*

i) *Personal requirements for working with Yellow fever virus (YFV) in BSL-3, including vaccination*

(a) *IBC approved April 29, 2019*

3) ***New requests***

a) *Pathogen Registration Documents*

i) ***New***

(a) *Bloom (LV)*

(a) ***PRD-19-215**: Lymphocytic choriomeningitis Virus*

b) *Inactivation Validation Testing data review*

i) *Feldmann (LV)*

(a) *Inactivation of RG4 viral families (Orthomyxo -, Bunya -, Arena -, and Paramyxo -) with AVL, PFA, RLT, and formalin*

ii) *Hinnebusch (LB)*

(a) *Inactivation of Yersinia pestis with 10% formalin*

4) ***Standard Operating Procedures***

i) ***Update***

(a) *SOP#4-28-32: Removal of specimens for nucleic acid extraction*

(a) *Update procedures for additional viral families*

(b) *SOP#4-28-33: Removal of specimens for Fluorescence, Immunofluorescence, Histopathology, Immunohistopathology, and Flow Cytometry*

(a) *Update procedures for additional viral families*

(c) *Draft ABSL-3 Plague animal SOP*

(a) *Add procedures for inactivation with 10% formalin*

5) ***Animal Study Protocols Review***

Title	***Associated PRD***	***Associated RD***	***Reviewer***
Control of Allergic Inflammation with Francisella lipids and Francisella Inspired Liposomes	*NA*	*NA*	*N. Hoe*
Defining the minimal dose of VSV-EBOV that provides rapid protection in cynomolgus macaques	*18-90 (Ebola virus)*	*15-404*	*N. Hoe*

Title	*Associated PRD*	*Associated RD*	*Reviewer*
Establishment of a mouse model for Alkhurma virus infection	*18-135 (Tick-borne encephalitis virus - Alkhurma hemorrhagic fever virus)*	*N/A*	*R. Anderson*
Prophylactic efficacy of Nipah virus F monoclonal antibodies against Nipah virus Bangladesh and Hendra virus in Syrian hamsters	*18-91 (Nipah, Hendra virus)*	*N/A*	*M. Brose*
Pilot study to evaluate Pigtail macaques as a severe disease model for Middle East Respiratory Syndrome (MERS)	*17-143 (MERS-CoV)*	*NA*	*R. Anderson*
Protective efficacy of a subunit vaccine against lethal Ebola and Marburg virus infection in mice	*18-90 (Ebola, Marburg virus) 18-82 (VSV)*	*15-404*	*N. Hoe*

6) ***Biosafety Training Performed – Rebecca Anderson***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
BSL-3 Laboratory Biosafety	*3*	*4*

7) ***Safety Audits and Inspections***

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

a) *Biological Incident Report:*
   i) *None*

8) ***Select Agent Issues***

a) *Summary of FSAP BSL-4 inspection, April 1-5, 2019*
b) *NBL/RBL Network meeting, April 29-30, Galveston, TX*

9) ***Other Issues –***

a) *Providence St. Patrick Hospital National Ebola Training and Education Center (NETEC) Readiness Consultation, May 8-9, Missoula*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 6/20/2019
Meeting Time: 1:03 PM **Adjourned:** 2:25 PM
Building A Library, (b)(6)

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Greg Saturday	☒	☐
Bob Heinzen, Vice Chair	☒	☐	Heinz Feldmann (EO)	☐	☒	Alexandra Scranton	☐	☒
Becky Anderson (EO)	☒	☐	Nancy Hoe	☐	☒	Brian Vickrey	☐	☒
Alan Applebury	☐	☒	Erik Hoover	☐	☒			
Chris Bosio	☐	☒	Clay Jarrett	☒	☐			
Marshall Bloom (EO)	☐	☒	Josh Kellar (EO)	☐	☒			
Megan Brose	☒	☐	Scott Kobayashi	☐	☒			
Larry Brouwer	☐	☒	Jamie Lovaglio	☐	☒			
Carol Calderwood	☐	☒	Andrea Marzi	☒	☐			
Marcie Caldwell (EO)	☐	☒	Alida Merritt	☒	☐			
Bruce Chesebro (EO)	☐	☒	Karin Peterson	☒	☐			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 5/16/19 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 5/16/19** Action: Meeting minutes for 5/16/19 were unanimously approved with the following minor modification: 1. Sue Priola stated that in Item 1, bullet 2, the description of DAG1 should also state that it is the receptor for LCMV. 2. Sue Priola also noted that in Item 2, bullet 4, the statement that Ebola virus was a surrogate for "everything" should be changed to "enveloped viruses."

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New)

	▪ Feldmann (LV) ▪ **PRD#19-216: Yellow Fever Virus** ▪ Becky Anderson presented the risk assessment. The Feldmann lab proposes to study the molecular details of the life cycle of Yellow Fever viruses and their pathogenesis for the purpose of developing vaccines and evaluating medical countermeasures. It is estimated that 15 to 50% of people infected with Yellow Fever develop illness, beginning abruptly about 3-6 days post exposure with fever, chills and headache, body aches, fatigue, and vomiting. Of the individuals that develop illness, about 57 to 85% abort infection and recover without developing classic Yellow Fever. Severe cases result in high fever, jaundice, bleeding, shock and organ failure. Those that develop severe disease have a mortality rate of 30-60%. Treatment is supportive care; however, it can vary depending on each case. The natural route of transmission is through the bite of an infected mosquito. The primary lab hazards include direct or indirect exposure to aerosols, infected animals and animal tissues. ▪ The following precautions apply to work with Yellow Fever virus: ○ All personnel who work with this agent, infected animals, and those entering rooms where agent is actively being worked with must be offered the Yellow Fever vaccine. ○ For those working in BSL-3 (b)(6) a sign must be posted on the door when Yellow Fever virus is actively being worked with. Incubators with Yellow Fever virus must be labeled clearly. ○ All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the hepatitis B vaccine. For more information, please contact the OMS Nurse at 375-9755. ▪ Alex Scranton submitted questions by email to Sue Priola. She questioned why the vaccine was not mandatory. The committee discussed and stated that the NIH cannot make vaccines mandatory. ▪ Animal studies with mice were proposed. ▪ Work with the 17D strain of Yellow Fever virus can be approved at BSL-2/ABSL-2. All other listed strains are BSL-3/ABSL-3. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **PRD#19-216** as written.
Item 2:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals</u>

	(Renew) ▪ Bloom (LV) ▪ **PRD#19-75: Powassan and Deer Tick Virus** ▪ Becky Anderson presented the risk assessment. The Bloom lab proposes to elucidate the biological changes and/or mechanisms associated with acute and persistent tick-borne flavivirus infection. Powassan virus infection causes tick-borne encephalitis or encephalomeningitis. Typical signs and symptoms include headache, fever, muscular aches, pains and weakness as well as involvement of the central nervous system including slurred speech, drowsiness or clumsiness. Patients with severe infections have symptoms of stupor, disorientation, coma, tremors, convulsions and spastic paralysis. The natural route of transmission is by the bite of infected ticks (*Ixodes scapularis)*. Powassan virus is not directly transmitted from person to person. Primary lab hazards include: exposure to aerosols, accidental sharps injuries and accidental parenteral inoculation. Long-term sequelae are common, and the case-fatality rate in reported cases is approximately 10%. ▪ Animal studies with mice were proposed. ▪ BSL-3/ABSL-3 is appropriate for work with Powassan virus and Deer Tick virus. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#19-75** as written.
Item 3:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renew) ▪ Bloom (LV) ▪ **PRD#19-58: Langat virus** ▪ Becky Anderson presented the risk assessment. The Bloom lab will examine and characterize changes caused by acute or persistent Langat virus infection in mammalian and tick cells to determine which specific viral proteins are responsible for morphological changes seen upon infection. ▪ Incidence of disease with Langat virus is extremely low; there are no registered cases of human disease. It is a naturally attenuated member of the Tick-borne encephalitis virus serogroup. The virus is completely non-virulent for adult mice following subcutaneous or IP inoculation and primates following intracerebral inoculation. In the few encephalitis cases that arose from a live attenuated LGTV based vaccine, the encephalitis was similar to that seen following infection with typical European strains of TBEV.

	The natural route of transmission is through an infected tick bite, there is no evidence of person to person transmission. The primary lab hazards include accidental parenteral inoculation, contact with broken skin or mucous membranes, and accidental sharps injuries. ▪ Sue Priola noted that the NIH Guidelines should be deleted in the Eukaryote cell section since this is a PRD. ▪ No animal studies were submitted, reviewed, or approved. ▪ BSL-2/ABSL-2 is appropriate for work with Langat virus. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#19-58** with the following minor modifications: 1. Delete the NIH rDNA Guidelines from the Eukaryote Cell section.
Item 4:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Hinnebusch (LB) ▪ **RD#15-303 Amend**: Mutagenesis of virulent *Yersinia pestis* for plague pathogenesis studies ▪ Reviewers: Bob Heinzen, Sue Priola ▪ **Summary:** The RD amendment describes generating *Y. pestis* strains that are fluorescently labeled. ▪ Bob Heinzen summarized the RD. The amendment for the Hinnebusch lab is straightforward. They will express fluorescent proteins in *Y. pestis* using approved plasmids and antibiotic resistance markers. Bob Heinzen had no concerns with the amendment and there were no DURC issues. ▪ Sue Priola stated that since they are using fluorescent tags, they need to add III-D-1-b in Section B. Sue Priola questioned if they will be making these strains or getting them from somewhere else. Clay Jarret stated that they will be making them in their lab with the commercially purchased plasmid. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Clay Jarrett abstained) **RD#15-303 Amend** with the following minor modifications: 1. Add III-D-1-b to section B NIH rDNA Guidelines.

	Research using prokaryotic hosts is approved at BSL-2 and BSL-3 under section III-D-1-b and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-3 under III-D-1-a and III-D-1-b of the NIH Guidelines.
Item 5:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Bloom (LV) ▪ **RD#19-201**: Langat virus ▪ Reviewers: Andrea Marzi, Karin Peterson ▪ **Summary:** Characterization of Langat virus infection in mammalian and tick cells. ▪ Andrea Marzi summarized the RD. This is an RD renewal for Langat virus. The purpose of the study is to characterize and analyze acute or persistent infection. They will perform cloning work and then assess the changes during infection. Overall there were no issues with the RD. In the Eukaryote cell section, it states that cells will be infected and/or transfected. This should be clarified if it is both or either. ▪ Karin Peterson had no additional concerns with the RD, she agreed that the and/or needs to be clarified. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#19-201** with the following minor modifications: 1. Clarify the and/or in the Eukaryote cell section. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a, and III-E-1 of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 and BSL-2 under III-D-1-a of the NIH Guidelines.
Item 6:	Full Committee Review of BSL-4 Inactivation Data ▪ Sue Priola informed the committee that there is inactivation data to review for the BSL-4. Included in this month's submission are 4 separate inactivation methods. ▪ The inactivation data for this review includes: 1. Orthomyxoviridae inactivated by 2% PFA of tissues ($\leq$1 cm^3), and 10% formalin fixation of tissues ($\leq$1 cm^3). 2. Flaviviridae inactivated by 10% formalin fixation of NHP brain

	3. Flaviviridae inactivated by 10% formalin fixation of tissue (≤1 cm^3) 4. Arenaviridae inactivated by 10% formalin fixation of NHP brain ▪ Orthomyxoviridae inactivated by 2% PFA of tissues, and 10% formalin fixation of tissues ▪ Sue Priola confirmed with the committee that the surrogates were appropriate, the samples and titers tested were appropriate, all necessary controls were included and that the procedures matched what is listed in the SOP. ▪ Flaviviridae inactivated by 10% formalin fixation of NHP brain ▪ The committee discussed the use of pig tailed macaque brain as a surrogate tissue for all NHP brains. They agreed that that pig tails are larger than any other NHP they would use in the MCL. ▪ Sue Priola confirmed with the committee that the surrogates were appropriate, the samples and titers tested were appropriate, all necessary controls were included and that the procedures matched what is listed in the SOP. ▪ Flaviviridae inactivated by 10% formalin fixation of tissue 1cm^3 or smaller ▪ Sue Priola questioned (b)(6) where the tissue for the positive control was taken from. (b)(6) informed the committee that the positive control was taken from a piece of the mouse brain that was inactivated (taken prior to placement in 10% formalin). Becky Anderson stated that was not clear in the write-up, but was the appropriate control. ▪ The committee expressed concern that this set of data relies on historical data for the average titer of brain tissue. It was requested that the titers for these specific brains be submitted to the IBC. This data will be used for the maximum titer that can be inactivated with this method. The committee approved the procedure pending titer data. ▪ Arenaviridae inactivated by 10% formalin fixation of NHP brain ▪ The committee expressed the same concern as above about the use of historical data for average titers of the brain tissue. It was requested that the titers for these specific brains be submitted to the IBC. This data will be used for the maximum titer that can be inactivated with this method. The committee approved the procedure pending titer data. ▪ The committee discussed that the table in SOP#4-28-33 needs to be updated to include the large tissue types in a subcategory under the heading "10% formalin—tissues, 30 days". The committee further discussed that the max titers be included in the table for tissue inactivation.

	Action: The committee approved (Andrea Marzi abstained) the following BSL-4 inactivation data as presented: 1. Orthomyxoviridae inactivated by 2% PFA of tissues, and 10% formalin fixation of tissues 2. Flaviviridae inactivated by 10% formalin fixation of NHP brain Action: The committee approved (Andrea Marzi abstained) the following BSL-4 inactivation data pending receipt of titer data: 1. Flaviviridae inactivated by 10% formalin fixation of tissue $1cm^3$ or smaller 2. Arenaviridae inactivated by 10% formalin fixation of NHP brain
Item 7:	**Standard Operating Procedure: SOP#4-28-33 Removal of Specimens for Fluorescence, Immunofluorescence, Histopathology, Immunohistochemistry, and Flow Cytometry (Update)** ▪ Sue Priola summarized the changes to the SOP to the committee. The update to the SOP was the addition of the submitted inactivation procedures for IBC approval. ▪ The committee discussed that only the approved procedures could be added to the table at this time. The committee also decided that the table should be updated to include rows under the 30-day tissues to indicate the large tissue types that are approved. Each tissue that has been approved will no longer have an "x" but instead state the max titer that is approved. ▪ There were no comments or concerns with the updated procedures. Action: The committee approved (Andrea Marzi abstained) the **SOP#4-28-33 Removal of Specimens for Fluorescence, Immunofluorescence, Histopathology, Immunohistochemistry, and Flow Cytometry (Update)** with the following minor modifications: 1. Update table to include rows under the 30-day tissues to indicate the large tissue types that are approved. Each tissue that has been approved will no longer have an "x" but instead state the max titer that is approved.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Not present.
Report:	**Occupational Safety and Health Manager Report/** (b)(6) ▪ Not present.

Report	**IRF Biosafety Manager Report/Megan Brose** ▪ The BSL-4 (b)(6) annual shutdown is complete. During the shutdown BSL-4 staff practiced medical emergency training. ▪ RML is continuing to test larger formaldehyde generators for decon in the BSL-4. RML's maintenance staff have done a wonderful job to work to improve the equipment. ▪ NIAID purchased the Steramist Units and we will begin testing them when they are onsite.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ None

Other issues	▪ Sue Priola informed the committee that there would be no IBC meeting in July.

Next Meeting:

- Date: 8/15/19
- Place: Library conference room
- Time: 1:00 PM

The IBC did not have a July 2019 meeting.

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 08/15/2019
Meeting Time: 1:05 PM **Adjourned:** 2:15 PM
Building A Library, (b)(6)

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Greg Saturday	☒	☐
Bob Heinzen, Vice Chair	☒	☐	Heinz Feldmann (EO)	☐	☒	Alexandra Scranton	☐	☒
Becky Anderson (EO)	☒	☐	Nancy Hoe	☒	☐	Brian Vickrey	☐	☒
Alan Applebury	☐	☒	Erik Hoover	☒	☐			
Chris Bosio	☒	☐	Clay Jarrett	☒	☐			
Marshall Bloom (EO)	☐	☒	Josh Kellar (EO)	☐	☒			
Megan Brose	☒	☐	Scott Kobayashi	☒	☐			
Larry Brouwer	☒	☐	Jamie Lovaglio	☒	☐			
Carol Calderwood	☐	☒	Andrea Marzi	☒	☐			
Marcie Caldwell (EO)	☐	☒	Alida Merritt	☐	☒			
Bruce Chesebro (EO)	☐	☒	Karin Peterson	☒	☐			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 6/20/19 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 6/20/19** Action: Meeting minutes for 6/20/19 were unanimously approved with the following minor modification: 1. Nancy Hoe noted the following: a. In Item 4, the title of the RD should make it clear that this applies to "virulent" *Y. pestis* strains. b. In Item 4, research using prokaryotes section, the biosafety level should be BSL-2 and BSL-3.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals

	(Amend) ▪ Feldmann (LV) ▪ **PRD#18-90 Amend: Filoviridae** ▪ Becky Anderson presented the risk assessment. The amendment is to add work with Mengla virus (MLAV) and animal work with bats. The Feldmann lab has already obtained CDC DSAT approval for work with Filoviruses in bats and SOPs for this work have already been developed and used in the BSL-4 with other agents. Mengla virus genetic material was identified in the bat liver samples from Mengla County China and the sequence was determined by next-gen sequencing. This sequence data has been published. At the genomic level, MLAV shares 39, 41 and 54% nucleotide sequence identity with LLOV, Ebola virus and Marburg virus, respectively. The sequence was then commercially synthesized by U. of Wisconsin collaborators. They will provide the Mengla virus full length plasmid and helper plasmids so that the Feldmann lab can generate the virus via reverse genetics. Mengla virus uses the same entry receptor and demonstrated a similar cell tropism as the other filoviruses ▪ Animal studies with bats were proposed. Animal studies are approved at ABSL-4. ▪ Work with Mengla virus is approved at BSL-4/ABSL-4. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Andrea Marzi abstained) **PRD#18-90 Amend** as written.
Item 2:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renew) ▪ Peterson (LPVD) ▪ **PRD#19-154: Diphtheria toxin** ▪ Becky Anderson presented the risk assessment. Proposed studies include the use of diphtheria toxin to deplete specific cell types from transgenic mice. These mice express an inducible diphtheria toxin receptor, treatment of mice with diphtheria toxin ablates specific cell types so that they can study how various cell types affect La Crosse virus pathogenesis. The toxin, when absorbed, affects organs and tissues distant from the site of invasion. The most frequent complications of diphtheria are myocarditis and neuritis. The overall case-fatality rate for diphtheria is 5%–10%, with higher death rates (up to 20%) among persons older than 40 years of age. Treatment with hyperimmune antiserum has been shown to reduce mortality from 7 to 2.5%. Antibodies only neutralize toxin before its entry into cells, so rapid

	treatment is essential. Because the diphtheria antiserum is produced in horses, up to 10 percent of treated individuals may develop serum sickness. Primary lab hazards include contact with skin, inhalation, and accidental needlesticks. ▪ The recommendations section also includes the statement that preparative work with the toxin should be done in a ducted BSC or chemical fume hood at BSL-2 with proper PPE (lab coat/gloves). Refer to BMBL appendix I for more details on toxins. ▪ Nancy Hoe pointed out that the statement in the recommendations section should be updated to the following, "Preparative work should be done in a ducted BSC or chemical fume hood wearing appropriate PPE (gloves/eye protection) and all toxin-containing waste should be inactivated by autoclaving at 121C/15psi/60 min or chemical inactivation prior to disposal". ▪ Sue Priola noted that DTX needs to be defined in the Synopsis section. ▪ Sue Priola also informed the committee that the company should be listed with the product number in the pathogen section. Karin Peterson asked if that locked her in to purchasing from that specific vendor. The IBC agreed that it would give Karin Peterson more flexibility to remove the product number so she was not restricted to one company for purchasing. ▪ Animal studies with mice were proposed. ▪ BSL-2/ABSL-2 is appropriate for work with diphtheria toxin. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved (Karin Peterson abstained) **PRD#19-154** with minor modifications: 1. Define diphtheria toxin in the synopsis section. 2. Update statement in the recommendations section to, "Preparative work should be done in a ducted BSC or chemical fume hood wearing appropriate PPE (gloves/eye protection) and all toxin-containing waste should be inactivated by autoclaving at 121C/15psi/60 min or chemical inactivation prior to disposal". 3. Remove catalog number from Pathogen section.
Item 3:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renew)</u> ▪ Peterson (LPVD) ▪ **PRD#19-162: Herpes simplex virus 1 (HSV-1)**

	▪ Becky Anderson presented the risk assessment. The proposed studies are to examine how the innate immune response affects HSV-1 infection and pathogenesis of the central nervous system (CNS). HSV-1 is associated mainly with above the waist Herpes infections involving the mouth pharynx, face, eye, and CNS. HSV-2 is associated mainly with genital herpes. Primary infections with HSV-1 are usually acquired in childhood and may be asymptomatic or subclinical. Symptomatic primary infections present mainly as gingivostomatitis with fever, sore throat, fetor oris, anorexia, cervical adenopathy, and mucosal edema and vesicular and ulcerative painful lesions involving the buccal mucosa, tongue, gums, and pharynx. Ulcers heal within 2-3 weeks. Recurrent infections have generally milder symptoms and clinical course. Ocular infections can occur, and more serious infections of the CNS can occur in both children and adolescents. If HSV encephalitis is left untreated, mortality can be as high as 70%. HSV-1 can also cause genital herpes, although it is not as common as HSV-2. Infections are transmitted through contact with HSV in herpes lesions, mucosal surfaces, genital secretions, or oral secretions. Antiviral drugs can inhibit viral replication. The primary lab hazards include: direct contact with viral isolates, aerosolization, droplet or inhalation exposure of mucous membranes of the eyes, nose, or mouth, ingestion, accidental parenteral inoculation. ▪ Precautions that have been added to the recommendations section state: "When working with purified virus or conducting any procedures that might create splashes, goggles should be worn. Aerosol generation with tissue homogenizer; have a plan to look before opening and for opening if there is a broken/ruptured tube". ▪ Sue Priola informed the committee that the NIH Guidelines in the Eukaryote Cell section should be removed and replaced with N/A. ▪ Animal studies with mice were proposed. ▪ BSL-2/ABSL-2 is appropriate for work with HSV-1. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved (Karin Peterson abstained) **PRD#19-162** with the following minor modifications: 1. Delete the NIH rDNA Guidelines from the Eukaryote Cell section and replace with N/A.
Item 4:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment)</u> ▪ Peterson (LPVD)

	▪ **PRD#18-103 Amend: Bunyaviruses** ▪ Becky Anderson presented the risk assessment. The amendment to the PRD is to allow for co-infections and reassortments of different members of the California Serogroup (CSG) of orthobunyaviruses. These viruses have overlapping geographical distributions in nature and have the potential to infect the same animals. The Peterson lab would like to study the effect of reassortment and coinfection of these viruses. The IBC extensively discussed the dual use potential of these types of experiments. The biggest concern was for dual use question 5, i.e. could this expand the host range. The committee discussed and determined that since reassortants already occur naturally these experiments do not pose dual use research of concern. ▪ Becky Anderson explained that the amendment for this meeting is split into Amend 0002 and Amend 0001 (as automatically numbered by the HealthRx system). Amend 002 describes co-infections and reassortants. Amend 0001 describes co-infections in mice in greater detail. ▪ Nancy Hoe stated that Amend 0001 should have question 7C in the dual use questionnaire clarified. The wording as written makes it sound like co-infections with the more virulent strain cannot occur. This is just a wording issue and the sentence should just be made clearer. ▪ Animal studies with mice were proposed. ▪ BSL-2/ABSL-2 is appropriate for work with Bunyaviruses. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved (Karin Peterson abstained) **PRD#18-103 Amend** with the following minor modifications: 1. Add justification for Q5 not being dual use of concern in Amend 001, provided by Karin Peterson and discussion during the IBC meeting. 2. Clarify sentence in justification of Question 7C in the Amend 002.
Item 5:	<u>Registration Documents for Recombinant DNA Experiments (Renew)</u> ▪ Peterson (LPVD) ▪ **RD#19-221**: Lentivirus ▪ Reviewers: Chris Bosio, Bob Heinzen ▪ **Summary:** Lentiviruses ▪ Chris Bosio summarized the RD. This is an RD renewal for lentiviral work, there are no changes to the renewal. The Peterson lab will use the system to express SARM1 or portions of it to repress expression. They will investigate the

	mechanisms of SARM1-mediated cell death. ▪ Bob Heinzen asked if we need to register lentiviral systems. Nancy Hoe stated that according to the NIH, they must be registered. Bob Heinzen had no comments or concerns with the renewal. ▪ Sue Priola pointed out in the Research Product section that III-D-3-a should be added. ▪ BSL-2/ABSL-2 is appropriate for the described work with Lentiviruses. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved (Karin Peterson abstained) **RD#19-221** with the following minor modifications: 1. Add III-D-3-a to the Research Product section. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a, and III-E-1 of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-2-a and III-E-1 of the NIH Guidelines.
Item 6:	<u>Registration Documents for Recombinant DNA Experiments (Renew)</u> ▪ Peterson (LPVD) ▪ **RD#19-214**: Retroviruses ▪ Reviewers: Sue Priola, Scott Kobayashi ▪ **Summary:** Retroviruses ▪ Sue Priola summarized the RD. This is an RD renewal for work with murine retroviruses. There have been no changes to the RD for the renewal. The proposed work includes studies with neurovirulent and non-neurovirulent viruses. Studies will include generating various recombinants for 9 specific amino acid residues that influence neurologic disease. These viruses will be studied to determine how differences in the virus envelope protein influence the host response to virus infection. ▪ Scott Kobayashi had no additional comments or concerns. ▪ BSL-1/ABSL-1 is appropriate for the described work with murine retroviruses. Theses labs however, are registered as BSL-2 laboratories. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns

	with the proposal. Action: The committee approved (Karin Peterson abstained) **RD#19-214** as written. Research using prokaryotic hosts is approved at BSL-1 under Appendix C-II of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-1 under III-D-3-e of the NIH Guidelines.
Item 7:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Feldmann (LV) ▪ **RD#16-450 Amend**: Lloviu virus Reverse Genetics ▪ Reviewers: Karin Peterson, Sue Priola ▪ **Summary:** This RD describes the reverse genetics system for work with Lloviu virus. ▪ Karin Peterson summarized the RD. The amendment to this RD is to add Mengla virus. Mengla virus was described earlier in the PRD amendment for the Feldmann lab. This RD describes a reverse genetics system that is used for Lloviu virus and they will use the same for Mengla virus. University of Wisconsin has made most of the Mengla virus, the rest will be done at RML. The Feldmann lab answered yes to DURC question 7B because the virus will be synthesized and is being reverse engineered. ▪ Sue Priola stated that the registration also included an email from (b) (6) (b) (6) confirming that the University of Wisconsin IBC approved the generation of these clones. She had no additional comments or concerns. ▪ BSL-4/ABSL-4 is appropriate for the described work with Mengla virus. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Andrea Marzi abstained) **RD#16-450 Amend** as written. Research using prokaryotic hosts is approved at BSL-2 under Section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-4 under Sections III-D-1-a, III-D-1-c, and III-D-3-c of the NIH Guidelines.
Item 7:	**Working Group Summary** ▪ Sue Priola presented the Working Group summary and associated SOP (see Item 4 below). Andrea Marzi and Clay Jarrett were the working group members that reviewed the inactivation methods from Bob Heinzen's lab. ▪ The purpose of the validation was to be able to extract LPS from *Coxiella*

	burnetii using phenol and to remove those samples from BSL-3 containment for downstream LPS extraction. ▪ See attached summary. The Heinzen lab tested the ability of phenol at room temperature to inactivate *C. burnetii*. They tested 400 ml of $1x10^9$ bacteria/ml and demonstrated in three different experiments that all the bacteria were inactivated. Sue Priola described the carryover controls that were used in the studies and the discussions that the working group had about the controls. ▪ The Working Group recommended changes to SOP-BSL-3-Cb-5 that were incorporated in the draft document. ▪ The committee agreed with the WG group recommendation that treatment of *C. burnetii* with phenol for 5 minutes at room temperature was a validated method for inactivating *C. burnetii*. Action: The committee approved (Bob Heinzen abstained) the Working Group recommendation that treatment with phenol completely inactivated *C burnetii* and approved the validation studies as written.
Item 8:	**Standard Operating Procedure: BSL-3-Cb-5 Inactivation of Coxiella burnetii and subcomponents for removal from the BSL-3 laboratory (Update)** ▪ Sue Priola summarized the changes to the SOP to the committee. The update to the SOP was the addition of the submitted inactivation procedures for IBC approval. The working group requested the maximum titer should be included and the procedures for pelleting the bacteria should be included. Both of those were added in the version that was submitted to the committee. ▪ There were no comments or concerns with the updated procedures. Action: The committee approved (Bob Heinzen abstained) the **BSL-3-Cb-5 Inactivation of Coxiella burnetii and subcomponents for removal from the BSL-3 laboratory (Update)** as written.
Item 9:	Full Committee Review of BSL-4 Inactivation Data ▪ Sue Priola informed the committee that there is inactivation data to review for the BSL-4. Included in this month's submission are 4 separate inactivation methods/viral families. ▪ The inactivation data for this review includes the following: ▪ Flaviviridae inactivated by 2% PFA of cells, and 10% formalin fixation of cells ▪ Sue Priola confirmed with the committee that the surrogates were appropriate, the samples and titers tested were appropriate, all necessary controls were included and that the procedures matched what is listed in the SOP.

	▪ Bunyaviridae inactivated by 10% formalin fixation of cells ▪ Sue Priola confirmed with the committee that the surrogates were appropriate, the samples and titers tested were appropriate, all necessary controls were included and that the procedures matched what is listed in the SOP. ▪ Arenaviridae inactivated by 10% formalin fixation cells and 2% PFA fixation of cells ▪ Sue Priola confirmed with the committee that the surrogates were appropriate, the samples and titers tested were appropriate, all necessary controls were included and that the procedures matched what is listed in the SOP. ▪ Paramyxoviridae inactivated by 10% formalin fixation of cells and 2% PFA fixation of cells ▪ Sue Priola confirmed with the committee that the surrogates were appropriate, the samples and titers tested were appropriate, all necessary controls were included and that the procedures matched what is listed in the SOP. Action: The committee approved (Andrea Marzi abstained) the following BSL-4 inactivation data as presented: 1. Flaviviridae inactivated by 2% PFA of cells, and 10% formalin fixation of cells 2. Bunyaviridae inactivated by 10% formalin fixation of cells 3. Arenaviridae inactivated by 10% formalin fixation cells and 2% PFA fixation of cells 4. Paramyxoviridae inactivated by 10% formalin fixation of cells and 2% PFA fixation of cells
Item 10:	**Standard Operating Procedure: SOP#4-28-33 Removal of Specimens for Fluorescence, Immunofluorescence, Histopathology, Immunohistochemistry, and Flow Cytometry (Update)** ▪ Sue Priola summarized the changes to the SOP to the committee. The update to the SOP was the addition of the submitted inactivation procedures for IBC approval. ▪ Becky Anderson noted that this update includes the removal of an inactivation method, 2% glutaraldehyde. ▪ There were no comments or concerns with the updated procedures. Action: The committee approved (Andrea Marzi abstained) the **SOP#4-28-33 Removal of Specimens for Fluorescence, Immunofluorescence, Histopathology,**

	Immunohistochemistry, and Flow Cytometry (Update) as written.
Item 6:	**Standard Operating Procedure: BSL-3-Cb-7 Spectramax iD3 Plate Reader (New)** ▪ Becky Anderson summarized the new SOP to the IBC. The SOP is new for the Heinzen lab, they will be using a new plate reader in their BSL-3 lab. This SOP describes transport from the BSC to the benchtop and back as well as indicates that the shaking mechanism must be turned off. ▪ Nancy Hoe asked what type of 96 well plate will be used and how secure the lid is. Bob Heinzen showed the IBC the type of plate they intend to use. The committee expressed concern that if dropped the plate could allow for some small splashes. Several members of the committee suggested different plates as well as an adhesive lid that might work better. ▪ The committee agreed that the Heinzen lab should test plates with secured lids prior to approving the SOP. Action: The committee TABLED (Bob Heinzen abstained) the **BSL-3-Cb-7 Spectramax iD3 Plate Reader (New).** 1. Identify an improved lid for the plates to be used in the plate reader.
Item 7:	**RML Exposure Control Plan (ECP) (Annual Review)** ▪ Becky Anderson informed the committee of the updates to the ECP. ▪ Becky Anderson presented to the committee the safer sharps devices that were evaluated by lab staff that perform animal work in the BSL-4. Of the three devices tested, the group seemed to prefer a retractable needle design that was easy to use. ▪ There were no comments or concerns with the updated document. Action: The committee unanimously approved the **RML Exposure Control Plan (Annual Review)** as written.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Reviewed the BSO report. ▪ Informed the committee that USAMRIID was issued a letter from CDC DSAT to cease and desist Select Agent work.
Report:	**Occupational Safety and Health Manager Report/**(b) (6) ▪ Not present.

Report	**IRF Biosafety Manager Report/Megan Brose** ▪ Becky Anderson and I attended the RO/ARO Workshop in July. It sounds like other entities have the same inactivation frustrations with CDC DSAT that we have at RML. CDC DSAT still did not provide justification for use of viral families as surrogate for inactivation.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ None

Other issues	▪ None

Next Meeting:

- Date: 9/19/19
- Place: Library conference room
- Time: 1:00 PM

RML Biosafety Committee Meeting
August 15, 2019
Biosafety Officer/Responsible Official Report

1) ***Requests approved by BSO since last meeting:***
   a) *None*
2) ***New requests approved by committee via electronic review:***
   a) *Validation Studies*
      (a) *Validation studies and associated SOPs for formalin inactivation of large tissues infected with filoviruses or paramyxoviruses*
         (a) *IBC approved August 6, 2019*
3) ***New requests***
   a) *Pathogen Registration Documents*
      i) ***Amend***
         (a) *Feldmann (LV)*
            (a) ***PRD-18-90****: Filoviridae*
               (i) Add Mengla virus
               (ii) Add animal work with bats
      ii) ***Renewals***
         (a) *Peterson (LPVD)*
            (a) ***PRD-19-154****: Diptheria toxin*
            (b) ***PRD 19-162****: Herpes simplex virus (HSV-1)*
            (c) ***PRD 18-103****: Bunyaviruses*
   b) *Registration Documents for Recombinant Nucleic Acid Experiments*
      i) ***Amend***
         (a) *Feldmann (LV)*
            (a) ***RD-16-450****: Lloviu virus reverse genetics*
               (i) Add Mengla virus
      ii) ***Renewals***
         (a) *Peterson (LPVD)*
            (a) ***RD-19-221****: Use of lentiviral vector transduction of small hairpin RNAs (shRNA) and cDNAs to examine mechanisms of La Crosse Virus infection and cell death*
            (b) ***RD-19-214****: recombinant polytropic retroviruses*
   c) *Working Group Summaries of Inactivation Validation Testing Review*
      i) *Heinzen (LB)*

(a) *Inactivation of Coxiella burnetii in LPS purifications*

d) *Inactivation Validation Testing Review*

i) *Feldmann (LV)*

(a) *Inactivation of RG4 viral families (Flavi -, Bunya -, Arena -, and Paramyxo -) with formalin and PFA*

4) ***Standard Operating Procedures***

i) ***Update***

(a) *SOP#BSL-3-Cb-5: Inactivation of Coxiella*

(a) *Add procedures for inactivation of Coxiella for LPS purification*

(b) *SOP#BSL-3-Cb-7: Use of Spectramax iD3 Plate Reader*

(a) *Add procedures for use of Spectramax iD3 Plate Reader*

(c) *SOP#4-28-33: Removal of specimens for Fluorescence, Immunofluorescence, Histopathology, Immunohistopathology, and Flow Cytometry*

(a) *Update procedures for additional viral families*

5) ***Exposure Control Plan Annual Review***

6) ***Animal Study Protocols Review***

Title	***Associated PRD***	***Associated RD***	***Reviewer***
Competence of B. burgdorferi Variants in the Mouse/tick Infectious Cycle	*18-24 (Borrelia burgdorferi)*	*14-308*	*N. Hoe*
Effect of Mosquito Salivary Gland extract and proteins on Zika virus pathogenesis in mice	*16-184 (Zika virus)*	*18-IV-05 (NIH RD)*	*N. Hoe*
Protective efficacy of a VSV-based Yellow Fever vaccine against challenge in the mouse model	*19-216 (Yellow fever viruses) 18-90 (Ebola virus) 18-82 (VSV)*	*15-404*	*N. Hoe*
Sex-dependent survival of hDPP4 mice infected with MERS-CoV	*17-143 (MERS-CoV)*	*N/A*	*M. Brose*
Control of Allergic Inflammation with Francisella lipids and Francisella Inspired Liposomes	*NA*	*N/A*	*N. Hoe*
Defining the minimal dose of VSV-EBOV that provides rapid protection in cynomolgus macaques	*15-442 (Cytomegalovirus)*	*N/A*	*N. Hoe*
Experimental Ebola and Marburg virus infection in Artibeus jamaicensis bats	*18-90 (Ebola, Marburg virus)*	*N/A*	*R. Anderson*
Experimental Nipah and Hendra virus infection in Artibeus jamaicensis bats	*18-91 (Nipah, Hendra virus)*	*N/A*	*R. Anderson*
Study of the evolution of HIV-1 in TKO-BLT humanized mice during antiretroviral therapy and post withdrawal	*18-55 (HIV)*	*N/A*	*N. Hoe*
Shedding of Salmonella in a mouse chronic disease model	*18-44 (Salmonella enterica serovar Typhimurium)*	*15-108*	*M. Brose*
Transmission of MERS-CoV within immunocompromised hDPP4 transgenic mice	*17-143 (MERS-CoV)*	*N/A*	*M. Brose*
Evaluation of a nanoparticle delivered RNA replicon encoding anti-MERS-CoV antibody VHH-83 in mice	*17-143 (MERS-CoV)*	*17-452*	*M. Brose*

RML Biosafety Committee Meeting
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7) ***Biosafety Training Performed – Megan Brose, Rebecca Anderson***

Type of Training	***Number of Sessions***	***Number of Employees Trained***
BSL-3 Laboratory Biosafety	*2*	*5*
BSL-3 Practical	*3*	*3*
BSL-4 Laboratory Biosafety	*7*	*8*
BSL-4 Annual Refresher Training	*1*	*1*
Select Agent Initial	*2*	*7*
Select Agent Visitor	*2*	*2*
Full-Length Clone Lab Initial Training	*1*	*1*
BSL-4 Emergency Medical Extraction	*2*	*8*
Biosafety Brief	*1*	*WIP*

8) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
a) *Biological Incident Report:*
   i) *None*

9) ***Select Agent Issues***
a) *None*

10) ***Other Issues –***
a) *USAMRIID cessation of select agent research*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 09/19/2019
Meeting Time: 1:01 PM **Adjourned:** 2:00 PM
Building A Library, (b)(6)

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Greg Saturday	☒	☐
Bob Heinzen, Vice Chair	☒	☐	Heinz Feldmann (EO)	☐	☒	Alexandra Scranton	☐	☒
Becky Anderson (EO)	☒	☐	Nancy Hoe	☒	☐	Brian Vickrey	☐	☒
Alan Applebury	☐	☒	Erik Hoover	☐	☒			
Chris Bosio	☒	☐	Clay Jarrett	☒	☐			
Marshall Bloom (EO)	☐	☒	Josh Kellar (EO)	☐	☒			
Megan Brose	☒	☐	Scott Kobayashi	☒	☐			
Larry Brouwer	☐	☒	Jamie Lovaglio	☐	☒			
Carol Calderwood	☐	☒	Andrea Marzi	☒	☐			
Marcie Caldwell (EO)	☐	☒	Alida Merritt	☒	☐			
Bruce Chesebro (EO)	☐	☒	Karin Peterson	☐	☒			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 8/15/19 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 8/15/19** Action: Meeting minutes for 8/15/19 were unanimously approved with the following minor modifications: 1. Nancy Hoe & Sue Priola noted a few minor typos.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amend) ▪ de Leo (LB) ▪ **PRD#18-1 Amend: *Staphylococcus aureus***

	▪ Becky Anderson presented the risk assessment. The amendment is to add work with *Staphylococcus epidermidis*. The proposed studies are to evaluate evasion of innate immunity by human bacterial pathogens. Infections caused by *S. epidermidis* and other coagulase-negative staphylococci are chronic, which contrasts the potential of *S. aureus* to cause acute disease. *S. epidermidis* infections are commonly nosocomial and typically develop in the immune compromised. *S. epidermidis* is known for causing infections on indwelling medical devices. The coagulase-negative staphylococci have been implicated as the causative agents in urinary tract disease, catheter related infections, shunt infections, pneumonia, endophthalmitis, surgical wound infections, breast abscess, osteomyelitis, and native valve endocarditis. Antibiotics are effective against *S. epidermidis*, but there are some antibiotic resistant strains that are typically treated with vancomycin. ▪ No animal studies were submitted, reviewed, or approved. ▪ Work with *S. epidermidis* is approved at BSL-1/ABSL-1, however this lab is registered as a BSL-2 lab because of work with other pathogens. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved (Scott Kobayashi abstained) **PRD#18-1 Amend** as written.
Item 2:	<u>Registration Documents for Recombinant DNA Experiments (Amendment)</u> ▪ Steele-Mortimer (LB) ▪ **RD#14-126 Amend**: Salmonella cancer vaccine ▪ Reviewers: Andrea Marzi, Sue Priola ▪ **Summary:** Antigen delivery system with recombinant attenuated Salmonella Vaccine (RASV) ▪ Andrea Marzi summarized the RD. This is an RD amendment to their antigen delivery (RASV) platform that was previously approved. Now they want to make visual confirmation of antigen delivery with fluorescence. The RD describes modifying the plasmid in four different ways, but all the changes are straightforward. They also would like to include one more antigen to deliver, the Lassa virus nucleoprotein. ▪ Sue Priola stated that she did not see any problems with the RD. The fluorescence is so that they can track antigen delivery. ▪ Clay Jarrett asked about the basis for the attenuation of Salmonella. He wanted to know why they are adding virulence genes back into the bacterium. The committee discussed and agreed there are multiple genes that are involved in the attenuation of the Salmonella strain and that the mammalian promoter will

	drive expression of the antigens within the mammalian cells only. ▪ BSL-2/ABSL-2 is appropriate for the described work with Salmonella. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#14-126 Amend** as written. Research using prokaryotic hosts is approved at BSL-2 under section III-D-1-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a of the NIH Guidelines.
Item 3:	Full Committee Review of Bosio 10X Genomics Single Cell Sequencing Inactivation Data ▪ Sue Priola informed the committee that there is inactivation data to review for the Bosio lab. Included in this month's submission is testing data for inactivation of *Francisella tularensis* SchuS4 infected murine tissue during 10X Genomics single cell sequencing library preparation. ▪ Sue Priola summarized the testing results for treating mouse tissues infected with *F. tularensis* with 10X genomics single cell sequencing reagents. Sue Priola confirmed with the committee that the samples and titers tested were appropriate, all necessary controls were included and that the procedures matched what is listed in the SOP. ▪ (b)(6) explained to the committee what type of information they can gain from performing single cell sequencing experiments. She also described the limitations on testing additional samples because of the kit design and cost. The committee agreed that the controls used were appropriate. Action: The committee approved (Chris Bosio abstained) the inactivation data using the 10X genomics single cell sequencing reagents as presented.
Item 4:	**Standard Operating Procedure: BSL3-C-8 Inactivation of Francisella spp. (Update)** ▪ Sue Priola summarized the SOP changes to the committee. The update to the SOP was the addition of the submitted inactivation procedures for IBC approval. ▪ There were no comments or concerns with the updated procedures. Action: The committee approved (Chris Bosio abstained) the **BSL3-C-8 Inactivation of Francisella spp. (Update)** as written.
Item 5:	**Standard Operating Procedure: BSL-3-Cb-7 Spectramax iD3 Plate Reader (New)** ▪ Sue Priola summarized the SOP changes to the committee. This SOP was tabled

	last month because the Heinzen lab was going to look at options for sealing the 96 well plates that will be placed in the Spectramax iD3 plate reader. The Heinzen lab will seal the plates with optical sealing tape as described in the SOP. ▪ There were no comments or concerns with the updated procedures to the new SOP. Action: The committee approved (Bob Heinzen abstained) the **BSL-3-Cb-7 Spectramax iD3 Plate Reader (New)** as written.
Item 6:	**Standard Operating Procedure: ABSL-3 Operations and Safety Procedures (OSP) (Annual Review)** ▪ Becky Anderson summarized the changes to the ABSL-3 OSP. The text for the minimum PPE for the ABSL-3 was clarified. The fever description was updated to match the OMS language for a fever. The number of mouse carcasses that can be bagged together for autoclaving has been increased from 10 to 15 after re-validation by biosafety. Biosafety also tested a total load weight for autoclaving carcasses that has been included in the OSP. ▪ Sue Priola asked why it states, "if applicable" after the listing of minimum PPE on page 25. Becky Anderson stated the "if applicable" applied to the respiratory protection. The committee agree that "if applicable" should be moved before respiratory protection to make the statement clearer. ▪ Alex Scranton submitted minor typos by email. ▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved the **ABSL-3 Operations and Safety Procedures (OSP) (Annual Review) with the following minor modifications:** 1. Correct minor typos. 2. Move "if applicable" to immediately before respiratory protection on page 25.
Item 7:	**Standard Operating Procedure: BSL-3 Operations and Safety Procedures (OSP) (Annual Review)** ▪ Becky Anderson summarized the changes to the BSL-3 OSP. The maintaining select agent inventories section was updated to clarify that the date on a vial may differ from the date added to inventory and included procedures for noting this difference. ▪ Alex Scranton submitted minor typos by email. ▪ There were no comments or concerns with the updated procedures.

	Action: The committee unanimously approved the **BSL-3 Operations and Safety Procedures (OSP) (Annual Review) with the following minor modifications:** 1. Correct minor typos.
Item 8:	**Standard Operating Procedure: SOP#4-28-12 Dunk Tank Operation (Update)** ▪ Becky Anderson summarized the change to the SOP. The changes are to the Dunk Tank Activity Log/Inactivation Certificate (Clean Side). The changes specify that the full name should be written, and "Approval" was spelled out. ▪ There were no comments or concerns with the updated procedures. Action: The committee approved (Andrea Marzi abstained) the **SOP#4-28-12 Dunk Tank Operation (Update)** as written.
Item 9	**Standard Operating Procedure: SOP#4-28-14 Maintaining Select Agent Inventories (Update)** ▪ Becky Anderson summarized the change to the SOP. Computer listing and lab notebook examples of a reference ID were removed and replaced with the computer database. The Attachment E was removed as the computer database replaced this method of written record. ▪ There were no comments or concerns with the updated procedures. Action: The committee approved (Andrea Marzi abstained) the **SOP#4-28-14 Maintaining Select Agent Inventories (Update)** as written.
Item 10:	**Standard Operating Procedure: SOP#4-28-33 Removal of Specimens for Fluorescence, Immunofluorescence, Histopathology, Immunohistochemistry, and Flow Cytometry (Update)** ▪ Becky Anderson summarized the changes to the SOP. The SOP has been updated to include procedures from SOP#4-28-42 for neutralization of formalin and paraformaldehyde waste using FORMALEX GREEN. With this change, SOP#4-28-42 will be inactivated. ▪ Greg Saturday stated that the SOP uses more Formalex than the manufacturer's instructions state. The committee discussed and agreed that Becky Anderson should verify with the staff that did the initial testing to see if it was their intent to use more Formalex. The committee was fine with keeping the SOP the same if there was reason to do so or updating the SOP if the BSL-4 wanted to change to match manufacturer's instructions. ▪ Alex Scranton submitted a comment by email. She questioned why absorbent pads were listed as material needed, but never used. Becky Anderson

	responded that they would use them if there was a spill, but they do all the pouring in the sink. Absorbent pads will be removed from the list of materials. ▪ There were no additional comments or concerns with the updated procedures. Action: The committee approved (Andrea Marzi abstained) the **SOP#4-28-33 Removal of Specimens for Fluorescence, Immunofluorescence, Histopathology, Immunohistochemistry, and Flow Cytometry (Update)** with minor modifications: 1. Potentially update the amount of Formalex to add based on response from BSL-4 users. 2. Remove absorbent pads from list of materials.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Reviewed the BSO report. ▪ Reviewed an incident from the ABSL-3 lab. A researcher sustained a needlestick while inoculating mice with *Y. pestis* in the ABSL-3. The individual followed procedures for responding to a needlestick and reported as appropriate.
Report:	**Occupational Safety and Health Manager Report** ▪ Not present.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ Not present.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ Alida Merritt informed the committee that Marcus Daly Memorial Hospital (MDMH) decided to assess their staff immunity to measles. Staff had to provide proof of two MMR vaccinations or proof of titer. It has been a long process but MDMH wanted to be ahead of the curve if there were to be an outbreak in Ravalli County. ▪ The pertussis outbreak in Missoula is steady and Ravalli County has 3 cases (2 adults and 1 child). There has been one positive influenza case in Ravalli County as well.

Other issues	▪ None

Next Meeting:

- Date: 10/17/19
  Place: Library conference room
- Time: 1:00 PM

RML Biosafety Committee Meeting
September 19, 2019
Biosafety Officer/Responsible Official Report

1) ***Requests approved by BSO since last meeting:***
    a) ***Update***
        i) *Standard Operating Procedures Coxiella burnetii, Rickettsia spp. BSL-3 Facility*
            (a) *Removed references to Roccal-D*
            (b) *Approved September 4, 2019*
2) ***New requests approved by committee via electronic review:***
    a) *None*
3) ***New requests***
    a) *Pathogen Registration Documents*
        i) ***Amend***
            (a) *DeLeo (LB)*
                (a) ***PRD-18-1****: Staphylococcus aureus*
                    (i) Add Staphylococcus epidermidis
    b) *Registration Documents for Recombinant Nucleic Acid Experiments*
        i) ***Amend***
            (a) *Steele-Mortimer (LB)*
                (a) ***RD-14-126****: Salmonella cancer vaccine*
                    (i) Add use of Cre recombinase as the delivery gene/protein to enable visual detection of antigen delivery in vitro
    c) *Inactivation Validation Testing Review*
        i) *Bosio (LB)*
            (a) *Inactivation of Francisella tularensis SchuS4 infected murine tissue during 10X Genomics single cell sequencing library preparation*
    d) ***Standard Operating Procedures***
        i) ***Update***
            (a) *SOP#BSL-3-C-8: Inactivation of Francisella tularensis*
                (a) *Add procedures for inactivation of Francisella tularensis SchuS4 in murine tissue by 10X Genomics GEM generation and GEM-RT PCR*
            (b) *SOP#BSL-3-Cb-7: Use of Spectramax iD3 Plate Reader*
                (a) *Add procedures for use of Spectramax iD3 Plate Reader (**TABLED** from 8-15-19 mtg)*

(c) ***Annual Biosafety Plan Review***

(a) *ABSL-3 Operations and Safety Procedures*

(i) Annual review

(b) *BSL-3 Operations and Safety Procedures*

(i) Annual review

(c) *SOP#: 4-28-12 Dunk Tank Operation*

(i) Update inactivation certificate

(d) *SOP#: BSL-4-28-14 Maintaining Select Agent Inventories*

(i) Remove example of experimental sample computer list

(e) *SOP#: 4-28-31 Removal of Specimens for Protein Analysis*

(i) Remove section on tissue specimens

(f) *SOP#: 4-28-33 Removal of Specimens for Fluorescence, Immunofluorescence, Histopathology, Immunohistopathology, and Flow Cytometry*

(i) Add procedures for collecting and neutralizing formalin and paraformaldehyde waste from SOP#4-28-42

4) ***Animal Study Protocols Review***

Title	***Associated PRD***	***Associated RD***	***Reviewer***
Assessing T-705 as a countermeasure to Lassa fever in Cynomolgus macaques	*17-138 (Lassa virus)*	*N/A*	*N. Hoe*
Amplification and isolation of a unique rodent cytomegalovirus in Mastomy Natalensis	*15-442 (Cytomegalovirus)*	*N/A*	*R. Anderson*
Role of Salmonella virulence factors in invasion of mouse meninges	*18-44 (Salmonella enterica)*	*15-108*	*R. Anderson*
Normal Laboratory Animal Blood and Tissue Donors to Support Ongoing Research	*N/A*	*N/A*	*N. Hoe*
Development of Guinea Pig Reagents	*NA*	*N/A*	*M. Brose*
Protective efficacy of the rVSV-EBOV-HA vaccine against highly pathogenic H5N1 influenza A virus infection in mice	*17-202 (Influenza A virus H5N1) 18-82 (VSV)*	*15-404*	*N. Hoe*
Characterizing the humoral response induced by ChAdOx1-vectored vaccines encoding Lassa virus glycoprotein and/or nucleoprotein	*N/A*	*17-410*	*N. Hoe*

5) ***Biosafety Training Performed – Megan Brose, Rebecca Anderson, Nancy Hoe***

RML Biosafety Committee Meeting
September 19, 2019
Biosafety Officer/Responsible Official Report

Type of Training	*Number of Sessions*	*Number of Employees Trained*
BSL-3 Practical	*2*	*3*
BSL-3 Visitor	*1*	*1*
BSL-4 Laboratory Biosafety	*10*	*6*
BSL-4 Annual Refresher Training	*2*	*27*
Biosafety for Support Personnel	*1*	*1*
Select Agent Visitor	*1*	*1*
Select Agent Refresher	*4*	*92*
Biosafety Brief	*1*	*WIP*

6) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
   a) *Biological Incident Report:*
      i) *Needlestick with exposure to Yersinia pestis*

7) ***Select Agent Issues***
   a) *None*

8) ***Other Issues –***
   a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 10/17/2019
Meeting Time: 1:03 PM **Adjourned:** 1:39 PM
Building A Library, (b)(6)

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Greg Saturday	☒	☐
Bob Heinzen, Vice Chair	☒	☐	Heinz Feldmann (EO)	☐	☒	Alexandra Scranton	☐	☒
Becky Anderson (EO)	☒	☐	Nancy Hoe	☐	☒	Brian Vickrey	☐	☒
Alan Applebury	☐	☒	Erik Hoover	☐	☒			
Chris Bosio	☒	☐	Clay Jarrett	☒	☐			
Marshall Bloom (EO)	☐	☒	Josh Kellar (EO)	☐	☒			
Megan Brose	☒	☐	Scott Kobayashi	☒	☐			
Larry Brouwer	☒	☐	Jamie Lovaglio	☒	☐			
Carol Calderwood	☐	☒	Andrea Marzi	☒	☐			
Marcie Caldwell (EO)	☐	☒	Alida Merritt	☐	☒			
Bruce Chesebro (EO)	☐	☒	Karin Peterson	☒	☐			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 9/19/19 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 9/19/19** Action: Meeting minutes for 9/19/19 were unanimously approved with the following minor modifications: 1. Sue Priola noted a few minor typos.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New) ▪ Munster (LV) ▪ **PRD#19-217: *Bacillus anthracis* (exempt)**

	▪ Becky Anderson presented the risk assessment. The Munster lab plans to work with *B. anthracis* exempt strains in order to prepare positive controls for a field diagnostic qRT-PCR assay. This assay is being developed to test for the presence of various pathogens in field samples collected from animal carcasses encountered during field work. *Bacillus anthracis* is a spore-forming bacterium that causes anthrax in humans and animals. *B. anthracis* has 3 main virulence factors coded on two plasmids, pXO1 and pXO2. If one of these two plasmids is missing, the organism cannot produce all of its virulence factors and the resulting organism is attenuated. The Sterne strain which they will be using was discovered in the 1930s and naturally lost its pXO2 plasmid, and its ability to produce a capsule. The Sterne strain has an excellent safety record and has been used safely by laboratory staff veterinarians. The Munster lab will use a Sterne strain prep that contains two bacterial isolates, one that still has the pXO2 plasmid and one that lacks the pXO2 plasmid. ▪ No animal studies were submitted, reviewed, or approved. ▪ Work with *B. anthracis* exempt strains is approved at BSL-2. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **PRD#19-217** as written.
Item 2:	<u>Registration Documents for Recombinant DNA Experiments (Amendment)</u> ▪ Feldmann (LV) ▪ **RD#17-410 Amend**: Adenovirus vaccine vector renewal ▪ Reviewers: Chris Bosio, Sue Priola ▪ **Summary:** Vaccine delivery through the use of adenoviral vectors ▪ Chris Bosio summarized the RD. This is an RD amendment to the Feldmann lab adenoviral vaccine vector RD. The amendment is to add reporter genes that were not previously approved and to introduce mutations of interest. The example that is provided in the description was a mutation to allow easier processing of Lassa virus glycoprotein. There are no changes to methodology and no changes to the NIH Guidelines or DURC issues. ▪ Sue Priola stated that everything is less than 2/3 of the genome because they are using single genes. Sue Priola had no additional comments or concerns. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal.

	Action: The committee approved (Andrea Marzi abstained) **RD#17-410 Amend** as written. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a and III-E-1 of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a and III-D-3-a of the NIH Guidelines.
Item 3:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Feldmann (LV) ▪ **RD#16-436 Amend**: Arenavirus Reverse Genetics System ▪ Reviewers: Karin Peterson, Scott Kobayashi ▪ **Summary:** Reverse genetics and minigenome systems for Arenaviruses ▪ Scott Kobayashi summarized the RD. This RD amendment describes using a new reverse genetics system for Arenaviruses. The plasmids and system description are included in the amendment. It is nicely outlined in the amendment description. The GFP reporter gene may be used in a cleavable form. There are no safety changes with the amendment and Scott Kobayashi reviewed the safety section with the IBC. Scott Kobayashi had no concerns with the amendment and stated that there are no DURC concerns. ▪ Karin Peterson had no additional comments or concerns. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Andrea Marzi abstained) **RD#16-436 Amend** as written. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 & BSL-4 under III-D-1-a, b, c and III-D-3-a, b, c and III-E-1 of the NIH Guidelines.
Item 4:	Working Group Summary ▪ Sue Priola informed the committee that a Working Group met August 7 which included, Andrea Marzi, Clay Jarrett, Sue Priola, Nancy Hoe, Megan Brose and Becky Anderson to review inactivation data from the Heinzen lab. ▪ Sue Priola summarized the testing results for inactivation of skin biopsies from guinea pigs infected with *C. burnetii* using 10% formalin. The working group reviewed the data at that time but expressed concern that 100% of the sample was not assayed for growth. The working group asked the Heinzen lab for two additional items: test the formalin fixed skin by PCR for any *C. burnetii* genomes and then test the remaining part of the sample for growth of *C. burnetii*. Both

	assays were completed and yielded negative results demonstrating that 10% formalin fixation is effective at inactivation of *C. burnetii* in skin biopsies. ▪ Sue Priola confirmed with the committee that the samples and titers tested were appropriate, all necessary controls were included and that the procedures matched what is listed in the SOP. Action: The committee approved (Bob Heinzen abstained) the inactivation data using the 10% formalin fixation of skin biopsies from *C. burnetii* infected guinea pigs presented.
Item 5:	**Standard Operating Procedure: BSL3-Cb-5 Inactivation of *C. burnetii* and subcomponents for removal from the BSL-3 laboratory (Update)** ▪ Sue Priola summarized the SOP changes to the committee. The update to the SOP was the addition of the submitted inactivation procedures for IBC approval. ▪ There were no comments or concerns with the updated procedures. Action: The committee approved (Bob Heinzen abstained) the **BSL3-Cb-5 Inactivation of *C. burnetii* and subcomponents for removal from the BSL-3 laboratory (Update)** as written.
Item 6:	**Standard Operating Procedure: ABSL-3 *Francisella tularensis* SOP (Update)** ▪ Becky Anderson summarized the SOP changes to the committee. This SOP was updated to include the intradermal route of inoculation as well as procedures for whole animal imaging with the IVIS Lumina XR. The Bosio lab previously had an SOP for ex vivo imaging of infected organs with the IVIS Lumina XR but could not perform whole animal imaging because they could not maintain the animals in primary containment while imaging. They recently purchased a Biobubble to enclose the IVIS Lumina XR. The Biobubble is setup and Biosafety staff performed smoke testing of the unit to ensure it maintains directional airflow even when ports are open. The SOP updates describe the procedures to perform these animal studies. ▪ Alex Scanton submitted questions to Sue Priola by email. She asked if the fever wording needed to be updated to the newer wording we have added to similar SOPs. The committee agreed this should be updated. ▪ Sue Priola questioned why 2.3.2 is listed, it does not make sense as written. The committee agreed that sentence should be deleted. ▪ Jamie Lovaglio asked why there are specific volumes listed for ketamine/xylazine. (b)(6) stated that is the volume the Bosio lab uses and what was listed elsewhere. The committee agreed that the specific volume should be removed because the volume is based on the weight of the animals

	and may vary. ▪ Clay Jarrett asked why the Bosio lab disinfects the syringe prior to disposal? He questioned why anyone would manipulate a syringe any more than necessary. Megan Brose stated that the BSL-4 lab also does this and there have been discussions on whether it is better to immediately dispose or disinfect. It was decided to let the labs choose what they want to do. ▪ Alex Scranton questioned why the BSL3-2 SOP does not describe *ex vivo* imaging for the LN or thymus? (b)(6) stated that they have no plans to image those organs. ▪ Alex Scranton stated that on page 22 in section 1.1.13 the SOP gives instructions for what to do if a mouse wakes up during imaging but does not give instructions for getting the re-sedated mouse back to the imaging platform. Perhaps referencing 1.1.10? The committee agreed that 1.1.13 should reference 1.1.10 for steps to follow if an animal had to be sedated again. ▪ There were no comments or concerns with the updated procedures to the new SOP. Action: The committee approved (Chris Bosio abstained) the **ABSL-3 *Francisella tularensis* SOP (update)** with the following minor modifications: 1. Update fever wording at the beginning of the SOP. 2. Delete the sentence in 2.3.2 on page 22. 3. Remove specific volumes for xylazine/ketamine throughout the SOP. 4. Add reference to 1.1.10 in section 1.1.13.
Item 7:	**Standard Operating Procedure: SOP#2/3-28-01 Handling Field Collected Fluid Blood and Tissue Samples (Update)** ▪ Becky Anderson summarized the changes to the SOP. The Munster lab would like to enrich field samples by filtering samples with a syringe attached filter or by using spin column filters. The new procedures are described in the SOP; however biosafety has two concerns: 1) the syringe attached filters need to be Luer lock so they do not accidentally come off when pressure is applied, 2) the syringe attached filters can easily become plugged if there debris in the samples. These concerns were relayed to the Munster lab and they will only use Luer lock so that requirement can be added to the SOP in E.2. The Munster lab decided that they will centrifuge samples to remove the debris prior to applying sample to the filters. The proposed wording for this should be added to the SOP.

	▪ Alex Scranton submitted questions to Sue Priola by email. Alex Scranton noted that the fever wording should also be updated in this SOP in section 7.0 on page 9. ▪ There were no additional comments or concerns with the updated procedures. Action: The committee unanimously approved the **SOP#2/3-28-01 Handling Field Collected Fluid Blood and Tissue Samples (Update)** with the following minor modifications: 1. State in E.2 that filter syringes must be Luer lock. 2. Add language to E.3 that samples will be centrifuged prior to enrichment. 3. Add the updated fever language in section 7.0 on page 9.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Becky Anderson reviewed the BSO report.
Report:	**Occupational Safety and Health Manager Report** ▪ Not present.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ The BSL-4 (b)(6); shutdown starts next week. ▪ RML has a new Steramist system and we have received training and are testing BSL-3 and BSL-4 lab spaces. Our end goal is to replace formaldehyde with ionized hydrogen peroxide (iHP). iHP acts like a gas because it is ionized and should work well for our application. If we use it at BSL-3 or BSL-4, we will confirm effectiveness with biological indicators. The process will significantly reduce time for decon and will eliminate the need for cleanup.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ Around the room.

Other issues	▪ None

Next Meeting:

- Date: 11/21/19
  Place: Library conference room
- Time: 1:00 PM

RML Biosafety Committee Meeting
October 17, 2019
Biosafety Officer/Responsible Official Report

1) ***Requests approved by BSO since last meeting:***
   a) ***Update***
      i) *Bosio PRD 14-157 Amend*
         (a) *Add intravenous route of inoculation for mice*
      ii) *Hinnebusch PRD 18-86 Amend*
         (a) *Add procurement of human blood from alternative source*
2) ***New requests approved by committee via electronic review:***
   a) *Validation Studies*
      i) *Validation studies and associated SOPs for formalin inactivation of small and large tissues infected with flaviviruses. Additional testing included paraformaldehyde inactivation of small tissues.*
         (a) *IBC Approved 10/8//19*
3) ***New requests***
   a) *Pathogen Registration Documents*
      i) ***New***
         (a) *Munster (LV)*
            (a) ***PRD-19-217****: Bacillus anthracis (exempt)*
   b) *Registration Documents for Recombinant Nucleic Acid Experiments*
      i) ***Amend***
         (a) *Feldmann (LV)*
            (a) ***RD-17-410****: Adenovirus vaccine vector*
               (i) Add mutation of genes of interest and add various reporter genes to genes of interest list
         (b) *Feldmann (LV)*
            (a) ***RD-16-436:*** *Arenavirus minigenome systems*
               (i) Add a new reverse genetics system
   c) *Inactivation Validation Testing Review*
      i) *Heinzen (LB)*
         (a) *Inactivation of Coxiella burnetii infected skin biopsy with 10% formalin*
   d) ***Standard Operating Procedures***
      i) ***Update***
         (a) *SOP#BSL-3-Cb-b: Inactivation of Coxiella burnetii and subcomponents for removal from BSL-3 laboratory*

(a) *Add procedures for inactivation of Coxiella burnetii infected skin biopsies from mice with 10% formalin*

(b) *ABSL-3 Tularemia animal SOP*

(a) *Add the intradermal route of inoculation throughout the SOP*

(b) *Add ex vivo imaging to BSL3-2 Removal and manipulation of mouse organs following infection with F. tularensis*

(c) *Add ex vivo imaging to BSL3-4 Pre-clinical imaging of bacterial infections, inflammation, and metabolism in vivo using the IVIS Lumina XR*

(c) *2/3-28-01 Handling Field Collected Fluid Blood and Tissue Samples*

(a) *Add virus enrichment of field collected samples using filtration*

4) ***Animal Study Protocols Review***

Title	*Associated PRD*	*Associated RD*	*Reviewer*
Validation and characterization of a susceptibility allele for Ebola hemorrhagic fever pathogenesis and resistance in mice	*18-90 (Ebola virus)*	*N/A*	*B. Anderson*
Durability of pLASV-mediated anti-LASV immunity and protection from LASV	*18-94 (Lassa virus)*	*N/A*	*M. Brose*
The effect of enhanced retinal proteasomal function on prion-induced retinal degeneration in mice	*16-190 (Scrapie)*	*N/A*	*M. Brose*
Characterization of Lassa virus infection in the host species Mastomys natalensis	*18-94 (Lassa virus)*	*N/A*	*M. Brose*
Manipulation of host lipid metabolism in F. tularensis pathogenesis in mice	*18-71 (Francisella tularensis)*	*N/A*	*B. Anderson*
Ultrastructural Pathology of the Epididymis and Accessory Sex Glands During Acute Infection with Zika Virus in Mice	*16-182 (Zika virus)*	*N/A*	*M. Brose*
Antimicrobial role of nitric oxide during Rickettsia rickettsii-infection of guinea pigs	*14-38 (Rickettsia rickettsia)*	*N/A*	*M. Brose*
Imaging metabolism and associated inflammation in vivo following infection	*18-71 (Francisella tularensis, Schus4)* *18-73 (Francisella tularensis, LVS)* *17-195 (B. pertussis)* *14-157 (Listeria monocytogenes)*	*N/A*	*B. Anderson*
Analysis of host and viral factors involved in the pathogenesis of	*18-103 (California serogroup orthobunyaviruses)*	*18-225*	*M. Brose*
Anti-CD47 treatment mice with Staphylococcus spp.-infected surgical mesh implants	*18-1 (Staphylococcus epidermidis)* *(Staphylococcus aureus)*	*N/A*	*B. Anderson*

RML Biosafety Committee Meeting
October 17, 2019
Biosafety Officer/Responsible Official Report

5) ***Biosafety Training Performed – Megan Brose, Rebecca Anderson, Nancy Hoe***

Type of Training	***Number of Sessions***	***Number of Employees Trained***
BSL-3 Practical	*1*	*2*
BSL-4 Laboratory Biosafety	*3*	*4*
BSL-4 Annual Refresher Training	*13*	*36*
Select Agent Initial	*1*	*6*
Select Agent Visitor	*2*	*4*
Select Agent Refresher	*3*	*100*
Biosafety Brief	*3*	*2 All Hands (RMVB), 1 LV WIP*

6) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
   a) *Biological Incident Report:*
      i) *None*

7) ***Select Agent Issues***
   a) *None*

8) ***Other Issues –***
   a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 11/21/2019
Meeting Time: 1:02 PM **Adjourned:** 1:45 PM
Building A Library, (b)(6)

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Greg Saturday	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Heinz Feldmann (EO)	☐	☒	Alexandra Scranton	☐	☒
Becky Anderson (EO)	☒	☐	Nancy Hoe	☐	☒	Brian Vickrey	☐	☒
Alan Applebury	☐	☒	Erik Hoover	☐	☒			
Chris Bosio	☒	☐	Clay Jarrett	☒	☐			
Marshall Bloom (EO)	☒	☐	Josh Kellar (EO)	☐	☒			
Megan Brose	☒	☐	Scott Kobayashi	☒	☐			
Larry Brouwer	☐	☒	Jamie Lovaglio	☒	☐			
Carol Calderwood	☐	☒	Andrea Marzi	☒	☐			
Marcie Caldwell (EO)	☐	☒	Alida Merritt	☐	☒			
Bruce Chesebro (EO)	☐	☒	Karin Peterson	☒	☐			

(P=present; A=absent)

Guests (b)(6)

Minutes: Meeting minutes from 10/17/19 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 10/17/19** Action: Meeting minutes for 10/17/19 were unanimously approved with the following minor modification: 1. Bob Heinzen noted that in Item 4, it should be clarified that the skin biopsies were from *C. burnetii* infected guinea pigs instead of stating C. burnetii infected skin biopsies. 2. Sue Priola pointed out a couple of typos.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New)

	▪ Bosio (LB) ▪ **PRD#19-218: *Klebsiella pneumoniae*** ▪ Becky Anderson presented the risk assessment. The proposed studies are to examine the innate and adaptive pulmonary immune response to *Klebsiella pneumoniae* as comparative pathogen to other established models in the lab. *K. pneumoniae* is a bacteria that can cause different types of healthcare-associated infections, including pneumonia, bloodstream infections, wound or surgical site infections, and meningitis. Increasingly, *Klebsiella* bacteria have developed antimicrobial resistance, most recently to the class of antibiotics called carbapenems. Some of these strains include naturally acquired antibiotic resistance, which is listed in the product sheets attached with the PRD. Infections with *Klebisella* can be treated with antibiotics. The natural route of transmission is through person to person and contact with contaminated surfaces. The primary lab hazards include ingestion of infected material, generation of aerosols, and accidental sharps injury. ▪ Immunocompromised individuals should be warned of the risks of working with *K. pneumoniae*. Precautions for working with human blood and body fluids have been added to the PRD recommendations section. ▪ No animal studies were submitted, reviewed, or approved. ▪ Work with *K. pneumoniae* is approved at BSL-2. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved (Chris Bosio abstained) **PRD#19-218** as written.
Item 2:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New)</u> ▪ Hackstadt (LB) ▪ **PRD#19-38: Rickettsia spp.** ▪ Becky Anderson presented the risk assessment. The Hackstadt lab proposes to study the differences between virulent and avirulent strains of Rickettsiae through comparative genomics and directed knockout and complementation studies of suspected virulence determinants. Specific genes/proteins will be deleted or complemented and differences in virulence determined. ▪ *R. rickettsii* infection causes Rocky Mountain Spotted Fever, a potentially fatal tick-borne disease that normally causes moderate to severe illness. Other Rickettsia can cause spotted fever or Typhus related disease. Spotted fever group rickettsiae can appear as an abrupt onset of fever, malaise, headache, anorexia, nausea, vomiting, abdominal pain, photophobia, diarrhea and neck stiffness. The characteristic maculopapular rash usually appears 2-5 days after the other symptoms, starting on wrists and ankles

	before progressing to the rest of the body. Approximately 95% of children and 80% of adults have the rash; however, absence of the rash is more common in fatal cases and cases involving the elderly or African-Americans. The symptoms can last 2 weeks although some patients have neurological sequelae lasting up to one year after disease onset. Transmission naturally occurs through blood feeding arthropods like ticks, fleas, lice, and mites. The primary lab hazards include parenteral contact, accidental sharps injuries, and exposure to aerosols. ▪ Sue Priola stated that the storage space, listed by rooms, should have the biosafety level added to clarify how each space is registered. ▪ *Rickettsia rickettsii, R. conorii, , R. akari, R. australis, R. helvetica, R. parkeri, R. slovaka, R. sibirica, Tillamook, Orientia* (formerly Rickettsia) *tsutsugumushi, R. typhi*, and attached strain list and several unclassified rickettiae all approved for work at BSL-3. ▪ *Wolbachia andersoni, W. persica* are for storage only at BSL-3. ▪ *R. montana, R. rhipicephali, R. bellii, R. canada*, are not known to cause human disease and are approved at BSL-2. Propagation and work with large quantities of these agents will be conducted at BSL-2 with BSL-3 practices. ▪ Animal studies with guinea pigs were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **PRD#19-38** with the following minor modifications: 1. Clarify the biosafety level for each room listed as storage.
Item 3:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment)</u> ▪ Peterson (LPVD) ▪ **PRD#18-103 Amend: Bunyaviruses** ▪ Becky Anderson presented the risk assessment. The amendment is to add two new viruses to the PRD, Cache Valley virus and California Encephalitis virus. Cache Valley virus was first isolated from *Culiseta inornata* mosquitoes collected in Cache Valley, Utah, in 1956. A high prevalence of neutralizing antibody to this virus can often be found in ungulates, including deer, sheep, horses, and cattle. The virus has been isolated from a healthy cow, sick sheep and a healthy horse in Michigan. It is teratogenic in sheep. There have been a few reports of human illness. Symptoms in humans include severe headache, nausea, vomiting, and fatigue and causes encephalitis. California encephalitis virus is very similar to La Crosse virus. It was discovered in Kern County California and causes encephalitis in humans. Symptoms of California encephalitis virus infection include headaches, fever,

	nausea, vomiting. ▪ No new animal studies were proposed. ▪ BSL-2/ABSL-2 is appropriate for work with Cache Valley virus and California Encephalitis virus. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Karin Peterson abstained) **PRD#18-103 Amend** as written.
Item 4:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Hackstadt (LB) ▪ **RD#19-110**: Virulence determinants of spotted fever group rickettsia ▪ Reviewers: Bob Heinzen, Clay Jarrett ▪ **Summary:** Defining the molecular determinants of virulence in spotted fever group rickettsia. ▪ Bob Heinzen summarized the RD. Bob Heinzen stated that this is a renewal of the genetics system for spotted fever Rickettsia for the Hackstadt lab. The Hackstadt labs wants to understand the differences in the Rickettsia strains. The Hackstadt lab will perform gene inactivation, complementation and gene swapping. Their readout for virulence is through infection of guinea pigs. They will use established genetics systems to perform these studies. The antibiotic resistance markers are appropriate since they are not used to clinically treat infections. There are no DURC issues with this registration. ▪ Clay Jarrett questioned why they added G-II-B and G-II-C to the NIH Guidelines section. Sue Priola stated that it is ok, it just refers to BSL-2 and BSL-3 practices. Clay Jarrett had no additional comments or concerns. ▪ Sue Priola stated that the foreign genes listed in the Research Product section should be added to the Eukaryote Cell section of the RD. ▪ Animal studies with guinea pigs were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#19-110** with the following minor modifications: 1. Add the list of foreign genes to the Eukaryote cell section. Research using prokaryotic hosts is approved at BSL-2 under section III-D-1-a, III-D-

	1-b, and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-3 under Appendices G-II-B and G-II-C of the NIH Guidelines.
Item 5:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Priola (LPVD) ▪ **RD#19-222**: Lentiviruses ▪ Reviewers: Karin Peterson, Andrea Marzi ▪ **Summary:** Lentiviruses ▪ Karin Peterson summarized the RD. This is an RD renewal for lentiviral work. They will use commercial lentiviral vectors to put PRP into mice and hamster cell lines. They will use the commercial packaging systems that do not create replication competent lentiviruses so they cannot replicate in the cell. There are no DURC issues. In the Research Product section, Explain expression product and/or study details, delete the word "cell" at the end of the paragraph. ▪ Andrea Marzi had no additional comments or concerns. ▪ Sue Priola noted that there is one vector map that is missing that needs to be added. ▪ BSL-2/ABSL-2 is appropriate for the described work with Lentiviruses. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Sue Priola abstained) **RD#19-222** with the following minor modifications: 2. Add the missing vector map. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a and III-D-3-a of the NIH Guidelines.
Item 6:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Rosa (LPVD) ▪ **RD#19-308**: Molecular genetic approaches to elucidate the mechanisms of adaptation and variation used by *B. burgdorferi*. ▪ Reviewers: Scott Kobayashi, Chris Bosio ▪ **Summary:** Determining the virulence determinants required for infection by *Borrelia burgdorferi*.

	▪ Scott Kobayashi summarized the RD. This is an RD renewal for work with their primary RD for Borrelia. They will continue to develop basic genetic tools, make plasmids and tools to perform knock outs and cloning. They want to understand the structure and function of plasmids in Borrelia, how Borrelia is responsive to environmental factors and want to conduct experiments with OspC from other Borrelia strains. The vectors they use have selectable markers and none of the antibiotics used for selection are used for clinical treatment. The proposed NIH Guidelines are appropriate and there are no DURC issues. ▪ Chris Bosio had no additional comments or concerns. ▪ Sue Priola stated that she could not find two of the plasmids, pCR-Blunt and pGEM-T, they need to be attached. Sue Priola also questioned the use of ampicillin for selection in some of the attached vectors. The committee discussed extensively, and Clay Jarrett and Scott Kobayashi clarified that the vectors that include ampicillin are only used in *E. coli*. Furthermore, those vectors will not work in Borrelia spp. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **RD#19-308** with the following minor modifications: 1. Add the missing vector maps: pCR-Blunt and pGEM-T Research using prokaryotic hosts is approved at BSL-2 under III-D-1-a and III-D-2-a of the NIH Guidelines.
Item 7:	<u>Registration Documents for Recombinant DNA Experiments (New)</u> ▪ Munster (LV) ▪ **RD#19-455**: Development of lipid nanoparticle-formulated mRNA vaccine candidates ▪ Reviewers: Sue Priola, Karin Peterson ▪ **Summary:** This RD describes an mRNA vaccine platform. ▪ Sue Priola summarized the RD. The RD submission describes an mRNA vaccine that is coated in a lipid nanoparticle that elicits a good immune response. The Munster lab will obtain this vaccine from the company CureVac. They have developed an mRNA vaccine that produces a response to a Lassa virus protein that they will be testing in guinea pigs with a Lassa virus challenge. If the Munster lab starts doing recombinant work at RML, they will have to amend the RD to include cloning information. The insert will be less than 2/3, and the

	NIH Guidelines are listed appropriately. ▪ Karin Peterson had no additional comments or concerns. ▪ Sue Priola stated that the RD should list CureVac as the source of recombinant material in the recombinant DNA section. ▪ Animal studies with guinea pigs were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#19-455** with the following minor modifications: 1. Add the source of the recombinant material to the recombinant DNA section. It should list CureVac. Research using prokaryotic hosts is approved at BSL-2 under Section III-E-1 of the NIH Guidelines.
Item 8:	**Full Committee Review of MCL Inactivation Data with Formalin/PFA** ▪ Sue Priola informed the committee that there is inactivation data to review for the MCL. Included in this month's submission is testing data for inactivation of Paramyxoviridae infected NHP lung tissue with formalin and tissues ≤1cm3 inactivated with formalin or PFA. The repeat testing was performed to increase the IBC approved viral titer for inactivation. ▪ Sue Priola summarized the testing results for the inactivation of tissues. Sue Priola confirmed with the committee that the samples and titers tested were appropriate, all necessary controls were included and that the procedures matched what is listed in the SOP. There were no comments or concerns with the inactivation data. Action: The committee unanimously approved the inactivation data using the 10% formalin or 2% PFA on Paramyxoviridae infected tissues with the increased viral titer.
Item 9:	**Standard Operating Procedure: SOP#4-28-33 Removal of Specimens for Fluorescence, Immunofluorescence, Histopathology, Immunohistopathology, and Flow Cytometry (Update)** ▪ Sue Priola summarized the changes to the SOP to the committee. The update to the SOP was the change in viral titer for already approved inactivation procedures. ▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved the **SOP#4-28-33 Removal of**

	Specimens for Fluorescence, Immunofluorescence, Histopathology, Immunohistopathology, and Flow Cytometry (Update) as written.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Becky Anderson reviewed the BSO Report
Report:	**Occupational Safety and Health Manager Report/** (b)(6) ▪ Not present.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ The BSL-4 (b)(6), lab shutdown is complete. ▪ The BSL-3 (b)(6) shutdown is occurring this week. We will start to plan for the (b)(6) shutdown in January, this shutdown will include replacing flooring in the small room.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ Sue Priola informed the committee that (b)(6) will be leaving the IBC to be part of the (b)(6) We will be looking to find a replacement for (b)(6) position.

Other issues	▪ None

Next Meeting:

- Date: 12/19/19
- Place: Library conference room
- Time: 1:00 PM

RML Biosafety Committee Meeting
November 21, 2019
Biosafety Officer/Responsible Official Report

1) ***Requests approved by BSO since last meeting:***
   a) ***None***
2) ***New requests approved by committee via electronic review:***
   a) ***None***
3) ***New requests***
   a) <u>*Pathogen Registration Documents*</u>
      i) ***New***
         (a) *Bosio (LB)*
            (a) ***PRD-19-218****: Klebsiella pneumoniae*
      ii) ***Renew***
         (a) *Hackstadt (LB)*
            (a) ***PRD-19-38;*** *Rickettsia spp.*
      iii) ***Amend***
         (a) *Peterson (LPVD)*
            (a) ***PRD-18-103;*** *Bunyaviruses*
   b) <u>*Registration Documents for Recombinant Nucleic Acid Experiments*</u>
      i) ***New***
         (a) *Munster (LV)*
            (a) ***RD-19-455:*** *Development of lipid nanoparticle-formulated mRNA vaccine candidates*
      ii) ***Renew***
         (a) *Hackstadt (LB)*
            (a) ***RD-19-110****: Virulence determinants of spotted fever group rickettsia*
         (b) *Priola (LPVD)*
            (a) ***RD-19-222:*** *Lentiviruses*
         (c) *Rosa (LPVD)*
            (a) ***RD-19-308:*** *Molecular genetic approaches to elucidate the mechanisms of adaptation and variation used by B. burgdorferi*
   c) <u>*Inactivation Validation Testing Review*</u>
      i) *Feldmann (LV)*
         (a) *Inactivation of RG4 viral family (Paramyxoviridae) with formalin and PFA*
   d) ***Standard Operating Procedures***

i) ***Update***

(a) *SOP#4-28-33: Removal of Specimens for Fluorescence, Immunofluorescence, Histopathology, Immunohistopathology, and Flow Cytometry*

(i) Add procedures for inactivation of of Paramyxoviruses with formalin and PFA

4) ***Animal Study Protocols Review***

Title	*Associated PRD*	*Associated RD*	*Reviewer*
Field Study in Ghana	*14-158*	*N/A*	*M. Brose*
Generation of polyclonal antibodies against La Crosse Virus and other Orthobunyaviruses in mice and rabbits	*18-1*	*N/A*	*R. Anderson*
Establishing a Wild Caught Colony of Mastomys natalensis in Mali	*N/A*	*N/A*	*R. Anderson*
Establishing a model of CCHFV Using a mouse adapted strain of CCHFV	*18-92*	*N/A*	*R. Anderson*
Efficacy of two novel lipid nanoparticle-formulated mRNA vaccines against LASV in guinea pigs	*18-94*	*19-455*	*R. Anderson*
Establishing novel strains of CCHFV in a non-human primate model	*18-92*	*N/A*	*M. Brose*

5) ***Biosafety Training Performed – Megan Brose, Rebecca Anderson, Nancy Hoe***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
BSL-3 Practical	*4*	*7*
BSL-4 Laboratory Biosafety	*7*	*3*
BSL-4 Annual Refresher Training	*2*	*2*
Select Agent Initial	*1*	*5*
BSL-3/BSL-4 Biosafety for Support Personnel (initial)	*1*	*3*
BSL-3/BSL-4 Biosafety for Support Personnel (Refresher)	*1*	*20*
New Employee Training	*2*	*5*
Annual Refresher Training	*5*	*All lab/office staff*

6) ***Safety Audits and Inspections***

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

a) *Biological Incident Report:*

i) *None*

7) ***Select Agent Issues***

a) *None*

8) ***Other Issues –***
   a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 12/19/2019
Meeting Time: 1:03 PM **Adjourned:** 1:36 PM
Building A Library, (b)(6)

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☐	☒	Frank DeLeo (EO)	☐	☒	Alexandra Scranton	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Heinz Feldmann (EO)	☐	☒	Brian Vickrey	☐	☒
Becky Anderson (EO)	☒	☐	Nancy Hoe	☐	☒	Clayton Winkler	☒	☐
Alan Applebury	☐	☒	Erik Hoover	☒	☐			
Chris Bosio	☒	☐	Clay Jarrett	☒	☐			
Marshall Bloom (EO)	☐	☒	Josh Kellar (EO)	☐	☒			
Megan Brose	☒	☐	Scott Kobayashi	☒	☐			
Larry Brouwer	☐	☒	Jamie Lovaglio	☒	☐			
Carol Calderwood	☐	☒	Andrea Marzi	☒	☐			
Marcie Caldwell (EO)	☐	☒	Alida Merritt	☒	☐			
Bruce Chesebro (EO)	☐	☒	Greg Saturday	☒	☐			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 11/21/19 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 10/17/19** Action: Meeting minutes for 11/21/19 were unanimously approved as written.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment) ▪ Feldmann (LV) ▪ **PRD#18-92 Amend:** *Bunyaviridae* ▪ Becky Anderson presented the risk assessment. The amendment is to add

	animal work with Rift Valley Fever virus. The PRD already covered animal work for Crimean Congo Hemorrhagic Fever virus. There are approved SOPs for the BSL-4 that cover the proposed animal work with Rift Valley Fever Virus. ▪ Animal studies with mice, hamsters, and NHPs were proposed. ▪ Work with Rift Valley Fever virus is approved at BSL-4/ABSL-4. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Andrea Marzi abstained) **PRD#18-92 Amend** as written.
Item 2:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment) ▪ Feldmann (LV) ▪ **PRD#18-90 Amend: Filoviridae** ▪ Becky Anderson presented the risk assessment. The amendment is to add the intravaginal route of inoculation for Filoviridae for mice and rats. This route of inoculation is currently not approved for Dr. Feldmann through CDC DSAT, so the IBC approval will be pending DSAT approval. In the next month or so the IBC should expect to see SOPs that describe procedures for the intravaginal route of inoculation. ▪ Filoviridae studies are approved for work at BSL-4/ABSL-4. ▪ Animal studies with mice and rats were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#18-90 Amend** as written **PENDING CDC DSAT approval**.
Item 3:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New) ▪ Feldmann (LV) ▪ **PRD#19-219: Mastomys Cytomegalovirus** ▪ Becky Anderson presented the risk assessment. The Feldmann lab proposes to develop a vaccine against Lassa virus that is a self-disseminating animal vaccine in the *Mastomys natalensis* rodent population in West Africa. The Mastomys Cytomegalovirus (CMV) is not known to cause disease in humans. CMV is a highly species-specific virus due to adaptation to their host so there is no cross species infection. Transmission in rodents occurs vertically or through contact with the saliva or urine of an infected animal. The primary

	lab hazards include avoiding contact with urine or saliva from infected animals. ▪ Becky Anderson pointed out that the animal section states ABSL-3, which is incorrect and should be changed to ABSL-2. ▪ Animal studies with Mastomys rodents were proposed. ▪ BSL-2/ABSL-2 is appropriate for work with Mastomys CMV. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Andrea Marzi abstained) **PRD#19-219** with the following minor modifications: 1. Change the biosafety level in the animal section to ABSL-2.
Item 4:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Feldmann (LV) ▪ **PRD#19-110: Bunyamwera** ▪ Becky Anderson presented the risk assessment. The Feldmann lab proposes to continue to study the molecular basis of the Orthobunyavirus viral life cycle, pathogenesis, mechanisms of virulence acquisition and evolution. Some of the orthobunyaviruses cause disease in humans. Most commonly, the orthobunyaviruses that are worked with at BSL-2 cause a self-limiting illness that presents with fever, headache, photophobia, stiff neck, arthralgia, rash and back or joint pain. The BSL-2 classified viruses that can cause a more severe illness in humans include: Cache Valley virus, La Crosse virus, and Ilesha virus. Cache Valley virus has 1 reported case where a severe systemic infection was reported. La Crosse virus can cause severe illness with encephalitis, especially in children under 16 years old. Ilesha virus causes a febrile illness with exanthema and erythema. For the BSL-3 classified viruses: Ngari, Germiston, Oropouche, Iquitos, Madre de Dios, and Enseada viruses: disease can range from febrile illness to severe headache, myalgia, arthralgia, anorexia, nausea, vomiting, weakness, dizziness, and photophobia, some patients can even exhibit meningitic symptoms. Treatment is typically supportive care. ▪ Animal studies with hamsters and rabbits were proposed. ▪ BSL-2 or BSL-3 is appropriate for work with Bunyamwera depending on the virus. BSL-3 Bunyamwera viruses include the following and will be handled at BSL-3: Ngari virus, Germiston virus, Oropouche virus, Iquitos virus, Madre de Dios virus, and Enseada virus. All other Bunyamwera viruses listed on this

	PRD are to be handled at BSL-2. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Andrea Marzi abstained) **PRD#19-110** as written.
Item 5:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Feldmann (LV) ▪ **PRD#19-158: Field Samples** ▪ Becky Anderson presented the risk assessment. This PRD is for the Feldmann lab to obtain and manipulate field samples from various field study sites from various animal species for assessment of the presence of viruses of interest. The PRD covers the collection of field samples and has ASPs attached that describe the animal species that will be sampled and samples types to be collected. This PRD also gives the IBC a mechanism to associate ASPs to field samples for Dr. Feldmann and his group. The PRD does not describe handling of samples at RML, the attached SOP describes the sample processing. The newer ASPs have improved descriptions of PPE worn in the field and how samples are processed in the field prior to being shipped back to RML. Biosafety reviews all these ASPs prior to ACUC review so we can ensure that the procedures are appropriate to mitigate the hazards. The recommendation section also covers the reminder that appropriate permits need to be obtained by the PI prior to import of any samples. ▪ Field sample ASPs are attached for sample collection. ▪ BSL-2 with BSL-3 practices is appropriate for handling field samples. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Andrea Marzi abstained) **PRD#19-158** as written.
Item 6:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Feldmann (LV) ▪ **PRD#19-159: Modified Vaccinia Ankara strain (MVA)** ▪ Becky Anderson presented the risk assessment. This is a renewal for the Feldmann lab for work with MVA. The MVA strain will be used to infect cells in comparison with recombinant MVA vaccine strains expressing virus

	proteins. MVA does not cause disease in humans. The attenuated MVA virus was passaged more than 570 times in chicken embryo fibroblast cells and became deficient for replication in most mammalian cells including human cells. ▪ No animal studies were submitted, reviewed, or approved. ▪ BSL-1 is appropriate for working with MVA if no other human orthopoxviruses are being used. This lab space is BSL-2 so the approved level is BSL-2. There is no vaccine requirement for working with MVA. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Andrea Marzi abstained) **PRD#19-159** as written.
Item 7:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Feldmann (LV) ▪ **PRD#19-160: Borrelia spp.** ▪ Becky Anderson presented the risk assessment. This is a renewal for the Feldmann lab for working with Borrelia species including *crocidurae, hermsii*, and *turicatae*. The goal of this study is to determine the duration of infection of *Borrelia crocidurae* in lab-reared *Mastomys natalensis* with the goal of better defining how long these animals are infectious and capable of transmitting the spirochetes to ticks. Studies in Mali determined that a large number of wild-captured mastomys are infected with or seropositive for *Borrelia crocidurae*. Tick borne relapsing fever is caused by the Borrelia spp. listed and is characterized by recurring febrile episodes that last approximately 3 days and are separated by afebrile periods of 7 days. Borrelia infections can be treated with antibiotics. The natural route of transmission is through the bite of an infected tick. The primary lab hazards include parenteral contact, accidental sharps injuries, and exposure to aerosols. ▪ Animal work with *Mastomys natelensis* rodents were proposed. ▪ Borrelia species are approved at BSL-2/ABSL-2. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Andrea Marzi abstained) **PRD#19-160** as written.
Item 8:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals

	(Renewal) ▪ Feldmann (LV) ▪ **PRD#19-163: Nairoviruses** ▪ Becky Anderson presented the risk assessment. This is a renewal for the Feldmann lab for work with Nairoviruses. The proposed studies are to understand the molecular basis of Nairovirus viral life cycle, pathogenesis, and mechanisms of virulence acquisition and evolution. Not all Nairoviruses are known to be human pathogens. Infection with the BSL-2 classified Nairoviruses typically leads to self-limiting illness with symptoms such as fever, headache, photophobia, nausea, and back/joint pains. Illness is short lived in duration and lasts 2-8 days. Issyk-Kul virus is characterized with symptoms of abrupt onset of high fever for 3-8 days, headache, dizziness, pharyngitis, cough, muscle pain, nausea and vomiting, rash abdominal pain, chills, pain in the eyes and photophobia. For Kasokero virus there is not much information available, when the virus was first isolated, laboratory acquired infections occurred resulting in mild to severe illness. Lab infections presented with fever, headache, abdominal pain, diarrhea, chest pain, myalgia and arthralgia. Symptoms lasted approximately 7 to 10 days with a complete recovery. Some patients had joint pain for over a month after recovery. ▪ No animal studies were submitted, reviewed, or approved. ▪ Work with Nairoviruses is approved at BSL-2/ABSL-2 except for Issyk-Kul and Kasokero which are BSL-3. All BSL-2 work with infectious material is performed in a BSC, PPE includes a disposable gown, surgical mask, face shield, double gloves, and disposable shoe covers. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Andrea Marzi abstained) **PRD#19-163** as written.
Item 8:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Feldmann (LV) ▪ **RD#17-452 Amend**: Use of Alphavirus replicon system to produce vaccines ▪ Reviewers: Scott Kobayashi, Clay Jarrett ▪ **Summary:** Vaccine production with Alphavirus replicons ▪ Scott Kobayashi summarized the RD amendment. This amendment is to add a plasmid for the production of Ross River virus and other Alphaviruses. The plasmid map is attached to the RD. This will create a full-length virus with GFP in frame and they do not need a helper virus to rescue the progeny. None of the Alphaviruses are select agent strains and they will use the appropriate

	biosafety level for the strain (according to PRD). ▪ Clay Jarrett pointed out that there is a DURC question marked yes because they will be performing reverse genetics studies, but there are no overall dual use issues. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Andrea Marzi abstained) **RD#17-452 Amend** as written. Research using prokaryotic hosts is approved at BSL-2 under Section III-D-2-a and III-E-1 of the NIH Guidelines. Research using eukaryotic hosts is approved at BSL-2 under Section III-D-1-a and III-D-3-a of the NIH Guidelines.
Item 9:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Feldmann (LV) ▪ **RD#19-402**: Lentiviral vectors ▪ Reviewers: Chris Bosio, Bob Heinzen ▪ **Summary:** This RD describes the use of lentiviral vectors. ▪ Chris Bosio summarized the RD. This is the renewal for the use of lentiviral vectors to express viral proteins or host proteins or iRNA. There is no new work added, this is just a renewal of the lentiviral expression system. There are no DURC issues and the NIH Guidelines are appropriate. ▪ Bob Heinzen had no additional concerns. Bob Heinzen noted that this system is a commercial system with lots of safeguards. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Andrea Marzi abstained) **RD#19-402** as written. Research using prokaryotic hosts is approved at BSL-2 under Section III-D-2-a of the NIH Guidelines. Research using eukaryotic hosts is approved at BSL-2 under Section III-D-1-a and III-D-3-a of the NIH Guidelines.
Item 10:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Steele-Mortimer (LB) ▪ **RD#19-126**: Salmonella Cancer Vaccine

	▪ Reviewers: Andrea Marzi, Bob Heinzen ▪ **Summary:** Development of Salmonella as a vaccine ▪ Andrea Marzi summarized the RD. This is a renewal for the Steele-Mortimer lab. They use recombinant attenuated Salmonella typhimurium vaccine (RASV) as a platform for vaccination. RASV uses two plasmids that allow bacteria to be released in the cytosol of the cell so the antigens can be expressed, and a host response can be developed. All the antigens are listed that they will work with. They are actively working with mastomys rodents and Lassa virus. All of the plasmid maps are included, and the NIH Guidelines are appropriate. There are no DURC issues. ▪ Bob Heinzen stated that it was a very long and detailed description of their work. He had no concerns with the proposed studies. ▪ Clay Jarrett noted that this is not a PRD, and the top of the first page should be changed to RD. ▪ Animal studies with mice and mastomys rodents were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#19-126** with the following minor modification: 1. Change on the first page, PRD to RD. Research using prokaryotic hosts is approved at BSL-2 under Section III-D-2-a of the NIH Guidelines. Research using eukaryotic hosts is approved at BSL-2 under Section III-D-1-a and III-D-3-a of the NIH Guidelines.
Item 8:	**Full Committee Review of MCL Inactivation Data with Formalin/PFA** ▪ Bob Heinzen summarized the inactivation data provided by Dr. Feldmann. The testing included inactivation of Arena-, Bunya-, and Paramyxo- viral families with Trizol. The samples included stock virus, infected cells, and infected tissues with each of the viral families. ▪ Bob Heinzen confirmed with the committee that the samples and titers tested were appropriate, all necessary controls were included and that the procedures matched what is listed in the SOP. There were no comments or concerns with the inactivation data provided. Action: The committee unanimously approved the inactivation data using Trizol as described on Arena-, Bunya-, and Paramyxo- virus infected tissues or cells.
Item 9:	**Standard Operating Procedure: SOP#4-28-32 Removal of Specimens for Nucleic Acid Extraction (Update)**

	▪ Bob Heinzen summarized the changes to the SOP to the committee. The update to the SOP was the revised table to include the inactivation procedures with Trizol on Arena-, Bunya-, and Paramyxo- virus infected tissues or cells. ▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved the **SOP#4-28-32 Removal of Specimens for Nucleic Acid Extraction (Update)** as written.
Item 10:	**Operations and Safety Procedures: MCL Operations and Safety Procedures (Annual Review)** ▪ Bob Heinzen summarized informed the committee that this is the annual review of the MCL OSP. There were no changes proposed for this year's annual review. ▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved the **Operations and Safety Procedures: MCL Operations and Safety Procedures (Annual Review)** as written.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Becky Anderson reviewed the BSO Report ▪ Becky Anderson informed the IBC that there was an unannounced CDC DSAT inspection on December 3-5. The inspection went well and the out brief from the inspectors listed very few findings. The official inspection report should be received within 30 days.
Report:	**Occupational Safety and Health Manager Report/**(b)(6) ▪ Not present. Submitted comments to Becky Anderson by email. (b)(6) (b)(6) noted that the (b)(6) safety surveys will be complete by 12/31/19.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ The (b)(6) BSL-3 shutdown dates are being finalized. The shutdown will be a little longer than a week to replace some flooring in a small room in the suite.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ Bob Heinzen informed the committee that (b)(6), a research associate in his lab will sit in on the IBC meetings to see how the biosafety program runs.

Other issues	▪ None

Next Meeting:

- Date: 01/16/2020
- Place: Library conference room
- Time: 1:00 PM

RML Biosafety Committee Meeting
December 19, 2019
Biosafety Officer/Responsible Official Report

1) Requests approved by BSO since last meeting:

a) ***None***

2) ***New requests approved by committee via electronic review:***

a) ***None***

3) ***New requests***

a) *Pathogen Registration Documents*

i) ***New***

(a) *Feldmann (LV)*

(a) ***PRD-19-219****:* Cytomegalovirus - mastomys

ii) ***Renew***

(a) *Feldmann (LV)*

(a) ***PRD-19-110;*** *Bunyamwera*

(b) *Feldmann (LV)*

(a) ***PRD-19-158;*** *Field samples*

(c) *Feldmann (LV)*

(a) ***PRD-19-159;*** *Vaccinia modified Ankara virus (MVA)*

(d) *Feldmann (LV)*

(a) ***PRD-19-160;*** *Borrelia spp.*

(e) *Feldmann (LV)*

(a) ***PRD-19-163;*** *Nairovirus*

iii) ***Amend***

(a) *Feldmann (LV)*

(a) ***PRD-18-92;*** *Bunyaviridae*

(b) *Feldmann (LV)*

(a) ***PRD 18-90;*** *Filoviridae*

b) *Registration Documents for Recombinant Nucleic Acid Experiments*

i) ***Renew***

(a) *Feldmann (LV)*

(a) ***RD-19-402****: Lentiviral vectors*

(b) *Steele-Mortimer (LB)*

(a) ***RD-19-126:*** *Recombinant attenuated Salmonella typhimurium vaccine*

ii) ***Amend***

(a) *Feldmann (LV)*

(a) ***RD-17-452:*** *Alphavirus reverse genetics*

c) *Inactivation Validation Testing Review*

i) *Feldmann (LV)*

(a) *Inactivation of RG4 viral family (Arena, Bunya, Paramyxo- viral families) with Trizol*

d) ***Standard Operating Procedures***

i) ***Update***

(a) *SOP#4-28-32: Removal of Specimens for Nucleic Acid Extraction*

(i) Add procedures for inactivation of Arena, Bunya, Paramyxo- viral families with Trizol

4) ***Animal Study Protocols Review***

Title	*Associated PRD*	*Associated RD*	*Reviewer*
Establishing a model of CCHF using a mouse adapted strain of CCHFV	*18-92*	*N/A*	*R. Anderson*
Post exposure efficacy of rVSV-expressed miRNA as treatment of Ebola virus infection in the host species Mastomys natalensis	*18-90* *18-82*	*15-404*	*M. Brose*
Characterization of Mastomys CMV infection in the host species mastomys natalensis	*19-219*	*15-422*	*M. Brose*
Establishment of a mouse model for Rift Valley Fever virus infection	*18-92*	*N/A*	*M. Brose*
Intravaginal inoculation of IFN R1-/- mice as a potential route of Ebola virus transmission	*18-90*	*N/A*	*R. Anderson*

5) ***Biosafety Training Performed – Megan Brose, Rebecca Anderson, Nancy Hoe***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
BSL-4 Laboratory Biosafety	*1*	*2*
Full Length Clone Lab Annual Refresher	*3*	*9*
Select Agent visitor/BSL-3 visitor	*2*	*5*
BSL-3/BSL-4 Biosafety for Support Personnel (initial)	*1*	*3*
BSL-3/BSL-4 Biosafety for Support Personnel (Refresher)	*5*	*61*
New Employee Training	*2*	*5*

6) ***Safety Audits and Inspections***

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

a) *Biological Incident Report:*
   i) *None*

7) ***Select Agent Issues***
   a) *Unannounced CDC DSAT Inspection December 3-5, 2019*

8) ***Other Issues –***
   a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 01/16/2020
Meeting Time: 1:02 PM **Adjourned:** 1:51 PM
Building A Library, (b)(6)

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Alexandra Scranton	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Heinz Feldmann (EO)	☐	☒	Brian Vickrey	☐	☒
Becky Anderson (EO)	☒	☐	Nancy Hoe	☐	☒	Clayton Winkler	☐	☒
Alan Applebury	☐	☒	Erik Hoover	☐	☒			
Chris Bosio	☒	☐	Clay Jarrett	☒	☐			
Marshall Bloom (EO)	☐	☒	Josh Kellar (EO)	☐	☒			
Megan Brose	☐	☒	Scott Kobayashi	☒	☐			
Larry Brouwer	☐	☒	Jamie Lovaglio	☒	☐			
Carol Calderwood	☐	☒	Andrea Marzi	☐	☒			
Marcie Caldwell (EO)	☐	☒	Alida Merritt	☐	☒			
Bruce Chesebro (EO)	☐	☒	Greg Saturday	☒	☐			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 12/19/19 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 12/19/19** Action: Meeting minutes for 12/19/19 were unanimously approved with minor typos from Sue Priola.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment) ▪ Bosio (LB) ▪ **PRD#19-218 Amend: *Klebsiella pneumoniae*** ▪ Becky Anderson presented the risk assessment. The proposed studies are to

	add animal work with mice. The primary hazards include rodent bites or scratches and accidental sharps injuries. To mitigate these hazards, studies will be performed in the human pathogen wing of (b)(6) PPE includes lab coat, gloves, and a surgical mask. All manipulations must be performed in a BSC. ▪ Animal studies with mice were proposed. ▪ Work with *K. pneumoniae* is approved at BSL-2/ABSL-2. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Chris Bosio abstained) **PRD#19-218 Amend** as written.
Item 2:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment) ▪ Bloom (LV) ▪ **PRD#19-213 Amend: *Borrelia burgdorferi*** ▪ Becky Anderson presented the risk assessment. The proposed studies are to add animal work with mice. The primary hazards include rodent bites or scratches and accidental sharps injuries. To mitigate these hazards, studies will be performed in the human pathogen wing of (b)(6) PPE includes lab coat, gloves, and a surgical mask. All manipulations must be performed in a BSC. ▪ Work with *Borrelia burgdorferi* is approved at BSL-2/ABSL-2. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#19-213 Amend** as written.
Item 3:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment) ▪ Bloom (LV) ▪ **PRD#14-58 Amend: Langat virus** ▪ Becky Anderson presented the risk assessment. The proposed studies are to add animal work with mice. The primary hazards include rodent bites or scratches and accidental sharps injuries. To mitigate these hazards, studies will be performed in the human pathogen wing of (b)(6) PPE includes lab coat, gloves, and a surgical mask. All manipulations must be performed in a BSC.

	▪ Animal studies with mice were proposed. ▪ BSL-2/ABSL-2 is appropriate for work with Langat virus ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#14-58 Amend** as written.
Item 4:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment) ▪ Feldmann (LV) ▪ **PRD#17-143 Amend: Coronavirus (exempt, non-Select Agent)** ▪ Becky Anderson presented the risk assessment. The amendment is to add the novel Coronavirus from Wuhan, China. This is the virus that is causing a pneumonia outbreak in Wuhan China that started in December 2019. There have been at least 41 cases (dozens hospitalized) and 1 death associated with this virus (this individual had other serious underlying medical conditions). It does not appear that the virus is readily transmitted by person to person contact, however there is limited information on the virus at this time. It is thought that the outbreak started because of contact with animals in the city of Wuhan at a live animal market. There has been an additional case that suggests either there is some human to human transmission, or the recent case was picked up at a separate market in Wuhan. Symptoms of this infection include: fever followed by difficulty breathing. Upon chest x-ray, patients appear to have lesions in both lungs. This virus is 79% similar genetically to SARS-CoV. Because the novel Coronavirus is so similar to SARS-CoV and due to the lack of information available the recommendation for the biosafety level is BSL-3/ABSL-3 with the same PPE used for MERS-CoV at BSL-3. ▪ Sue Priola questioned the committee if they have concerns with the biosafety level. The committee agreed that BSL-3/ABSL-3 is appropriate for this novel virus. ▪ Sue Priola noted that the description section listed the addition of "one or more strains of Wuhan 2019 Coronavirus", strains should be changed to isolates. ▪ No animal studies were submitted, reviewed, or approved. ▪ BSL-3/ABSL-3 is appropriate for work with the new Wuhan 2019 Coronavirus ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal.

	Action: The committee unanimously approved **PRD#17-143 Amend** with the following minor modifications: 1. Change strains to isolates in the description section.
Item 5:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Chesebro (LPVD) ▪ **PRD#20-166: Human blood and body fluids** ▪ Becky Anderson presented the risk assessment. This is a renewal for the Chesebro lab. The Chesebro lab will test if brain homogenates from humans carrying the two independent mutations in prion protein genes described in the PRD are transmissible. Three most common bloodborne pathogens are HBV, HCV, and HIV. HBV is the most common of the three and causes a serious form of hepatitis. The symptoms include: jaundice, fatigue, abdominal pain, loss of appetite, intermittent nausea, vomiting. It can also lead to chronic liver disease, liver cancer, and death. There is a vaccine available for HBV, the vaccine is offered free of charge at RML through the OMS Nurses. HCV symptoms include jaundice, fatigue, abdominal pain, loss of appetite, intermittent nausea and vomiting. HCV can also lead to chronic liver disease and death. HIV is the virus that leads to AIDS. ▪ Animal studies with mice were proposed. ▪ Work with human blood and body fluids is approved at BSL-2/ABSL-2. ▪ The recommendations section also includes language for working with Bloodborne Pathogens. ▪ The committee discussed the dual-use potential of these experiments as described above. Dual use question 5 is marked yes because the Chesebro lab will passage the prions through mice. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#20-166** as written.
Item 6:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Gherardini (LB) ▪ **PRD#20-03: Borrelia spp.** ▪ Becky Anderson presented the risk assessment. The proposed studies are to develop a better understanding of the infectious cycle of *Borrelia burgdorferi*. *B. burgdorferi* causes Lyme disease, which is a tickborne zoonotic disease characterized by distinctive skin lesion, can present with fever, chills, headache, fatigue, muscle and joint aches, and swollen lymph

	nodes. The rash occurs in approximately 70 to 80 percent of infected individuals. It begins at the site of a tick bite and after a few days expands reaching up to 12 includes across. Sometimes the rash can have a bull's eye appearance as it grows. Approximately 10 to 20 percent of patients treated for Lyme disease with a 2-4 week course of antibiotics will have lingering symptoms of fatigue, pain, or joint and muscle aches. In some cases, these symptoms can last for more than 6 months. The natural route of transmission is through the bite of an infected tick. There is no evidence of human to human transmission. The primary lab hazards include: accidental needle stick, generation of aerosols. ▪ Sue Priola noted that the reference to LZP should be changed to LB. ▪ Sue Priola also stated that there are rabbits listed in the ASP, these animals should be added to the PRD. Becky Anderson stated that Frank Gherardini did not want rabbits included because he was not doing infectious work with them, but the attached ASPs look like they do. The committee agreed to add the ASP for rabbits and in order to make sure they are also properly registered. ▪ Animal studies with mice and rabbits were proposed. ▪ Work with Borrelia spp. is approved at BSL-2/ABSL-2. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **PRD#20-03** with the following modifications: 1. Change the reference from LZP to LB as these labs have re-organized. 2. Attach the ASP for animal work with rabbits.
Item 7:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal)</u> ▪ Hasenkrug (LPVD) ▪ **PRD#20-114: *Listeria monocytogenes*** ▪ Becky Anderson presented the risk assessment. The Hasenkrug lab uses *L. monocytogenes* as a control during *in vivo* infections. Specifically, they co-infect mice with Friend virus and *L. monocytogenes* to determine if FV induced immune suppression is confined to FV primary infections or extends to secondary infections as well. Although relatively rare, human listeriosis is often severe and mortality rates can approach 50%. Certain factors predispose individuals to infection with *L. monocytogenes*, such as neonates, pregnancy, leukemia, Hodgkin's disease, diabetes mellitus, alcoholism or cirrhosis and immunosuppressive or cytostatic therapy. Most commonly,

	listeria causes a mild febrile illness. There are currently no vaccines available. The primary choice of therapy includes ampicillin or amoxicillin together with gentamicin. The recommended course of treatment is 2 to 4 weeks. The predominate route of transmission is though consumption of contaminated foods. The primary lab hazards include: accidental sharps injuries, ingestion, or inhalation. ▪ Animal studies with mice were proposed. ▪ Work with *Listeria monocytogenes* is approved at BSL-2/ABSL-2. ▪ The following precautions have been added to the recommendations section: ○ Women who are pregnant or thinking of becoming pregnant are encouraged to notify the Lab supervisor and RML OMS Nurse. This is in order to assure that they are aware of any potential risks to themselves or the fetus and determine if any additional risk reduction measures should be taken. ○ All work with infectious materials is conducted in a BSC, centrifugation of infectious materials must be carried out in sealed safety cups or removable rotors that can be loaded and unloaded in a BSC. ○ Immunocompromised persons should be made aware of the risks of working with this material. RML OMS Nurses can help to determine if any additional risk reduction measures should be taken. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **PRD#20-114** as written.
Item 8:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal)</u> ▪ Hasenkrug (LPVD) ▪ **PRD#20-161: *Diphtheria toxin*** ▪ Becky Anderson presented the risk assessment. The Hasenkrug lab is using transgenic mice in which the immunosuppressive T cells or regulatory T cells (Tregs) express diphtheria toxin receptors. Treatment of these mice with diphtheria toxin specifically depletes the Tregs allowing them to study effects on other components of the immune response. The toxin, when absorbed, affects organs and tissues distant from the site of invasion. The most frequent complications of diphtheria are myocarditis and neuritis. The overall case-fatality rate for diphtheria is 5%–10%, with higher death rates (up to 20%) among persons older than 40 years of age. Treatment with

	hyperimmune antiserum has been shown to reduce mortality from 7 to 2.5 percent. Antibodies only neutralize toxin before its entry into cells, so rapid treatment is essential. ▪ Animal studies with mice were proposed. ▪ Work with diphtheria toxin is approved at BSL-2/ABSL-2. ▪ The following precautions have been added to the recommendations section: ○ Preparative work with the toxin should be done in a Class II B2 BSC or CFH at BSL-2 with proper PPE being worn. ○ Please see BMBL Appendix I. A recent DTP vaccination is recommended. ○ Sharps containers in animal rooms should be labeled, "contaminated with toxin". ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#20-161** as written.
Item 9:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Gherardini (LPVD) ▪ **RD#20-319**: *Borrelia burgdorferi* ▪ Reviewers: Chris Bosio, Clay Jarrett ▪ **Summary:** Characterization of the infectious cycle of *Borrelia burgdorferi* ▪ Chris Bosio summarized the RD. He stated that in the renewal, it was not clear what the new route of inoculation was. Chris Bosio noted that they need to enter N/A in the host prokaryote section for the question, "If you are working with viral rDNA, what percent sources genome. . ." The information can be deleted because they are not working with vRNA. ▪ Clay Jarrett stated that they listed the suicide vectors twice, but they are the same. The NIH Guidelines are appropriate and there are no dual use issues. ▪ Sue Priola noted the same comments as for the Gherardini PRD. The reference to LZP should be changed to LB. Add animal studies with rabbits. ▪ Animal studies with mice and rabbits were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#20-319** with the following

	minor modifications: 1. Delete the text in the, "If you are working with viral rDNA, what percent sources genome. . ." section and replace with N/A. 2. Change LZP to LB. 3. Add animal work with rabbits. Research using prokaryotic hosts is approved at BSL-2 under section III-D-1-a and III-D-2-a of the NIH Guidelines.
Item 10:	<u>Registration Documents for Recombinant DNA Experiments (Renewal)</u> ▪ Feldmann (LV) ▪ **RD#20-419**: Orthobunyaviruses ▪ Reviewers: Sue Priola, Scott Kobayashi ▪ **Summary:** Orthobunyavirus reverse genetics, minigenomes/replicons and trVLPs ▪ Sue Priola summarized the RD. The Orthobunyavirus RD is to characterize the pathogenesis of Orthobunyavirus and viral protein functions by three main strategies. They will make mutant and chimeric viruses, minigenomes and virus like particles. There is a dual use question marked yes because they will be using synthetic DNA techniques to study ancestral viruses. The DURC response was very extensive, the PI does not think they will create a virus that is any more virulent than the current viruses. There is no overall DURC. The NIH Guidelines are appropriate. Sue Priola noted that the dual use language references a PRD when it should be an RD. ▪ Scott Kobayashi noted that the Eukaryotic cells section for the NIH Guidelines has III-D-3-b listed which is for BSL-3. This makes the biosafety levels confusing. Becky Anderson stated that a comment could be entered to state the biosafety level will depend on the virus being studied. The committee agreed this would be appropriate. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **RD#20-419** with the following minor modifications: 1. In the Eukaryote Cell section, clarify that they biosafety level will vary depending on the virus being studied. 2. Remove the references to PRD in the dual use question 1 answers and change

	to RD. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 or BSL-3 (depending on the virus studied) under III-D-1-a, III-D-3-a, III-D-3-b, III-E-1, III-D-1-b of the NIH Guidelines.
Item 11:	**Full Committee Review of MCL Inactivation Data with AVL & SDS/Heat** ▪ Sue Priola informed the committee that there is inactivation data to review for the MCL. Included in this month's submission is testing data for inactivation of Coronaviridae (SARS as surrogate) inactivated with AVL. Also included for review is testing data for Arena-, Bunya-, and Paramyxo- virus and infected cells with SDS/Heat inactivation. ▪ Sue Priola summarized the testing results for the inactivation of tissues. Sue Priola confirmed with the committee that the samples and titers tested were appropriate, all necessary controls were included and that the procedures matched what is listed in the SOP. There were no comments or concerns with the inactivation data. Action: The committee unanimously approved the inactivation data using the AVL for Coronaviridae stock and SDS/Heat inactivation for Arena-, Bunya-, and Paramyxo- virus and infected cells as written.
Item 12:	**Standard Operating Procedure: SOP#4-28-31 Removal of Specimens for Protein Analysis (Update)** ▪ Sue Priola summarized the changes to the SOP to the committee. The update to the SOP was the addition of the table that lists the approved inactivation procedures. ▪ Sue Priola stated that plate size or cell number should be added to the SOP to reflect what was used in the validation testing. ▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved the **SOP#4-28-31 Removal of Specimens for Protein Analysis (Update)** with the following minor modifications: 1. Add plate size or cell number to the SOP in section 6.c.
Item 13:	**Standard Operating Procedure: SOP#4-28-32 Removal of Specimens for Nucleic Acid Extraction (Update)** ▪ Sue Priola summarized the changes to the SOP to the committee. The update to the SOP was the addition of the new inactivation procedure with Coronavirus to the table of approved procedures.

	▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved the **SOP#4-28-32 Removal of Specimens for Nucleic Acid Extraction (Update)** as written.
Item 14:	**Standard Operating Procedure: SOP#4-28-48 Inoculation/Infection and Blood Collection Procedures for Rodents in Level 4 Biocontainment (Update)** ▪ Becky Anderson summarized the changes to the SOP to the committee. The update to the SOP was the addition of the intravaginal route of inoculation. ▪ Jamie Lovaglio stated that there are several parts of the SOP that should be updated to more accurately reflect what is done in the BSL-4. Becky Anderson stated that this can be done and brought back to the IBC for review of those changes. At this time, we should focus on approving the additional language that was added. The committee agreed with this approach. ▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved the **SOP#4-28-48 Inoculation/Infection and Blood Collection Procedures for Rodents in Level 4 Biocontainment (Update)** as written.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Becky Anderson reviewed the BSO Report
Report:	**Occupational Safety and Health Manager Report/** (b)(6) ▪ Not present.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ Not present.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ None.

Other issues	▪ None

Next Meeting:

- Date: 2/20/2020
- Place: Library conference room
- Time: 1:00 PM

RML Biosafety Committee Meeting
January 16, 2020
Biosafety Officer/Responsible Official Report

1) ***Requests approved by BSO since last meeting:***
   a) ***None***
2) ***New requests approved by committee via electronic review:***
   a) ***None***
3) ***New requests***
   a) *Pathogen Registration Documents*
      i) ***Renew***
         (a) *Chesebro (LPVD)*
            (a) ***PRD-20-166;*** *Human blood and body fluids*
         (b) *Gherardini (LB)*
            (a) ***PRD-20-03;*** *B. burgdorferi*
         (c) *Hasenkrug (LPVD)*
            (a) ***PRD-20-114;*** *Listeria monocytogenes*
         (d) *Hasenkrug (LPVD)*
            (a) ***PRD-20-161;*** *Diphtheria toxin*
      ii) ***Amend***
         (a) *Bosio (LB)*
            (a) ***PRD-19-218;*** *K. pneumoniae*
         (b) *Bloom (LV)*
            (a) ***PRD 19-213;*** *B. burgdorferi*
         (c) *Bloom (LV)*
            (a) ***PRD 19-58;*** *Langat virus*
         (d) ***Feldmann (LV)***
            (a) ***PRD 17-43;*** *Coronavirus*
   b) *Registration Documents for Recombinant Nucleic Acid Experiments*
      i) ***Renew***
         (a) *Gherardini (LPVD)*
            (a) ***RD-20-319****: B. burgdorferi*
         (b) *Feldmann (LV)*
            (a) ***RD-20-419****: Orthobunyavirus*
   c) *Inactivation Validation Testing Review*

i) *Feldmann (LV)*

(a) *Inactivation of RG4 viral family (Corona- viral families) with AVL*

(b) *Inactivation of RG4 viral family (Arena-, Bunya-, Paramyxo- viral families) with SDS + heat*

d) ***Standard Operating Procedures***

i) ***Update***

(a) *SOP#4-28-31: Removal of Specimens for Protein Analysis*

(i) Add procedures for SDS & heat inactivation with Arena-, Bunya-, Paramyxo- viral families

(b) *SOP#4-28-32: Removal of Specimens for Nucleic Acid Extraction*

(i) Add procedures for inactivation of Coronaviruses with AVL

(c) *SOP#4-28-48 Inoculation/Infection and Blood Collection Procedures for Rodents in Level 4 Biocontainment*

(i) Add the intravaginal route of inoculation

4) ***Animal Study Protocols Review***

Title	*Associated PRD*	*Associated RD*	*Reviewer*
Establishment of a pneumonic model of Klebsiella pneumoniae in mice	*19-218*	*N/A*	*B. Anderson*
Efficacy of a Modified Vaccinia Ankara against Nipah virus Bangladesh in Syrian hamsters	*18-91, 19-159*	*15-447*	*M. Brose*
Establishing a rhesus macaque model for RVFV	*18-92*	*N/A*	*B. Anderson*
Determine the pathogenicity of Mengla virus & Bombali virus is mice	*18-90*	*14-407*	*B. Anderson*
Defining the peripheral route of infection and neuroinvation in the Bornavirus rhesus macaque model	*18-208*	*N/A*	*B. Anderson*
Investigating the role of Ajuba in DC migration from skin to draining lymph nodes in a mouse model	*17-108*	*N/A*	*M. Brose*
Infective cycle of Borrelia burgdorferi mutants in the mouse tick-mouse model of infection & transmission	*14-03*	*N/A*	*M. Brose*
Interactions of tickborne bacteria & viruses throughout the tick life cycle	*19-58, 19-213*	*N/A*	*M. Brose*

RML Biosafety Committee Meeting
January 16, 2020
Biosafety Officer/Responsible Official Report

5) ***Biosafety Training Performed – Megan Brose, Rebecca Anderson, Nancy Hoe***

Type of Training	***Number of Sessions***	***Number of Employees Trained***
BSL-4 Laboratory Biosafety Annual refresher	*1*	*1*
BSL-3 Laboratory Biosafety	*1*	*2*
Select Agent Initial Training	*1*	*2*
Select Agent visitor/BSL-3 visitor	*1*	*21*
New Employee Training	*1*	*1*

6) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
   a) *Biological Incident Report:*
      i) *None*

7) ***Select Agent Issues***
   a) *Tentative date for the BSL-4 CDC DSAT inspection April 6-10.*

8) ***Other Issues –***
   a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 02/20/2020
Meeting Time: 1:02 PM **Adjourned:** 2:40 PM
Building A Library, (b)(6)

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Alexandra Scranton	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Heinz Feldmann (EO)	☐	☒	Brian Vickrey	☐	☒
Becky Anderson (EO)	☒	☐	Nancy Hoe	☐	☒	Clayton Winkler	☒	☐
Alan Applebury	☐	☒	Erik Hoover	☒	☐			
Chris Bosio	☒	☐	Clay Jarrett	☐	☒			
Marshall Bloom (EO)	☐	☒	Josh Kellar (EO)	☐	☒			
Megan Brose	☒	☐	Scott Kobayashi	☒	☐			
Larry Brouwer	☐	☒	Jamie Lovaglio	☐	☒			
Carol Calderwood	☐	☒	Andrea Marzi	☒	☐			
Marcie Caldwell (EO)	☐	☒	Alida Merritt	☒	☐			
Bruce Chesebro (EO)	☐	☒	Greg Saturday	☐	☒			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 1/16/2020 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 1/16/2020** Action: Meeting minutes for 1/16/2020 were unanimously approved with minor typos from Sue Priola.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment) ▪ De Leo (LB) ▪ **PRD#16-180 Amend: *Klebsiella pneumoniae*** ▪ Becky Anderson presented the risk assessment. The proposed amendment

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	is to add a strain of *Klebsiella pneumoniae* ST258 to the registration. The strain is designated as MKP103 and was derived from the NIH clinical isolate KPNIH1. This strain will be acquired from the U. of Washington and no recombinant work will be performed at RML. There is no biosafety level change and no additional precautions necessary for this new strain. ▪ No animal studies were submitted, reviewed, or approved. ▪ Work with *K. pneumoniae* is approved at BSL-2/ABSL-2. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#16-180 Amend** as written.
Item 2:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New) ▪ Hackstadt (LB) ▪ **PRD#20-220: *Bartonella henselae*** ▪ Becky Anderson presented the risk assessment. The Hackstadt lab will use *Bartonella henselae* to express suspected *Rickettsia rickettsii* type IV secreted effectors to see if they are secreted. *B. henselae* is the causative agent of cat scratch fever. Symptoms include low grade fever, enlarged lymph nodes, and a papule/pustule at the site of the scratch. Less commonly, eye infections, muscle pain, or encephalitis may occur. ▪ Sue Priola stated that *Rickettsia rickettsii* should be removed from the Pathogen and/or Toxin section. ▪ Work with *Bartonella henselae* is approved at BSL-2/ABSL-2. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#20-220** with the following minor modifications: 1. Remove *Rickettsia rickettsii* from the pathogen section.
Item 3:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Hackstadt (LB) ▪ **ST-PRD#20-39: *Rickettsia prowazekii (Select Agent)*** ▪ Becky Anderson presented the risk assessment. This renewal is for the storage only of *Rickettsia prowazekii*. Prior to working with this agent, IBC approval is required. The "ST" on the PRD indicates that this is a storage

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	only registration. ▪ No animal studies were submitted, reviewed, or approved. ▪ BSL-3 is appropriate for storage of *Rickettsia prowazekii* ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **ST-PRD#20-39** as written.
Item 4:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Hackstadt (LB) ▪ **ST-PRD#20-41: *Coxiella burnetii (non-exempt, Select Agent)*** ▪ Becky Anderson presented the risk assessment. This renewal is for the storage only of *Coxiella burnetii*. Prior to working with this agent, IBC approval is required. The "ST" on the PRD indicate that this is a storage only registration. ▪ No animal studies were submitted, reviewed, or approved. ▪ BSL-3 is appropriate for storage of *Coxiella burnetii.* ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **ST-PRD#20-41** as written.
Item 5:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Best (LV) ▪ **PRD#20-154: Herpes Simplex Virus 1 (HSV-1)** ▪ Becky Anderson presented the risk assessment. This is a renewal for the Best lab. The proposed studies are to continue to evaluate how viruses suppress the early immune response. They wish to use HSV-1 to compare and contrast to their other virus models. HSV-1 is associated mainly with above the waist infections involving the mouth pharynx, face, eye, and CNS. Primary infections with HSV-1 are usually acquired in childhood and may be asymptomatic or subclinical. Symptomatic primary infections present mainly as gingivostomatitis with fever, sore throat, fetor oris, anorexia, cervical adenopathy, and mucosal edema and vesicular and ulcerative painful lesions involving the buccal mucosa, tongue, gums, and pharynx. Antiviral drugs are used for treatment. The natural route of transmission is through close

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	personal contact and direct contact with contaminated secretions. Sexual and vertical transmission can occur as well. The primary lab hazards include direct contact with viral isolates, aerosolization, droplet or inhalation exposure of mucous membranes of the eyes, nose, or mouth, ingestion, accidental parenteral inoculation. ▪ Work with HSV-1 is approved at BSL-2. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#20-154** as written.
Item 6:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Best (LV) ▪ **PRD#20-170: Yellow Fever Vaccine Strain 17D** ▪ Becky Anderson presented the risk assessment. This is a renewal for the Best lab. The proposed studies are to continue to understand how the early host innate immune response is activated by Flaviviruses, and how these viruses escape early immune response to cause disease. Reactions to 17D Yellow Fever vaccine are typically mild. After vaccination, vaccinees have reported mild headaches, myalgia, low-grade fevers, or other minor symptoms for 5-10 days. There is no know transmission of this vaccine strain. The primary lab hazards are accidental sharps injuries, ingestion, or generation of aerosols. ▪ Sue Priola noted that III-D-1-a needs to be removed from the NIH Guidelines section of the Eukaryote Cell section. ▪ No animal studies were submitted, reviewed, or approved. ▪ Work with Yellow Fever vaccine strain is approved at BSL-2. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#20-170** with the following modifications: 1. Remove NIH Guidelines from the Eukaryote Cell section.
Item 7:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal)

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	▪ Heinzen (LB) ▪ **PRD#20-43: *Coxiella burnetii (non-exempt, Select Agent)*** ▪ Becky Anderson presented the risk assessment. This is a renewal for the Heinzen lab. The Heinzen lab is continuing to better understand the function of *C. burnetii* genes with an emphasis on those involved in Q fever pathogenesis. Q fever can cause acute or chronic illness, and people are commonly exposed from contact with infected animals or exposure to contaminated environments. The acute symptoms usually develop within 2-3 weeks of exposure, about half of infected people remain asymptomatic. Symptoms include high fever, fatigue, severe headache, malaise, myalgia, chills, non-productive cough, nausea, vomiting, diarrhea, and chest pain. Chronic Q fever occurs in less than 5% of infected individuals. The natural route of transmission is through breathing in dust that is contaminated with infected animal feces, urine, milk, birth products that contain *C. burnetii*. Transmission can also occur by consuming unpasteurized diary products. The primary lab hazards include parenteral inoculation, generation of aerosols, and accidental sharps injuries. ▪ Sue Priola requested that the strain list be attached to be more specific than stating that many *C. burnetii* strains are employed. Bob Heinzen stated that it was previously attached to the paper version and can be attached to the PI Dashboard renewal. ▪ Animal studies with guinea pigs were proposed. ▪ Work with *Coxiella burnetii* is approved at BSL-3/ABSL-3. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved (Bob Heinzen abstained) **PRD#20-43** with the following modifications: 1. Attach strain list.
Item 8:	<u>Registration Documents for Recombinant DNA Experiments (New)</u> ▪ Hackstadt (LB) ▪ **RD#20-132**: *Bartonella henselae* as a Type IV secretions system surrogate ▪ Reviewers: Bob Heinzen, Clay Jarrett ▪ **Summary:** Expression of suspected *R. rickettsia* type IV secreted effectors in Bartonella to see if they are secreted. ▪ Bob Heinzen summarized the RD. He informed the committee the RD is to use *B. henselae* as a surrogate to screen for *R. rickettsia* type IV effector proteins. There is not a good biolgoiocal screen for these. They will clone the genes and

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	then perform a secretion assay. Bob Heinzen stated that there is not much detail in this registration. The IBC agreed that there was a lack of detail in the RD and the Hackstadt lab needs to add detail before the IBC can approve the RD. The RD will be tabled and can be reviewed electronically ▪ Animal studies with mice and rabbits were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously TABLED **RD#20-132** and agreed to review electronically once additional information is added.
Item 9:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Hackstadt (LB) ▪ **RD#20-120**: *Chlamydia trachomatis* ▪ Reviewers: Scott Kobayashi, Bob Heinzen ▪ **Summary:** Genetic modification of Chlamydia ▪ Scott Kobayashi summarized the RD. He stated that the RD describes a transposon system for Chlamydia, the Himar1 system. The antibiotics used are appropriate because they are not preferred for treatment. The NIH Guidelines are fine and the biosafety level is appropriate. There are also no DURC issues. ▪ Bob Heinzen stated that the last sentence in the "Briefly describe the details of your study section" is not appropriate for this RD. Bob Heinzen had no additional comments or concerns. ▪ No animal studies were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#20-120** with the following minor modifications: 1. Delete the last sentence in the Briefly describe the details of your study section. Research using prokaryotic hosts is approved at BSL-2 under section III-D-1-a and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 with BSL-3 practices under III-D-1-a of the NIH Guidelines.
Item 10:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Hackstadt (LB) ▪ **RD#20-128**: Chlamydial type III secretion for *Y. pseudotuberculosis*

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	▪ Reviewers: Bob Heinzen, Chris Bosio ▪ **Summary:** *Y. pseudotuberculosis* as a heterologous host for Chlamydial type III secreted effector proteins. ▪ Bob Heinzen summarized the RD. He informed the committee that this is another heterologous secretion system. They will be looking for secreted proteins by using *Y. pseudotuberculosis* as the system. They will be cloning the Chlamydial genes into *Y. pseudotuberculosis* and then doing a secretion assay to see what Chlamydial protein has been secreted into the medial. Bob Heinzen stated that they need to add III-D-2-a to the NIH Guidelines in the Prokaryote Hosts section. ▪ Chris Bosio had no additional comments or concerns. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#20-128** with the following minor modifications: 1. Add III-D-2-a to the NIH Guidelines for the Prokaryote Hosts section. Research using prokaryotic hosts is approved at BSL-2 under section III-D-1-a of the NIH Guidelines.
Item 11:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Best (LV) ▪ **RD#20-420**: Langat virus evasion of the host immune response ▪ Reviewers: Andrea Marzi, Clayton Winkler ▪ **Summary:** Langat virus evasion of the host immune response ▪ Andrea Marzi summarized the RD. She stated that this is a renewal to continue to investigate Langat virus in mice and cell lines. There is an ASP attached describing their animal work. The appropriate vector map is attached for their recombinant work. Andrea Marzi stated that she was unsure if the NIH Guidelines were appropriate. Sue Priola stated that III-E-1 and III-D-2-a should be added to the Research Product Section. ▪ Clayton Winkler informed the committee that the RD did not explain any of the mutations, so it is hard to evaluate dual use. Would any mutation impair the virus? The committee discussed in detail and determined that a sentence should be added to state, "The mutations are expected to attenuate, but likely will not exceed virulence of the parent virus." Also, Sonja Best should add some detail to the description of the mutations.

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	▪ Sue Priola added that GFP needs to be added to the list of foreign genes. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#20-420** with the following minor modifications: 1. Add III-E-1 and III-D-2-a to the Research Product Section. 2. Add statement that mutations are expected to attenuate, but likely will not exceed the parent virus. 3. Sonja Best to add description of mutations. 4. Add GFP to list of foreign genes. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a, III-D-3-a, and III-E-1 of the NIH Guidelines.
Item 12:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Best (LV) ▪ **RD#20-421**: Kunjin virus evasion of the host immune response ▪ Reviewers: Sue Priola, Andrea Marzi ▪ **Summary:** Kunjin virus evasion of the host immune response ▪ Sue Priola summarized the RD. She stated that this RD is exactly the same as the Langat virus RD, but for Kunjin. All the systems are the same as described previously. The same changes that were added for RD#20-420 should be applied to this RD. As a note, this RD did include a DURC explanation. ▪ Andrea Marzi had no additional comments or concerns. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#20-421** with the following minor modifications: 1. Add III-E-1 and III-D-2-a to the Research Product Section. 2. Add statement that mutations are expected to attenuate, but likely will not exceed the parent virus.

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	3. Sonja Best to add description of mutations. 4. Add GFP to list of foreign genes. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a, III-D-3-a, and III-E-1 of the NIH Guidelines.
Item 13:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Best (LV) ▪ **RD#20-422**: Use of lentiviruses to interrupt host immune response signaling pathways ▪ Reviewers: Sue Priola, Clayton Winkler ▪ **Summary:** Delivery of RNAs with lentiviruses ▪ Sue Priola summarized the RD. She informed the committee that the lentiviral system is to block host genes involved in immune response to virus infection. They will use commercially available systems. The RD is straightforward. The biosafety level is appropriate. The NIH Guidelines should have III-E-1 added to both the Prokaryote Host and Eukaryote Cell section. The list of foreign genes expressed should be added. ▪ Clayton Winkler asked if they should add the siRNA targets as well. Sue Priola stated that they do not need to be included because they are mammalian targets. Clayton Winkler had no additional comments or concerns. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#20-422** with the following minor modifications: 1. Add the list of foreign genes being expressed. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a, III-D-3-a of the NIH Guidelines.
Item 14:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Best (LV) ▪ **RD#20-439**: Investigating the pathogenesis and mechanisms of immune evasion of Dengue virus (1-4) ▪ Reviewers: Andrea Marzi, Sue Priola

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	▪ **Summary:** Dengue virus evasion of the host immune response ▪ Andrea Marzi summarized the RD. She stated that this RD is similar to the other RDs for Langat and Kunjin virus. This one focuses on expressing proteins from the 4 serotypes of Dengue virus. The Best lab has a viral clone to generate Dengue virus. There is no animal work associated with this RD. The Research Product and Prokaryote Host sections should have III-E-1 and III-D-2-a added. She also noted that the expression of foreign genes is not consistent throughout the document. GFP and mCherry need to be added to the list as they are talked about in different places in the RD. There are no DURC concerns. ▪ Sue Priola had no additional comments or concerns. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#20-439** with the following minor modifications: 1. Ensure the listing for foreign genes is consistent. Add GFP and mCherry to list of foreign genes. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a, III-E-1, of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a, III-D-3-a, and III-E-1 of the NIH Guidelines.
Item 15:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Heinzen (LB) ▪ **RD#20-106**: Genetic manipulation of *Coxiella burnetii* ▪ Reviewers: Chris Bosio, Scott Kobayashi ▪ **Summary:** Molecular mechanisms of *C. burnetii* survival and virulence ▪ Chris Bosio summarized the RD. He informed the committee that this is a renewal for the virulence determinants for C. burnetii. This describes all of the molecular tools that they use. It was nicely described why all of the different NIH Guidelines were added. Chris Bosio only had one concern; the Nucleic Acid insert section has some copy/paste issues. ▪ Sue Priola stated that this RD is similar to the PRD in that it says, "many *C. burnetii* strains will be employed" and the strain list should be attached. ▪ Scott Kobayashi had no additional comments or concerns. ▪ Animal studies with guinea pigs proposed.

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	▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Bob Heinzen abstained) **RD#20-106** with the following minor modifications: 1. Attach the strain list. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a, III-D-1-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a of the NIH Guidelines.
Item 16:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Heinzen (LB) ▪ **RD#20-107**: Introduction of *C. burnetii* genes into *L. pneumophila* and mammalian cell lines ▪ Reviewers: Clay Jarrett, Chris Bosio ▪ **Summary:** Deciphering the function of *C. burnetii* genes with an emphasis on those encoding proteins predicted to modulate host cell functions ▪ Chris Bosio summarized the RD. This RD is also a renewal. They will continue to look at expression of *C. burnetii* genes to and assess how they alter cell function. They will use Legionella to express the *C. burnetii* genes. Everything in this renewal looks good, the NIH Guidelines are appropriate. The only item that needs to be adjusted is to delete the viral RNA section. ▪ Clay Jarrett was not present. There were no additional comments or concerns from the committee. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Bob Heinzen abstained) **RD#20-107** with the following minor modifications: 1. Delete the entry in the viral RNA section. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a, III-D-1-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a of the NIH Guidelines.
Item 17:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Heinzen (LB)

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	▪ **RD#20-123**: Identification of proteins secreted by type IV secretion machinery ▪ Reviewers: Scott Kobayashi, Clay Jarrett ▪ **Summary:** Understanding the mechanisms of pathogen vacuole biogenesis ▪ Scott Kobayashi summarized the RD. This RD is another renewal. The Heinzen lab wants to evaluate and identify proteins secreted by the type IV secretion machinery. There are multiple BSL-2 organisms on the RD, none of them are Select Agents. When they are expressing genes in Coxiella (exempt strain), the antibiotics used for selection are appropriate. The NIH Guidelines are also appropriate for the work described. There are no DURC issues noted. The only comment is that the viral DNA section should be deleted. ▪ Clay Jarrett was not present but submitted comments. His comment was to also delete the viral DNA section. He had no additional comments or concerns. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Bob Heinzen abstained) **RD#20-123** with the following minor modifications: 1. Delete the entry in the viral RNA section. Research using prokaryotic hosts is approved at BSL-2 under section III-D-1-a, III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a and Appendix G-II-B of the NIH Guidelines.
Item 18:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Best (LV) ▪ **RD#20-456**: CPER clone of Powassan virus ▪ Reviewers: Sue Priola, Clay Jarrett ▪ **Summary:** Infectious molecular clone of Powassan virus ▪ Sue Priola summarized the RD. She stated that this is a new RD to generate an infectious clone of Powassan virus. They will mix together 7 overlapping dsDNA fragments and clone into the pUC19 vector. An eighth pUC19 plasmid will contain the untranslated region linker. Sue Priola informed the committee that III-D-2-a needs to be added to the research product section. She also noted that the first sentence in the synopsis section should have “amendment” removed as this is a new registration. The remaining NIH Guidelines are fine and there are no DURC issues. ▪ Clay Jarrett questioned the NIH Guidelines in his submitted comments. Sue Priola stated that they are appropriate. He had no additional comments or

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	concerns. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#20-456** with the following minor modifications: 1. Add III-D-2-a to the research product section. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a and III-D-1-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-2-a of the NIH Guidelines.
Item 19:	**Full Committee Review of MCL Inactivation Data with SDS/Heat** ▪ Sue Priola informed the committee that there is inactivation data to review for the MCL. Included in this month's submission is testing data for inactivation Flavivirus and Flavivirus infected cells with SDS/Heat inactivation. ▪ Sue Priola summarized the testing results for the inactivation of tissues. Sue Priola confirmed with the committee that the samples and titers tested were appropriate, all necessary controls were included and that the procedures matched what is listed in the SOP. There were no comments or concerns with the inactivation data. Action: The committee unanimously approved the inactivation data using SDS/Heat inactivation for Flavivirus and Flavivirus infected cells as written.
Item 20:	**Standard Operating Procedure: SOP#4-28-31 Removal of Specimens for Protein Analysis (Update)** ▪ Sue Priola summarized the changes to the SOP to the committee. The update to the SOP was the addition of the table that lists the approved inactivation procedures. ▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved the **SOP#4-28-31 Removal of Specimens for Protein Analysis (Update)** as written.
Item 21:	**Standard Operating Procedure: BSL-3 (b)(6) SOP (Update)** ▪ Becky Anderson summarized the new SOP to be added to the BSL-3 (b)(6) SOP, BSL-3-C-10 MACSQuant Tyto Sorter SOP. The Bosio lab would like to place a cell sorter in their BSL-3 lab. This is a newer design cell sorter called the MACSQuant Tyto. This sorter does not use the typical high-pressure fluidics

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	system that we normally see in cell sorters. Instead, samples are loaded into a sealed plastic cassette and the cells sorted never leave the cassette, instead they pass through to different compartments within the cassette. The movement of cells is by injection of air through 0.1 um filter with 3 psi of pressure. The biggest concern with using cell sorters to sort infected cells is the generation of infectious aerosols. While this cell sorter is advertised to not create aerosols, biosafety performed testing to ensure that no aerosols could be detected. In the packet, the results of that testing are included. Fluorescent beads were diluted to an approximate concentration of $67x10^6$ beads/ml. This sample was then sorted on the MACSQuant Tyto. During the sort, a Cyclex-d impactor was connected to a vacuum set at a constant volume of 20 liter/min. The coverslip within the impactor was then analyzed for fluorescent beads. Two conditions were monitored, both during the sort with the lid closed and after the sort when the lid opens. Neither condition tested resulted in any collection of fluorescent beads. A positive control was generated to ensure the assay worked; this was setup with a different, high fluidics cell sorter set to fail mode. Katy Bosio was available by cell phone for any questions the committee had. Sue Priola questioned how the cassette would be loaded and transported to the cell sorter. Katy Bosio stated that it would be loaded in the BSC and transported to the cell sorter within a containment box. Once a sort was complete the same containment box would be used. Katy Bosio also informed the committee that if the cassette has any leaks, it automatically shuts down and does not sort because it needs a sealed system for the airflow to move the cells. ▪ The committee discussed the results of the assays and agreed that the determined that aerosols were not generated during cell sorting procedures with the MACSQuant Tyto. The committee decided that the cell sorter does not require primary containment and can be placed on the benchtop. ▪ There were no additional comments or concerns with the updated procedures. Action: The committee approved (Chris Bosio abstained) the **BSL-3 (b)(6) OP (Update)** as written.
Item 22:	**Standard Operating Procedure: SOP#4-28-54 Operation of the Cytoflex LX (Update)** ▪ Becky Anderson summarized the changes to the SOP to the committee. LV has purchased a new flow cytometer. The only changes to the SOP are how to use the new cytometer. Samples are still fixed with 4% PFA as they were in the previous SOP.

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	▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved the **SOP#4-28-54 Operation of the Cytoflex LX (Update)** as written.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Becky Anderson reviewed the BSO Report
Report:	**Occupational Safety and Health Manager Report/**(b)(6) ▪ Not present.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ The (b)(6); (b)(3):42 shutdown is ongoing. The (b)(6) shutdown will start February 28. The (b)(6) will be the following week in March.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ Alida Merritt thanked (b) (6) for talking to the MT APEC group on Q fever. (b) (6) also spoke to the group about influenza. The group really appreciates the staff at RML to be such a great resource. The group is mostly nurses that are all studying for an infection control certification. Thank you for helping us out.

Other issues	▪ None

Next Meeting:

- Date: 3/19/2020
- Place: Library conference room
- Time: 1:00 PM

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RML Institutional Bio-Safety Committee Minutes

Due to the COVID-19 Pandemic, this meeting was conducted electronically by email. Documents were sent to the committee for comments on 3/16/20. An email including comments/questions/answers was sent to the committee to vote on the following documents. This request was sent on 3/23/20.

Minutes: Meeting minutes from 2/20/2020 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 2/20/2020** Action: Meeting minutes for 2/20/2020 were unanimously approved with the following minor modifications: ▪ Pg. 1 Clayton Winkler was present, not present and absent at the same time. ▪ Pg. 3, Item 5, last 2 lines. Change "Antiviral drugs can be treatment" to "Antiviral drugs are used for treatment. ▪ Pg. 4, Item 5, last bullet. Dual use potential paragraph refers to Chesebro lab, not Best lab. ▪ Pg. 5, Item 7, under Action. Should note that Bob Heinzen abstained. ▪ Pg. 6, Item 9, bullet 6. Delete "because it" in line 2 and put quotations around section name. ▪ Pg. 7, Item 10, bullet 4, line 2. "…they will be looked for secreted… " should be "…they will be looking for secreted…" ▪ Pg. 7, Item 10, bullet 4, line 4. Remove "the" in front of bacteria name. ▪ Pg. 14, 4th line from bottom of top paragraph. "sorted" should be "sorter". ▪ At the bottom of page 15, the date for the next meeting is the February date

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment)

	▪ Feldmann (LV) ▪ **PRD#19-159 Amend:** ***Modified Vaccinia Ankara (MVA)*** ▪ Amendment was to add animal work with hamsters. ▪ No comments. ▪ Animal studies with hamsters were proposed. ▪ Work with MVA is approved at BSL-2/ABSL-2. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#19-159 Amend** as written.
Item 2:	Registration Documents for Recombinant DNA Experiments (Amend) ▪ Steele-Mortimer (LB) ▪ **RD#15-108 Amend**: Salmonella Host Cell interactions ▪ Reviewers: Bob Heinzen, Chris Bosio ▪ Bob Heinzen: This amendment is simply to add guinea pigs and rabbits to an existing RD that examines Salmonella host cell interaction and pathogenesis. Animals will be examined as models of Salmonella gastroenteritis. I have no concerns with the proposed studies. ▪ Chris Bosio: Amendment also adds oral route of infection. ▪ Clayton Winkler: I recuse myself, because I am listed as an associated researcher on this document. ▪ Animal studies with guinea pigs and rabbits were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Clayton Winkler abstained) **RD#15-108 Amend** as written.
Item 3:	Registration Documents for Recombinant DNA Experiments (Amend) ▪ Feldmann (LV) ▪ **RD#17-452 Amend**: Use of Alphavirus replicon system to produce vaccines ▪ Reviewers: Andrea Marzi, Clay Jarrett ▪ Andrea Marzi: No comments or concerns. NHPs should be added to this RD. ▪ Alex Scranton: This amendment says the only new work is to add NHP to this RD. The original RD however does not include mention of SARS-CoV-2 – which

	the NHP will be challenged with – in order to test the potential vaccine. Seems important that these details also be included in the amendment to the RD (and not just in the Animal Study Proposal). It should be clearly reflected in the IBC records that the committee discussed a proposal to test a possible vaccine for SARS-CoV-2. Otherwise it may appear that in the records that we just approved adding NHP to a study on Ross River Virus. ▪ Also – I hope there can be some discussion (virtually at least) about the pros and cons of the expediency of this work. Clearly, the world could use a vaccine quickly – but on the other hand there is little we know – there isn't even a mouse model developed yet – and the ASP says the NHP model is still in development – so there are still a lot of questions there. It's a big decision to devote resources to NHP studies – and could be unfortunate to do so prematurely and waste those resources/opportunities by not waiting for more information on the NHP model that could better inform a study. ▪ It could also be clarified as to who/where the NHP model is being developed – and what coordination is expected between RML and whoever else is doing that work (is it Univ of Washington?). Given the many unknowns - coordination and collaboration would be a good idea. ▪ <u>Becky Anderson Response:</u> PRD 17-143, for Coronaviruses, was approved in October of 2017. At that time, animal studies with NHPs were approved. An amendment in January was to specifically add SARS-CoV-2 to the list of approved Coronaviruses on PRD 17-143. The animal models that were previously approved apply to any new virus that we add to this PRD. Any amendment is to add to the original RD, not an amendment to an amendment. The amendment for NHPs is not to the amendment to add Ross River Virus, rather to the original RD describing use of alphavirus as a vaccine platform. ▪ As to the animal research, it is the purview of the Animal Care and Use Committee, the PI and Lab Chief as to when it is appropriate (ethically) to do different animal models. The IBC sets the biosafety level, ensures that appropriate safety procedures are developed for various procedures. ▪ I'm not sure we can/should ask the PI to describe who and where all the animal models are being developed as this is not a requirement of the RD. I can tell you that they are having weekly (at a minimum) conference calls with several other research groups and each group is working on different NHP models so that they are not duplicating work in order to get the fastest possible results. ▪ <u>Clay Jarrett:</u> Dual Use question B (the synthetic biology question) is answered "No" on the current document but "Yes" on the previous version. Either answer is fine with me, since the general statement in the previous document

	explains things well enough. I bring it up only to see if we need to keep the answers consistent. Actually, this is the third amendment to the RD and only on the last one was B answered "Yes". You might just disregard my comments. Obviously, a timely study, with over two years of work, that should be approved. ▪ Animal studies with NHPs were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#17-452 Amend** as written.
Item 4:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Feldmann (LV) ▪ **RD#20-446:** Plasmodium spp. ▪ Reviewers: Scott Kobayashi, Sue Priola ▪ Sue Priola: The purpose of this RD is to develop a multiplex qPCR to detect multiple Plasmodium spp. This is a renewal and no changes have been made to the RD. No comments. ▪ Clayton Winkler: reference pdf appears to be largely missing. ▪ Sue Priola Response: Often, only the first page of a reference is included. The committee has accepted that in the past since they can use the first page to look up the whole reference. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#20-446** as written.
Item 5:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Feldmann (LV) ▪ **RD#20-447:** Plasmodium spp. ▪ Reviewers: Sue Priola, Clayton Winkler ▪ Andrea Marzi: We added hamsters to the MVA PRD above. Shouldn't this species with the above ASP being added here, too? ▪ Clayton Winkler: Overall, I see no major problems with this proposal and have no dual use concern. Vote to approve. ▪ Pg.2 in "purpose of study", they should indicate the meaning of MVA.

- Pg.2 near the bottom of "briefly describe your study" the authors make a redundant statement: "No cloning will be done on-site, and no work will be done in prokaryotic systems. The only eukaryotic work would be to grow the virus in cell culture to obtain sufficient volume of high titer material in preparation for vaccination." This should be removed.

- Pg.5 In this section the authors describe the use of their recombinant MVA and VACV vaccine viruses in eukaryotic cells, which they claim to be limited to amplifying/passaging virus. Then in the "proposed pertinent NIH guidelines" should they say III-D-1a rather than III-D-2a since they are not doing any of the cloning or homologous recombination in-house? Or does this section pertain to all the molecular biology done to generate the vaccine virus even if off-site?
- Becky Anderson Response: I think it is safer to include the NIH Guidelines for all of the molecular biology done for the proposed work, even if off-site. I would just keep the III-D-2-a so if there was an amendment to the registration at a later date to perform this work at RML, we would not miss including III-D-2-a.

- Clayton Winkler: Pg.22 In the section describing the viral gene insertion points, I was a little confused. They make the statement "This vaccine generates non-infectious virus-like particles (VLPs) in the cells of the vaccinated animal…", would this not also be the case in eukaryotic cell lines in which they are trying to amplify the virus? Or is there something special about the avian cell lines they propose to use that allow for generation of infectious virus? Or this this just a product of being in an animal system? I guess I'm just looking for some clarity since they don't discuss this point in any of their other study details.
- Andrea Marzi Response: The VLPs are expressed from any cell line that is infected with the MVA – no matter if avian or mammalian. Or in an animal for that matter. The important point is though that MVA will not replicate in an animal or in mammalian cell culture. MVA replicates only in avian cells. It is only the vehicle for the antigens.

- No animal studies were submitted, reviewed, or approved.

- The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal.

Action: The committee unanimously approved **RD#20-447** with the following minor modifications:

1. In "purpose of study", indicate the meaning of MVA.
2. Near the bottom of "briefly describe your study", delete the following statement: "No cloning will be done on-site, and no work will be done in prokaryotic systems. The only eukaryotic work would be to grow the virus in cell culture to obtain sufficient volume of high titer material in preparation for

	vaccination."
Item 6:	Transfer PI of currently approved registrations The following PRDs and RDs will be transferred from PI Heinz Feldmann to PI Andrea Marzi: ▪ PRD 19-216: Yellow Fever Virus ▪ PRD 16-182: Zika Virus ▪ PRD 18-082: Replication Competent wild-type Vesicular Stomatitis Virus (VSV). ▪ RD 15-404: Replication competent VSV. VSV is used to study the function of viral proteins derived from various viral pathogens (below) in virus replication and pathogenesis. Moreover, we have developed and are continuously developing vaccines based on VSV as a replication competent vaccine vector expressing proteins of interest originating from various viral pathogens that may be tested in animal disease models. We will also be using VSV as a delivery platform for miRNAs against these viruses to be tested as therapeutics. Foreign genes encoding viral proteins, and miRNAs, used in these studies will be derived from Filo-, Bunya-, Henipa-, Arena-, Retro-, and Coronaviruses. ▪ RD 15-406: Replication deficient VSV. To study the attachment and entry processes of various viral pathogens (below) by rescuing VSV pseudoparticles containing internal reporter genes (i.e. GFP, luciferase, or others) and carrying foreign viral glycoproteins on their surface. Moreover, we are developing vaccines based on VSV as a vaccine vector expressing proteins of interest derived from various viral pathogens that may be tested in animal disease models. The viral pathogens to be used in these studies are Filo-, Bunya-, Paramyxo-, Orthomyxo-, Flavi-, Arena-, and Coronaviruses. Foreign genes will also originate from these viruses. Action: The committee approved (Andrea Marzi abstained) transferring the PI for all of the above registrations from Feldmann to Marzi.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ None.
Report:	**Occupational Safety and Health Manager Report/**(b)(6) ▪ None.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ None.

Report	**Associate Director Report/Marshall Bloom** ▪ None.
Around the room	▪ None.

Other issues	▪ None

Next Meeting:

- Date: 4/16/2020
- Place: Library conference room
- Time: 1:00 PM

RML Biosafety Committee Meeting
April 8, 2020
Biosafety Officer/Responsible Official Report

1) ***Requests approved by BSO since last meeting:***
   a) ***None***
2) ***New requests approved by committee via electronic review:***
   a) ***None***
3) ***New requests***
   a) *Pathogen Registration Documents*
      i) ***New***
         (a) *Hasenkrug (LPVD)*
            (a) *PRD-20-221; HBBF-COVID19*
         (b) *Bosio (LB)*
            (a) *PRD-20-222; HBBF-COVID19*
         (c) *Bosio (LB)*
            (a) *PRD-20-223; SARS-CoV-2*
      ii) ***Renew***
            (a) *None*
      iii) ***Amend***
            (a) *None*
   b) *Registration Documents for Recombinant Nucleic Acid Experiments*
      i) ***New***
            (a) *None*
      ii) ***Renew***
            (a) *None*
      iii) ***Amend***
         (a) *Munster (LV)*
            (a) *RD-19-455*
         (b) *Feldmann (LV)*
            (a) *RD-17-431*
   c) ***Standard Operating Procedures***
      i) ***Update***
            (a) *Draft ABSL-3 SARS-CoV-2 SOP- New*
            (b) *Draft Suite C COVID19 SOP- New*

4) ***Animal Study Protocols Review***

RML Biosafety Committee Meeting
April 8, 2020
Biosafety Officer/Responsible Official Report

Title	Associated PRD	Associated RD	Reviewer
Protective efficacy of a VSV-based vaccine for SARS-CoV-2 in hamsters	*17-143* *18-82*	*15-404*	*M. Brose*
Assessing the role of innate immunity and mitophagy in pathogenesis of COVID-19 in mice	*17-143*	*17-410*	*M. Brose*
Prophylaxis and Treatment of COVID-19-like Disease in the Rhesus Macaque Model with Hydroxychloroquine and Azithromycin	*17-143*	*N/A*	*B. Anderson*
Production of antibodies against Lineage B (SARS-like) Betacoronaviruses including SARS-CoV-2	*N/A*	*17-431*	*M. Brose*
Sentinel Animal Surveillance Program	*N/A*	*N/A*	*B. Anderson*
Laboratory Animal Holding	*N/A*	*N/A*	*B. Anderson*
Laboratory Animal Care and Use Training Program (Small Lab Animals)	*N/A*	*N/A*	*B. Anderson*
Laboratory Animal Care and Use Training Program - Rabbits	*N/A*	*N/A*	*B. Anderson*
Laboratory Animal Breeding/Production	*N/A*	*N/A*	*B. Anderson*
Guinea pig antibodies against Coxiella burnetii proteins	*18-70*	*20-106*	*M. Brose*
Characterization of the cellular immune response following systemic and/or mucosal delivery of ChAdOx1 MERS and implications for the longevity of protection conferred against MERS-CoV	*17-143*	*17-410*	*M. Brose*
Evaluation of an RNA vaccine for SARS-CoV-2 in rhesus macaques	*17-143*	*17-452*	*M. Brose*
Protective efficacy of a VSV-based vaccine against nCoV-2019 in rhesus macaques	*17-143*	*15-404*	*B. Anderson*
Mouse- and hamster-adaptation of SARS-CoV-2	*17-143*	*N/A*	*B. Anderson*
Moderna mRNA-1273 vaccine efficacy in the rhesus macaque model	*17-143*	*N/A*	*M. Brose*
CureVac mRNA SARS2 vaccine efficacy in the rhesus macaque model	*17-143*	*19-455*	*M. Brose*
Squirrel Monkeys as a Disease Model for COVID-19	*17-143*	*N/A*	*B. Anderson*
Assessing hamster knock-out strains as a COVID-19 disease model	*17-143*	*N/A*	*B. Anderson*
Treatment of mouse adapted EBOLA virus (MA-EBOV) infections with anti-CD47 immunotherapy	*18-90*	*N/A*	*B. Anderson*
Immunogenicity and protective efficacy of a bivalent VSV-based vaccine for highly-pathogenic influenza virus and SARS-CoV-2 (2019-nCoV)	*17-143* *17-202* *18-82*	*15-404*	*M. Brose*
Determining the role of Helz2 in suppression of Ebola virus replication in mice	*18-90*	*N/A*	*B. Anderson*
Testing the protective efficacy of VSV-based vaccine against Kyasanur Forest Disease virus (KFDV) in pigtail macaques	*18-135* *18-82*	*15-404*	*B. Anderson*

5) ***Biosafety Training Performed – Megan Brose, Rebecca Anderson, Nancy Hoe***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
BSL-3 Laboratory Biosafety	*3*	*8*
BSL-4 Laboratory Biosafety	*9*	*2*
Select Agent Initial Training	*2*	*5*
Select Agent visitor/BSL-3 visitor	*2*	*2*
New Employee Training	*2*	*~5*

6) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
   a) *Biological Incident Report:*
      i) *None*

7) ***Select Agent Issues***
   a) *BSL-4 CDC DSAT inspection April 6-10- CANCELED*

8) ***Other Issues –***
   a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 04/08/2020
Meeting Time: 1:02 PM **Adjourned:** 2:08 PM
Due to the COVID19 pandemic, this meeting was conducted online via Skype for Business

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Alexandra Scranton	☒	☐
Bob Heinzen, Vice Chair	☒	☐	Heinz Feldmann (EO)	☐	☒	Brian Vickrey	☐	☒
Becky Anderson (EO)	☒	☐	Nancy Hoe	☐	☒	Clayton Winkler	☒	☐
Alan Applebury	☐	☒	Erik Hoover	☐	☒			
Chris Bosio	☒	☐	Clay Jarrett	☒	☐			
Marshall Bloom (EO)	☐	☒	Josh Kellar (EO)	☐	☒			
Megan Brose	☒	☐	Scott Kobayashi	☒	☐			
Larry Brouwer	☐	☒	Jamie Lovaglio	☐	☒			
Carol Calderwood	☐	☒	Andrea Marzi	☒	☐			
Marcie Caldwell (EO)	☐	☒	Alida Merritt	☒	☐			
Bruce Chesebro (EO)	☐	☒	Greg Saturday	☒	☐			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 3/23/2020 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from** 3/23/2020 Action: Meeting minutes for 3/23/2020 were unanimously approved as written

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New) ▪ Hasenkrug (LPVD) ▪ **PRD#20-221: Human blood and body fluids-COVID19 (HBBF-COVID19)** ▪ Becky Anderson presented the risk assessment. The Hasenkrug lab is going to develop a mouse model to develop and test therapeutics for COVID19. Mice do not express the proper ACE-2 receptor required for SARS-CoV-2 entry. They will obtain human lung tissues from patients receiving treatment for lung cancer. This tissue will be provided by a cardiothoracic surgeon in Kalispell. This healthy lung tissue

will be devitalized and used as a scaffold for reconstitution by differentiated induced pluripotent stem cells. These scaffolds will then be implanted into mice that will subsequently be used for *in vivo* infection of mice with SARS-CoV-2. The cancer cells will be homogenized into a single cell suspension. The cells will be analyzed for expression of the ACE-2 gene and frozen for later implantation into mice. These suspensions will be analyzed for SARS-CoV-2 RNA. The work with the healthy lung tissue that undergoes the harsh treatments with enzyme and detergents will be performed at BSL-2 with strict usage of a BSC. Work with the cancer cells will be performed in the Hasenkrug's HIV lab at BSL-2 with BSL-3 practices. Normally when evaluating human blood and body fluid PRDs, we are most concerned about HBV, HCV and HIV. Since the material the Hasenkrug lab will be receiving is lung tissue during this current pandemic, it is important to also think about precautions for SARS-CoV-2. Since SARS-CoV-2 is a respiratory illness that can be asymptomatic in some patients, precautions need to be taken for working with these materials. The following precautions have been added to the recommendations section.

- Work with healthy lung tissue is approved at BSL-2 with all handling and work with samples to be performed within a biological safety cabinet (BSC). Care should be taken to minimize worker exposure to aerosols, restricting any such procedures to a certified Class II BSC, and using gasketed bucket covers when centrifuging potentially infectious material and being sure to open up rotors within the BSC.
- Work with cancerous lung tissue that is homogenized for implantation into mice is approved at BSL-2 with BSL-3 practices in the HIV lab.
- If lung samples are identified as SARS-CoV-2 positive, strict inventory and record keeping practices must be in place for all potentially infected materials in case designation of the virus changes to that of a 'select agent' and all associated materials must be identified.
- All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 375-9755.

- Sue Priola questioned who would assess the samples for SARS-CoV-2 infection. Becky Anderson stated that likely LV will do the testing. The committee discussed that the samples should be inactivated prior to removal from the Hasenkrug lab. This needs to be added to the recommendations section.
- No animal studies were submitted, reviewed, or approved.
- Work with HBBF-COVID19 is approved at BSL-2 with the above stated precautions.
- The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.

Action: The committee unanimously approved **PRD#20-221** with the following minor modifications:

1. Add to the recommendations section that samples removed from the lab for analysis of SARS-CoV-2 infection need to be inactivated prior to removal.

Item 2:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New) ▪ Bosio (LB) ▪ **PRD#20-222: Human blood and body fluids-COVID19 (HBBF-COVID19)** ▪ Becky Anderson presented the risk assessment. The Bosio labs plans to perform metabolic profiling of human serum samples from COVID19 positive patients. SARS-CoV-2 symptoms can range from mild to severe. Symptoms can present 2-14 days post exposure. This is a respiratory illness and the symptoms include fever, cough, and shortness of breath. Many patients can be asymptomatic or have mild disease and recover, while others have a severe disease causing severe respiratory problems, kidney failure and death. The mortality rate at this time is difficult to determine as many areas are behind in reporting. A rough calculation from the numbers posted on the worldometer website would suggest that globally the average mortality rate is approximately 5.5%. Blood samples from these patients will be irradiated upon arrival at RML. Once these samples are irradiated, they can be worked with at BSL-2 with standard precautions. The Bosio lab will irradiate according to LV's validated irradiation protocol for Coronaviruses. The primary lab hazards include accidental parenteral inoculation, generation of aerosols and sharps injuries. The following precautions have been added to the recommendations section. o BSL-2 for these samples. Any manipulation prior to irradiation must be performed in a BSC. Strict inventory and record-keeping practices must be in place for all potentially infected materials in case designation of the virus changes to that of a 'select agent' and all associated materials must be identified. o All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 375-9755. ▪ Work with HBBF-COVID19 is approved at BSL-2 with the above stated precautions. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Chris Bosio abstained) **PRD#20-222** as written
	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment) ▪ Feldmann (LV) ▪ **PRD#17-83 Amend: Human blood and body fluids** ▪ Becky Anderson presented the risk assessment. The Feldmann lab plans to perform various analysis of human serum samples from COVID19 positive patients. SARS-CoV-2 symptoms can range from mild to severe. Symptoms can present 2-14 days post exposure. This is a respiratory illness and the symptoms include fever, cough,

	and shortness of breath. Many patients can be asymptomatic or have mild disease and recover, while others have a severe disease causing severe respiratory problems, kidney failure and death. The mortality rate at this time is difficult to determine as many areas are behind in reporting. A rough calculation from the numbers posted on the worldometer website would suggest that globally the average mortality rate is approximately 5.5%. Blood samples from these patients will be irradiated upon arrival at RML. Once these samples are irradiated, they can be worked with at BSL-2 with standard precautions. The Feldmann lab will irradiate according to LV's validated irradiation protocol for Coronaviruses. The primary lab hazards include accidental parenteral inoculation, generation of aerosols and sharps injuries. Becky Anderson informed the committee that the following precautions need to be added to the recommendations section in order to be consistent with the Bosio lab registration. ○ BSL-2 for these samples. Any manipulation prior to irradiation must be performed in a BSC. Strict inventory and record-keeping practices must be in place for all potentially infected materials in case designation of the virus changes to that of a 'select agent' and all associated materials must be identified. ○ All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 375-9755. ▪ Sue Priola stated that the amendment should clarify that the samples will be irradiated according to validated irradiation protocols for Coronaviruses. ▪ Work with HBBF from COVID19 positive patients is approved at BSL-2 with the above stated precautions. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **PRD#17-83 Amend** with minor modifications: 1. Add the same precautions to the recommendation section that were added to the Bosio PRD 20-222. 2. Clarify that the HBBF will be irradiated according to validated irradiation protocols for Coronaviruses.
Item 3:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New)</u> ▪ Bosio (LB) ▪ **PRD#20-223: SARS-CoV-2** ▪ Becky Anderson presented the risk assessment. The Bosio labs plans to perform metabolic profiling of human serum samples from COVID19 positive patients as well as to test novel therapeutics in cell cultures. SARS-CoV-2 symptoms can range from

	mild to severe. Symptoms can present 2-14 days post exposure. This is a respiratory illness and the symptoms include fever, cough, and shortness of breath. Many patients can be asymptomatic or have mild disease and recover, while others have a severe disease causing severe respiratory problems, kidney failure and death. The mortality rate at this time is difficult to determine as many areas are behind in reporting. A rough calculation from the numbers posted on the worldometer website would suggest that globally the average mortality rate is approximately 5.5%. ▪ The Bosio lab will work with SARS-CoV-2 in their current BSL-3 suite. Later in this meeting the IBC will review a new SOP for the Bosio lab that describes procedures for work with SARS-CoV-2. ▪ The PPE for work with SARS-CoV-2 will include N95 or PAPR, Tyvek gown, shoe covers, double gloves, and eye protection as needed. ▪ The following precautions have been added to the PRD. ○ Studies with SARS-CoV-2 are approved at BSL-3. All procedures must be performed following an IBC approved SOP. ○ Strict inventory and record-keeping practices must be in place for all potentially infected materials in case designation of the virus changes to that of a 'select agent' and all associated materials must be identified. ○ All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 375-9755. ▪ Scott Kobayashi questioned where cells and virus are coming from. Becky Anderson stated that the Bosio lab will obtain SARS-CoV-2 from BEI resources and the cells are commercial primary bronchia/tracheal epithelial cells (uninfected). ▪ Clayton Winkler asked if they were working with non-human primate samples as well. The HBBF section indicated they are. (b)(6) stated that they may receive samples from LV to perform metabolic testing. These samples will be irradiated prior to being obtained. Becky Anderson stated that this information could be added in the comment section of the HBBF section. ▪ Work with SARS-Cov-2 is approved at BSL-3 with the above stated precautions. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Chris Bosio abstained) **PRD#20-223** as written
Item 4:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Munster (LV) ▪ **RD#19-455 Amend**: *Development of lipid nanoparticle-formulated mRNA vaccine candidates* ▪ Reviewers: Chris Bosio, Bob Heinzen

	▪ **Summary:** mRNA vaccine will be tested for SARS-CoV-2 infection. ▪ Chris Bosio summarized the RD. The Munster lab would like to add SARS-CoV-2 to the list of viruses and open reading frames. In addition, they are adding animal work with non-human primates with the intramuscular route of inoculation. The NIH Guidelines are fine and the biosafety level is appropriate. There are also no DURC issues. ▪ Bob Heinzen had no additional comments or concerns. ▪ Sue Priola questions if they should state the ORFs they will be working with. Becky Anderson stated the table has already been updated. ▪ Sue Priola also noted that the amendment should state that the mRNA vaccine is provided by CureVac. ▪ Animal studies with non-human primates were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **RD#20-120** with the following minor modifications: 1. Add to the amendment description that the mRNA vaccine will be provided by CureVac. Research using prokaryotic hosts is approved at BSL-2 under section III-E-1 of the NIH Guidelines.
Item 5:	<u>Registration Documents for Recombinant DNA Experiments (Amendment)</u> ▪ Feldmann (LV) ▪ **RD#17-431 Amend**: *Molecular characterization of viral proteins of pathogenic RNA viruses* ▪ Reviewers: Clayton Winkler, Sue Priola ▪ **Summary:** Adding SARS-CoV-2 to the list of virus proteins studied ▪ Clayton Winkler summarized the RD. The Feldmann lab would like to add SARS-CoV-2 to the list of viruses and open reading frames. The Feldmann lab should clarify what the cross symbol means and add an asterisk to Coronaviruses. The NIH Guidelines are fine and the biosafety level is appropriate. There are also no DURC issues. ▪ Sue Priola stated that there were special precautions in the original RD for working with RNA and these should be added to the amendment. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **RD#17-431 Amend** with the following minor modifications:

	2. Update table to clarify what the cross symbol means and add an asterisk to Coronavirus. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-2-a and III-E-1 of the NIH Guidelines.
Item 6:	**Standard Operating Procedure: (b)(6) BSL-3 SOP Coronavirus (New)** ▪ Becky Anderson informed the committee that this SOP is for the Bosio lab to study SARS-CoV-2 in their BSL-3 lab. This SOP is copied from their West Nile Virus SOP so most of the procedures are the same. ▪ Bob Heinzen stated that there was not consistency between the work described in the PRD versus the SOP. The SOP lists unrelated procedures and includes inactivation that may not have been validated for SARS-CoV-2. The committee discussed and agreed that they could not approve inactivation procedures that have not been validated. Becky Anderson informed the committee that LV has only validated AVL and irradiation for the Coronavirus family. The remaining inactivation procedures will be removed from the SOP. ▪ Bob Heinzen also questioned if the baseline serum is collected from OMS or questioned what the policy is. Megan Brose stated that statement is taken from the BMBL. She stated that we can verify with OMS if they do collect baseline serum prior to starting work. ▪ Scott Kobayashi stated that Coronavirus should be changed to SARS-CoV-2 in the title and throughout the document (including 2.2 and 2.3) ▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved the (b)(6) **BSL-3 SOP Coronavirus (New)** with the following modifications: 1. Change Coronavirus to SARS-CoV-2 throughout the document. 2. Remove inactivation procedures from the SOP that are not validated.
Item 7:	**Standard Operating Procedure: ABSL-3 SARS-CoV-2 (New)** ▪ Becky Anderson informed the committee that this SOP is for LV to perform animal studies with rodents in the ABSL-3. To date, all of their animal studies have been performed in the ABSL-4 and they want to be able to do studies in the ABSL-3 in order to have more space. ▪ Alex Scranton questioned if an animal bite should be added in section 1.2. The committee agreed that would be appropriate. ▪ Clayton Winkler stated that in Section 1.1 there should be a comma between headache and diarrhea.

	▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved the **ABSL-3 SARS-CoV-2 (New)** with the following minor modifications: 1. Add animal bite to Section 1.2 2. Add a comma in Section 1.1 between headache and diarrhea.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Becky Anderson reviewed the BSO Report
Report:	**Occupational Safety and Health Manager Report/** (b)(6) ▪ Not present.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ There was an emergency decon in the BSL-4 to fix an autoclave this week. ▪ The BSL-3 (b)(6) shutdown is scheduled for next week and it needs to be determined if it will proceed or not.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ Alida Merritt informed the committee that Marcus Daly is setup and prepared for COVID19 patients. They screen people and do the swabbing while patients are in the car to minimize contact. At this time Ravalli County only has 3 cases. There has not been a surge yet so they have had time to prepare.

Other issues	▪ None

Next Meeting:

- Date: TBD
- Place: online via Skype for Business
- Time: TBD

RML Biosafety Committee Meeting
April 8, 2020
Biosafety Officer/Responsible Official Report

1) ***Requests approved by BSO since last meeting:***
   a) ***None***
2) ***New requests approved by committee via electronic review:***
   a) ***None***
3) ***New requests***
   a) *Pathogen Registration Documents*
      i) ***New***
         (a) *Hasenkrug (LPVD)*
            (a) *PRD-20-221; HBBF-COVID19*
         (b) *Bosio (LB)*
            (a) *PRD-20-222; HBBF-COVID19*
         (c) *Bosio (LB)*
            (a) *PRD-20-223; SARS-CoV-2*
      ii) ***Renew***
            (a) *None*
      iii) ***Amend***
            (a) *None*
   b) *Registration Documents for Recombinant Nucleic Acid Experiments*
      i) ***New***
            (a) *None*
      ii) ***Renew***
            (a) *None*
      iii) ***Amend***
         (a) *Munster (LV)*
            (a) *RD-19-455*
         (b) *Feldmann (LV)*
            (a) *RD-17-431*
   c) ***Standard Operating Procedures***
      i) ***Update***
         (a) *Draft ABSL-3 SARS-CoV-2 SOP- New*
         (b) *Draft* (b)(6) *COVID19 SOP- New*

4) ***Animal Study Protocols Review***

RML Biosafety Committee Meeting
April 8, 2020
Biosafety Officer/Responsible Official Report

Title	Associated PRD	Associated RD	Reviewer
Protective efficacy of a VSV-based vaccine for SARS-CoV-2 in hamsters	*17-143* *18-82*	*15-404*	*M. Brose*
Assessing the role of innate immunity and mitophagy in pathogenesis of COVID-19 in mice	*17-143*	*17-410*	*M. Brose*
Prophylaxis and Treatment of COVID-19-like Disease in the Rhesus Macaque Model with Hydroxychloroquine and Azithromycin	*17-143*	*N/A*	*B. Anderson*
Production of antibodies against Lineage B (SARS-like) Betacoronaviruses including SARS-CoV-2	*N/A*	*17-431*	*M. Brose*
Sentinel Animal Surveillance Program	*N/A*	*N/A*	*B. Anderson*
Laboratory Animal Holding	*N/A*	*N/A*	*B. Anderson*
Laboratory Animal Care and Use Training Program (Small Lab Animals)	*N/A*	*N/A*	*B. Anderson*
Laboratory Animal Care and Use Training Program - Rabbits	*N/A*	*N/A*	*B. Anderson*
Laboratory Animal Breeding/Production	*N/A*	*N/A*	*B. Anderson*
Guinea pig antibodies against Coxiella burnetii proteins	*18-70*	*20-106*	*M. Brose*
Characterization of the cellular immune response following systemic and/or mucosal delivery of ChAdOx1 MERS and implications for the longevity of protection conferred against MERS-CoV	*17-143*	*17-410*	*M. Brose*
Evaluation of an RNA vaccine for SARS-CoV-2 in rhesus macaques	*17-143*	*17-452*	*M. Brose*
Protective efficacy of a VSV-based vaccine against nCoV-2019 in rhesus macaques	*17-143*	*15-404*	*B. Anderson*
Mouse- and hamster-adaptation of SARS-CoV-2	*17-143*	*N/A*	*B. Anderson*
Moderna mRNA-1273 vaccine efficacy in the rhesus macaque model	*17-143*	*N/A*	*M. Brose*
CureVac mRNA SARS2 vaccine efficacy in the rhesus macaque model	*17-143*	*19-455*	*M. Brose*
Squirrel Monkeys as a Disease Model for COVID-19	*17-143*	*N/A*	*B. Anderson*
Assessing hamster knock-out strains as a COVID-19 disease model	*17-143*	*N/A*	*B. Anderson*
Treatment of mouse adapted EBOLA virus (MA-EBOV) infections with anti-CD47 immunotherapy	*18-90*	*N/A*	*B. Anderson*
Immunogenicity and protective efficacy of a bivalent VSV-based vaccine for highly-pathogenic influenza virus and SARS-CoV-2 (2019-nCoV)	*17-143* *17-202* *18-82*	*15-404*	*M. Brose*
Determining the role of Helz2 in suppression of Ebola virus replication in mice	*18-90*	*N/A*	*B. Anderson*
Testing the protective efficacy of VSV-based vaccine against Kyasanur Forest Disease virus (KFDV) in pigtail macaques	*18-135* *18-82*	*15-404*	*B. Anderson*

5) ***Biosafety Training Performed – Megan Brose, Rebecca Anderson, Nancy Hoe***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
BSL-3 Laboratory Biosafety	*3*	*8*
BSL-4 Laboratory Biosafety	*9*	*2*
Select Agent Initial Training	*2*	*5*
Select Agent visitor/BSL-3 visitor	*2*	*2*
New Employee Training	*2*	*~5*

6) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
   a) *Biological Incident Report:*
      i) *None*

7) ***Select Agent Issues***
   a) *BSL-4 CDC DSAT inspection April 6-10- CANCELED*

8) ***Other Issues –***
   a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 04/22/2020
Meeting Time: 3:03 PM **Adjourned:** 3:31 PM
Due to the COVID19 pandemic, this meeting was conducted online via Skype for Business

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Alexandra Scranton	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Heinz Feldmann (EO)	☐	☒	Brian Vickrey	☐	☒
Becky Anderson (EO)	☒	☐	Nancy Hoe	☐	☒	Clayton Winkler	☒	☐
Alan Applebury	☐	☒	Erik Hoover	☐	☒			
Chris Bosio	☒	☐	Clay Jarrett	☒	☐			
Marshall Bloom (EO)	☐	☒	Josh Kellar (EO)	☐	☒			
Megan Brose	☐	☒	Scott Kobayashi	☒	☐			
Larry Brouwer	☐	☒	Jamie Lovaglio	☐	☒			
Carol Calderwood	☐	☒	Andrea Marzi	☒	☐			
Marcie Caldwell (EO)	☐	☒	Alida Merritt	☐	☒			
Bruce Chesebro (EO)	☐	☒	Greg Saturday	☐	☒			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 4/08/2020 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from** 4/08/2020 Action: Meeting minutes for 4/08/2020 were unanimously approved as written.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New) ▪ Bloom (LV) ▪ **PRD#20-224: SARS-CoV-2** ▪ Becky Anderson presented the risk assessment. The Bloom labs plans study and characterize Coronaviruses in cell culture. This includes SARS-CoV-2 and MERS-CoV. Since their suite is not a select agent registered space, they will not be using SARS-CoV-1. SARS-CoV-2 symptoms can range from mild to severe. Symptoms can present 2-14 days post exposure. This is a respiratory illness and the symptoms

	include fever, cough, and shortness of breath. Many patients can be asymptomatic or have mild disease and recover, while others have a severe disease causing severe respiratory problems, kidney failure and death. The mortality rate at this time is difficult to determine as many areas are behind in reporting. A rough calculation from the numbers posted on the worldometer website would suggest that globally the average mortality rate is approximately 5.5%. ▪ The Bloom lab will work with SARS-CoV-2 and MERS-CoV in their current BSL-3 suite. Later in this meeting the IBC will review a new SOP for the Bloom lab that describes procedures for work with the stated Coronaviruses. ▪ The PPE for work with SARS-CoV-2 and MERS-CoV will include N95 or PAPR, Tyvek gown or coverall, shoe covers, double gloves, and eye protection as needed. ▪ The following precautions have been added to the PRD. o Studies with SARS-CoV-2 are approved at BSL-3. All procedures must be performed following an IBC approved SOP. o Strict inventory and record-keeping practices must be in place for all potentially infected materials in case designation of the virus changes to that of a 'select agent' and all associated materials must be identified. o All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 375-9755. ▪ Bob Heinzen stated that the title should be updated to state SARS-CoV-2 and MERS-CoV. ▪ Clayton Winkler asked if they will be concentrating the virus. The SOP describes procedures for concentrating virus, but the PRD states that they will not. Becky Anderson stated that they will potentially concentrate the virus so they wanted that section in the SOP. The PRD should be updated to match the SOP. ▪ Work with SARS-CoV-2 and MERS-CoV are approved at BSL-3 with the above stated precautions. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **PRD#20-224** with the following minor modifications: 1. Change project title to SARS-CoV-2 and MERS-CoV. 2. Update to state the virus will be concentrated.
Item 2:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal)</u> ▪ Tirloni (LB) ▪ **PRD#20-225: Human blood and body fluids (HBBF)** ▪ Becky Anderson presented the risk assessment. This is a new registration for a PI joining RML in the Laboratory of Bacteriology. The goal of this project is to study the effects of saliva from ticks on blood coagulation, inflammation, and the immune

	system of their hosts as well as its role on vector-borne pathogen transmission. The Tirloni lab also aims to characterize the individual salivary components responsible for these effects. The three most common bloodborne pathogens are HBV, HCV, and HIV. HBV is the most common of the three and causes a serious form of hepatitis. The symptoms include: jaundice, fatigue, abdominal pain, loss of appetite, intermittent nausea, vomiting. It can also lead to chronic liver disease, liver cancer, and death. There is a vaccine available for HBV, the vaccine is offered free of charge at RML through the OMS Nurses. HCV symptoms include jaundice, fatigue, abdominal pain, loss of appetite, intermittent nausea and vomiting. HCV can also lead to chronic liver disease and death. HIV is the virus that leads to AIDS. ▪ Becky Anderson stated that precautions for aerosol producing procedures should be added to the recommendations section. ▪ Sue Priola questioned where the RPD listed the biosafety level. Becky Anderson will check to make sure there is not an issue with the PDF rendering to show the approved biosafety level. ▪ No animal studies were submitted, reviewed, or approved. ▪ Work with human blood and body fluids is approved at BSL-2. ▪ The recommendations section also includes language for working with Bloodborne Pathogens. <u>Action:</u> The committee unanimously approved **PRD#20-225** with minor modifications: 1. Add the precautions for aerosol producing procedures to the recommendations section. 2. Check to make sure the biosafety level shows up on the rendered PDF.
Item 4:	<u>Registration Documents for Recombinant DNA Experiments (New)</u> ▪ Heinzen (LB) ▪ **RD#20-133**: *Host cell modulation by SARS-CoV-2* ▪ Reviewers: Andrea Marzi, Scott Kobayashi ▪ **Summary:** SARS-CoV-2 protein function ▪ Andrea Marzi summarized the RD. She informed the committee that this is a straightforward RD to assess the protein function of SARS-CoV-2. Individual genes will be expressed on the listed plasmids. Intracellular trafficking of viral proteins and cellular expression will be assessed. The appropriate plasmid maps are attached. The listed NIH Guidelines are appropriate and there are no issues with the RD. ▪ Scott Kobayashi stated that there is a minor typo throughout the document, the plasmid pLVX is mistyped as pLXV and this should be corrected. ▪ Sue Priola stated that III-E-1 should be added to the NIH Guidelines section. She also noted that the sequence is codon optimized for eukaryotic cells and this should probably be added to the RD. Bob Heinzen will add a sentence to describe this. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described

	above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Bob Heinzen abstained) **RD#20-133** with the following minor modifications: 1. Correct the type for plasmid pLVX. 2. Add III-E-1 to the NIH Guidelines. 3. Add a statement that the sequence will be codon optimized for eukaryotic cells. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a and III-E-1 of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-2-a of the NIH Guidelines.
Item 6:	**Standard Operating Procedure: (b)(6) BSL-3 Operations and Safety Procedures (OSP) (Update)** ▪ Becky Anderson informed the committee that the OSP is being updated for two reasons. The first is that LV wants to change the PPE requirements for this lab. The current PPE requirement is to wear a Tyvek coverall AND a Tyvek gown. They would like to change to state Tyvek coverall OR a Tyvek gown. This change is due to the reduced availability of PPE during the SARS-CoV-2 pandemic. The second update to the OSP is to add a new SOP for homogenization of tissues from rodents infected with SARS-CoV-2 or other viral pathogens. The SOP is called BSL-3-28-15 Homogenization of tissue infected with BSL-3 pathogens. ▪ Becky Anderson informed the committee that LV would like to change the language in SOP BSL-3-28-15 Homogenization of tissue infected with BSL-3 pathogens, item 10 to state that there is a 5 minute contact time with ethanol prior to removing equipment from the BSC. ▪ Sue Priola stated that the agent summary table needs to be updated to include SARS-CoV-2 in the Coronavirus section. She also noted that there are a few places throughout the document that need SARS-CoV-2 added. The summary of changes table needs to be updated with these changes as well. ▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved the (b)(6) **BSL-3 Operations and Safety Procedures (Update)**with the following modifications: 1. Update SOP BSL-3-28-15 Homogenization of tissue infected with BSL-3 pathogens, item 10 to state that there is a 5 minute contact time with ethanol prior to removing equipment from the BSC. 2. Update agent summary section with SARS-CoV-2. Add SARS-CoV-2 a couple places in the document where MERS-CoV is mentioned.
Item 7:	**Standard Operating Procedure: (b)(6) BSL-3 SOP Coronavirus (New)** ▪ Becky Anderson informed the committee that this SOP is for the Bloom lab to study

	SARS-CoV-2 and MERS-CoV in their BSL-3 lab. This SOP is copied from their Powassan virus SOP so most of the procedures are the same. ▪ Bob Heinzen stated that in 2.2 it was not clear why they are flipping the sign and if it allows less PPE. Becky Anderson will update the language to be clearer. ▪ Bob Heinzen stated that in the viral concentration SOP, it states that the swinging buckets are added to the rotor in the BSC and then transported to the centrifuge. This is not appropriate, and the buckets should be transported to the rotor at the centrifuge and then attached. Becky Anderson stated that she checked with the Bloom lab and they do the procedure as Bob Heinzen described. The SOP will be updated to reflect how the transport of those buckets occurs. ▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved the (b)(6) **BSL-3 SOP Coronavirus (New)** with the following modifications: 1. Update 2.2 to clarify flipping of the sign. 2. Change the procedure described in the viral concentration SOP to accurately reflect how the buckets are transported to the centrifuge.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Becky Anderson reviewed the BSO Report
Report:	**Occupational Safety and Health Manager Report/** (b)(6) ▪ Nothing to report.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ Not present.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ None.

Other issues	▪ None

Next Meeting:

- Date: TBD
- Place: online via Skype for Business

- Time: TBD

RML Biosafety Committee Meeting
May 21, 2020
Biosafety Officer/Responsible Official Report

1) Requests approved by BSO since last meeting:

a) Feldmann PRD 17-143 Amend

i) Add intranasal route of inoculation for hamsters

ii) Add intraperitoneal route of inoculation for hamsters

iii) Add intravenous route of inoculation for pigs

2) ***New requests approved by committee via electronic review:***

a) ***None***

3) ***New requests***

a) *Pathogen Registration Documents*

i) ***New***

(a) *Peterson (LPVD)*

(a) *PRD-20-226; Coronaviruses (OC43, 229E)*

ii) ***Renew***

(a) *None*

iii) ***Amend***

(a) *Bosio (LB)*

(a) *PRD-20-224 Amend; SARS-CoV-2*

b) *Registration Documents for Recombinant Nucleic Acid Experiments*

i) ***New***

(a) *Priola (LPVD)*

(i) RD-20-226

ii) ***Renew***

(i) None

iii) ***Amend***

(a) *Steele-Mortimer (LB)*

(i) RD-19-126 Amend

(b) *Priola (LPVD)*

(i) RD-19-223 Amend

c) ***Standard Operating Procedures***

i) ***New***

(a) *SARS-CoV-2 animal SOP ABSL-3- Bosio*

RML Biosafety Committee Meeting
May 21, 2020
Biosafety Officer/Responsible Official Report

4) ***Animal Study Protocols Review***

Title	*Associated PRD*	*Associated RD*	*Reviewer*
Pathogenesis and immune response in young versus older adult rhesus macaques	*17-143*	*N/A*	*M. Brose*
Evaluation of an RNA vaccine for SARS-CoV-2 in pigtail macaques	*17-143*	*17-452*	*B. Anderson*
Recombinant Attenuated Salmonella Vaccines against SARS-CoV-2 infection in Hamsters	*17-143* *18-44*	*19-126*	*M. Brose*
Evaluation of a DNA vaccine for SARS-CoV-2 in hamsters	*17-143*	*17-431*	*M. Brose*

5) ***Biosafety Training Performed – Megan Brose, Rebecca Anderson, Nancy Hoe***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
BSL-3 Laboratory Biosafety	*None*	*None*
BSL-4 Laboratory Biosafety	*6*	*1*
Select Agent Initial Training	*None*	*None*
Select Agent visitor/BSL-3 visitor	*None*	*None*
New Employee Training	*None*	*None*

6) ***Safety Audits and Inspections***

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

a) *Biological Incident Report:*
   i) *None*

7) ***Select Agent Issues***

a) *None*

8) ***Other Issues –***

a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 05/21/2020
Meeting Time: 1:01 PM **Adjourned:** 1:23 PM
Due to the COVID19 pandemic, this meeting was conducted online via Skype for Business

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Alexandra Scranton	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Heinz Feldmann (EO)	☐	☒	Brian Vickrey	☐	☒
Becky Anderson (EO)	☒	☐	Nancy Hoe	☐	☒	Clayton Winkler	☒	☐
Alan Applebury	☐	☒	Erik Hoover	☐	☒			
Chris Bosio	☐	☒	Clay Jarrett	☒	☐			
Marshall Bloom (EO)	☐	☒	Josh Kellar (EO)	☐	☒			
Megan Brose	☒	☐	Scott Kobayashi	☒	☐			
Larry Brouwer	☐	☒	Jamie Lovaglio	☒	☐			
Carol Calderwood	☐	☒	Andrea Marzi	☒	☐			
Marcie Caldwell (EO)	☐	☒	Alida Merritt	☐	☒			
Bruce Chesebro (EO)	☐	☒	Greg Saturday	☒	☐			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 4/22/2020 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from** 4/22/2020 Action: Meeting minutes for 4/22/2020 were unanimously approved as written

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New) ▪ Peterson (LPVD) ▪ **PRD#20-226: Coronaviruses (OC43 and 229E)** ▪ Becky Anderson presented the risk assessment. To establish *in vitro* cell line systems which will be used to examine the potential of therapeutic compounds (medicinal plant extracts as well as small molecules) to inhibit viral replication. The most active compounds will then be examined for their mode of activation by looking at different stages of virus replication using confocal and EM microscopy.

	These are common human coronaviruses which usually cause mild to moderate upper respiratory tract illnesses like the common cold. Most people get infected with one or more of these viruses at some point in their lives. They are responsible for approximately a quarter of all common colds. Human to human transmission is common and there are no vaccines or antivirals used for routine clinical use for these viral infections. The primary lab hazards include: accidental parenteral inoculation, generation of aerosol, sharps injuries. ▪ The following precautions should be added to the PRD. ○ Care must be taken to minimize worker exposure to aerosols by using a certified Biological Safety Cabinet (BSC) and by using gasketed bucket covers when centrifuging infectious material. ▪ Work with OC43 and 229E Coronaviruses is approved at BSL-2 with the above stated precautions. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved (Clayton Winkler abstained) **PRD#20-226** with the following minor modifications: 1. Add the precautions to the recommendations section for minimizing worker exposure to aerosols.
Item 2:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment)</u> ▪ Bosio (LB) ▪ **PRD#20-226 Amend: COVID-19** ▪ Becky Anderson presented the risk assessment. The amendment is to add animal work with mice to the PRD. The studies with SARS-CoV-2 will be conducted in the ABSL-3 according to agent specific SOPs, which have been submitted for review this meeting. The PPE for these studies will include Tyvek coverall or gown, N95 or PAPR, shoe covers, two pairs of gloves, and eye protection and hair cover if not wearing a PAPR. ▪ Animal studies with mice were proposed. ▪ Animal studies with SARS-CoV-2 are approved at ABSL-3. <u>Action:</u> The committee unanimously approved **PRD#20-226 Amend** as written.
Item 4:	<u>Registration Documents for Recombinant DNA Experiments (Amendment)</u> ▪ Steele-Mortimer (LB) ▪ **RD#19-126 Amend**: Salmonella Cancer Vaccine ▪ Reviewers: Scott Kobayashi, Bob Heinzen ▪ **Summary:** Vaccine delivery system with attenuated Salmonella. ▪ Scott Kobayashi summarized the RD amendment. Scott Kobayashi stated that the

	Steele-Mortimer lab wants to add the SARS-CoV-2 glycoprotein to their RASV system so they can use as a vaccine delivery system. Scott Kobayashi noted that they need to specify which or both glycoproteins because there are two glycoproteins in SARS-CoV-2. ▪ Bob Heinzen had no additional comments or concerns. ▪ No new animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#19-126 Amend** with the following minor modifications: 1. Specify which glycoprotein will be used in the RASV system. Research using prokaryotic hosts is approved at BSL-2 under section III-D-1-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a of the NIH Guidelines.
Item 6:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Priola (LPVD) ▪ **RD#19-222 Amend**: Lentiviruses ▪ Reviewers: Chris Bosio, Clay Jarrett ▪ **Summary:** Lentiviral system. ▪ Chris Bosio was not in attendance. ▪ Clay Jarrett summarized the RD amendment. The amendment is to add another expression system to the RD. It is a well described system with safety features included. There are no other changes to the RD. ▪ The committee had no additional comments or concerns. ▪ No new animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Sue Priola abstained) **RD#19-222 Amend** as written. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a and III-D-3-a of the NIH Guidelines.
Item 7:	Registration Documents for Recombinant DNA Experiments (New) ▪ Priola (LPVD) ▪ **RD#20-226**: SARS-CoV-2 Protein Folding

	▪ Reviewers: Andrea Marzi, Clayton Winkler ▪ **Summary:** SARS-CoV-2 protein folding analysis to develop a potential therapeutic ▪ Andrea Marzi summarized the RD. Andrea Marzi informed the committee that this is a new RD to study chaperones and their interaction with the SARS-CoV-2 spike protein. These studies will include pull-down assays, proteinase digestion, and surface association assays. The RD is clearly written and includes all cell lines, tags, and vector maps. Andrea Marzi had no concerns with the RD. ▪ Clayton Winkler noted that the Eukaryote Cell section referenced the Lentiviral system but is was not clear that work was described in another RD. This section should add more information regarding that. Becky Anderson stated that in the Associated Registrations section, the Lentiviral RD could be added to link the two registrations. Clayton Winkler also noted that there was a typo in the vector map pLVX-EF1a-IREsPURO vector. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#20-226** with the following minor modifications: 1. In the Eukaryote Cell section describe the Lentiviral system and/or reference the Lentiviral RD. 2. Add the Lentiviral RD to the Associated Registrations list. 3. Correct spelling of the pLVX-EF1a-IREsPURO vector. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a and III-E-1 of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-2-a, III-D-3-a, and III-E-1 of the NIH Guidelines.
Item 8:	**Standard Operating Procedure: ABSL-3 SARS-CoV-2 Animal SOP- Bosio (New)** ▪ Becky Anderson informed the committee that this SOP is for the Bosio lab to perform animal studies with SARS-CoV-2 in the ABSL-3. ▪ Becky Anderson pointed out in Section 3.2.3 the third bullet should be changed to reference the (b)(6) SOP. ▪ Becky Anderson also noted that in section 5.2.1 of the SOP should also include removal of N95, safety glasses and hair cover if not wearing a PAPR. ▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved the **ABSL-3 SARS-CoV-2 Animal SOP- Bosio (New)** with the following modifications: 1. Section 3.2.3 the third bullet should be changed to reference the (b)(6) SOP. 2. Section 5.2.1 of the SOP should also include removal of N95, safety glasses and hair

	cover if not wearing a PAPR.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Becky Anderson reviewed the BSO Report
Report:	**Occupational Safety and Health Manager Report/(b)(6)** ▪ (b)(6) introduced (b)(6) the new Occupational Safety and Health Manager for RML.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ We are working on scheduling the (b)(6); (b)(3):42 BSL-4 annual shutdown possibly in June. We are trying to work around all the SARS-CoV-2 studies. ▪ The BSL-3 (b)(6) annual shutdown has been postponed to a later date, its annual recertification date is not until October but the lab had requested an earlier date to have some new equipment installed.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ None.

Other issues	▪ Becky Anderson introduced Dr. (b)(6) she is the new DOHS Director and replaces Dr. Deborah Wilson. Dr. (b)(6) thanked the committee for all of their hard work on the IBC.

Next Meeting:

- Date: TBD
- Place: online via Skype for Business
- Time: TBD

RML Biosafety Committee Meeting
May 21, 2020
Biosafety Officer/Responsible Official Report

1) Requests approved by BSO since last meeting:

a) Feldmann PRD 17-143 Amend

i) Add intranasal route of inoculation for hamsters

ii) Add intraperitoneal route of inoculation for hamsters

iii) Add intravenous route of inoculation for pigs

2) ***New requests approved by committee via electronic review:***

a) ***None***

3) ***New requests***

a) *Pathogen Registration Documents*

i) ***New***

(a) *Peterson (LPVD)*

(a) *PRD-20-226; Coronaviruses (OC43, 229E)*

ii) ***Renew***

(a) *None*

iii) ***Amend***

(a) *Bosio (LB)*

(a) *PRD-20-224 Amend; SARS-CoV-2*

b) *Registration Documents for Recombinant Nucleic Acid Experiments*

i) ***New***

(a) *Priola (LPVD)*

(i) RD-20-226

ii) ***Renew***

(i) None

iii) ***Amend***

(a) *Steele-Mortimer (LB)*

(i) RD-19-126 Amend

(b) *Priola (LPVD)*

(i) RD-19-223 Amend

c) ***Standard Operating Procedures***

i) ***New***

(a) *SARS-CoV-2 animal SOP ABSL-3- Bosio*

RML Biosafety Committee Meeting
May 21, 2020
Biosafety Officer/Responsible Official Report

4) ***Animal Study Protocols Review***

Title	*Associated PRD*	*Associated RD*	*Reviewer*
Pathogenesis and immune response in young versus older adult rhesus macaques	*17-143*	*N/A*	*M. Brose*
Evaluation of an RNA vaccine for SARS-CoV-2 in pigtail macaques	*17-143*	*17-452*	*B. Anderson*
Recombinant Attenuated Salmonella Vaccines against SARS-CoV-2 infection in Hamsters	*17-143* *18-44*	*19-126*	*M. Brose*
Evaluation of a DNA vaccine for SARS-CoV-2 in hamsters	*17-143*	*17-431*	*M. Brose*

5) ***Biosafety Training Performed – Megan Brose, Rebecca Anderson, Nancy Hoe***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
BSL-3 Laboratory Biosafety	*None*	*None*
BSL-4 Laboratory Biosafety	*6*	*1*
Select Agent Initial Training	*None*	*None*
Select Agent visitor/BSL-3 visitor	*None*	*None*
New Employee Training	*None*	*None*

6) ***Safety Audits and Inspections***

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

a) *Biological Incident Report:*
   i) *None*

7) ***Select Agent Issues***

a) *None*

8) ***Other Issues –***

a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 06/18/2020
Meeting Time: 1:01 PM **Adjourned:** 2:11 PM
Due to the COVID19 pandemic, this meeting was conducted online via Skype for Business

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Alexandra Scranton	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Heinz Feldmann (EO)	☐	☒	Brian Vickrey	☐	☒
Becky Anderson (EO)	☒	☐	Nancy Hoe	☐	☒	Clayton Winkler	☒	☐
Alan Applebury	☐	☒	Erik Hoover	☐	☒			
Chris Bosio	☒	☐	Clay Jarrett	☒	☐			
Marshall Bloom (EO)	☐	☒	Josh Kellar (EO)	☐	☒			
Megan Brose	☒	☐	Scott Kobayashi	☒	☐			
Larry Brouwer	☒	☐	Jamie Lovaglio	☐	☒			
Carol Calderwood	☐	☒	Andrea Marzi	☒	☐			
Marcie Caldwell (EO)	☐	☒	Alida Merritt	☒	☐			
Bruce Chesebro (EO)	☐	☒	Greg Saturday	☒	☐			

(P=present; A=absent)

Guests: (b)(6)

Minutes: Meeting minutes from 4/22/2020 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from** 5/21/2020 Action: Meeting minutes for 5/21/2020 were unanimously approved with minor modifications: 1. In Item 6, the Clayton Winkler reference should be changed to Clay Jarrett.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New) ▪ Tirloni (LB) ▪ **PRD#20-227: *Borrelia burgdorferi*** ▪ Becky Anderson presented the risk assessment. The proposed studies are to understand how the tick feeding process is exploited by *Borrelia burgdorferi* to facilitate transmission. *Borrelia burgdorferi* causes Lyme disease. It is a tickborne

	zoonotic disease characterized by distinctive skin lesion, can present with fever, chills, headache, fatigue, muscle and joint aches, and swollen lymph nodes. The rash occurs in approximately 70 to 80 percent of infected persons and begins at the site of a tick bite after approximately 3 to 30 days. The rash expands over time and can reach up to 12 inches or greater. The rash can be warm to the touch and appear as a target or bull's eye shape and appear on any area of the body. ▪ Approximately 10 to 20% of patients treated for Lyme disease with a recommended 2–4 week course of antibiotics will have lingering symptoms of fatigue, pain, or joint and muscle aches. In some cases, these can last for more than 6 months. The primary lab hazards include accidental needle stick, parenteral inoculation, and generation of aerosols. ▪ Work with *Borrelia burgdorferi* is approved at BSL-2. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#20-227** as written.
Item 2:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New) ▪ Best (LV) ▪ **PRD#20-228: SARS-CoV-2** ▪ Becky Anderson presented the risk assessment. The proposed studies are to determine the molecular mechanisms by which the SARS-CoV-2 disrupts immune responses. The Best lab was previously covered under the Feldmann PRD for SARS-CoV-2, however they plan to do some recombinant work separate from the Feldmann lab so they wanted to establish their own PRD and RD. SARS-CoV-2 symptoms can range from mild to severe. Symptoms can present 2-14 days post exposure. This is a respiratory illness and the symptoms include fever, cough, and shortness of breath. Many patients can be asymptomatic or have mild disease and recover, while others have a severe disease causing severe respiratory problems, kidney failure and death. The mortality rate currently is difficult to determine as many areas are behind in reporting. A rough calculation from the numbers posted on the worldometer website would suggest that globally the average mortality rate is approximately 5.5%. The primary lab hazards include accidental parenteral inoculation, generation of aerosol and sharps injuries. ▪ Work with SARS-CoV-2 is approved at BSL-3/ABSL-3. ▪ Animal studies with mice and hamsters were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#20-228** with minor modifications: 1. In the Pathogen and/or Toxin section, change "strains" to "isolates".

Item 4:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Feldmann (LV) ▪ **RD#17-410 Amend**: Adenovirus vaccine vector ▪ Reviewers: Clayton Winkler, Bob Heinzen ▪ **Summary:** Addition of a new Adenovirus vaccine candidate. ▪ Clayton Winkler summarized the RD amendment. The amendment is to add a new Adenovirus, which is in line with the previous work approved on the RD. This adenovirus, like the others has E1 and E3 deleted so it is replication incompetent. There are some advantages to this new Adenovirus which is a type 26 and it will be tested in animal species that are already approved on the RD. Clayton Winkler questioned if the cloning vectors will be the same as the previous work. Andrea Marzi clarified that the Feldmann lab will be obtaining purified virus from the collaborators and that material will be directly tested in animals. There will be no recombinant work at RML. Clayton stated that should be made clearer in the amendment. Becky Anderson stated that if the work is not being performed at RML there is no need to include the cloning vectors. ▪ Bob Heinzen had no additional comments or concerns. ▪ No new animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#17-410 Amend** with the following minor modifications: 1. Clarify that no recombinant work will be performed at RML. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a and III-E-1 of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a and III-D-3-a of the NIH Guidelines.
Item 6:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Feldmann (LV) ▪ **RD#16-440 Amend**: Coronaviruses ▪ Reviewers: Andrea Marzi, Sue Priola ▪ **Summary:** Coronavirus reverse genetics system ▪ Andrea Marzi summarized the RD amendment. The amendment is to add a new system for preparing full-length recombinant Coronavirus using a yeast artificial chromosome. This new system is important because Coronaviruses are so large that traditional systems are not as effective. Andrea Marzi also stated that this RD should also include NIH Guideline III-D-2-a. The RD also needs to include the vector maps that are referenced in the attached paper. There are no dual use issues with the RD.

	▪ Sue Priola stated that III-E-1- also should be added because they are cloning fragments. ▪ The committee had no additional comments or concerns. ▪ No new animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#16-440 Amend** with minor modifications: 1. Add III-D-2-a and III-E-1 to the amendment. 2. Add the referenced vector maps. Research using eukaryotic cells is approved at BSL-2 to BSL-4 under III-D-3-a, III-D-3-b, III-D-1-a, III-D-2-a, and III-E-1 of the NIH Guidelines.
Item 7:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Feldmann (LV) ▪ **RD#20-432**: Phlebovirus ▪ Reviewers: Scott Kobayashi, Chris Bosio ▪ **Summary:** Phlebovirus VLPs, minigenomes, and reverse genetics ▪ Scott Kobayashi summarized the RD. Scott Kobayashi stated that this is a renewal and that the renewal does not include any new work. The Feldmann lab will continue developing minigenomes, virus like particles, and other reverse genetics systems. Some of these elements allow the Feldmann lab to study various processes without infectious virus. The viruses listed on the RD are BSL-2 and BSL-3. ▪ Chris Bosio had no additional comments or concerns. ▪ Sue Priola stated that this RD renewal combines RD 14-438 with the current RD. With this RD renewal, RD 14-438 can be inactivated. She also stated that in the Prokaryote Cell section, there is a reference to PRD XX-123. The XX should be changed to the correct number. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#20-432** with the following minor modifications: 1. In the Prokaryote cell section, change PRD XX-123 to the appropriate date for the XX. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-3-a and III-E-1 of the NIH Guidelines.

Item 8:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Feldmann (LV) ▪ **RD#20-442**: Cytomegalovirus ▪ Reviewers: Bob Heinzen, Clay Jarrett ▪ **Summary:** Cytomegalovirus vaccine platform ▪ Bob Heinzen summarized the RD renewal. This RD describes CMV as a vaccine to vaccinate animal reservoirs in the natural host to eliminate transmission to humans. This method elicits a strong mucosal immune response and a great benefit of this system is that CMV is species specific. The only change to this renewal is that they will be adding Lassa virus recombinant products in Mastomys natalensis. ▪ Clay Jarrett had no additional comments or concerns. ▪ Animal studies with mice, NHPs, mastomys natalensis were proposed ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#20-442** with the following minor modifications: 1. In the Prokaryote cell section, change PRD XX-123 to the appropriate date for the XX. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-3-a and III-E-1 of the NIH Guidelines.
Item 9:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Feldmann (LV) ▪ **RD#20-416**: Influenza virus ▪ Reviewers: Sue Priola, Andrea Marzi ▪ **Summary:** Generation of recombinant Influenza A viruses ▪ Sue Priola summarized the RD. She stated that this RD covers the reverse genetics systems for Influenza A, the generation of virus like particles, and minigenomes. In the previous review of this RD, the IBC requested a table that specifically describes the potential combination of amino acid mutations, insertions/deletions, recombinants and reassortants. The dual use is filled out appropriately, there she had no concerns. The only change is to add III-E-1 to the research product section. ▪ Andrea Marzi agreed that III-E-1 should be added to the RD. ▪ Animal studies with ferrets, mice, NHPs were proposed ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal.

	Action: The committee unanimously approved **RD#20-416** with the following minor modifications: 1. Add III-E-1 to the research product section. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-3-a III-D-3-b, and III-D-1-a of the NIH Guidelines.
Item 10:	Registration Documents for Recombinant DNA Experiments (New) ▪ Best (LV) ▪ **RD#20-457**: SARS-CoV-2 ▪ Reviewers: Chris Bosio, Clayton Winkler ▪ **Summary:** Infectious clones of SARS-CoV-2 ▪ Chris Bosio summarized the RD. This RD describes recombinant work with SARS-CoV-2 where the Best lab will express individual SARS-CoV-2 proteins to examine protein-protein interactions and use infectious clones of SARS-CoV-2 to understand how virus-host interactions contribute to virus replication and disease. The dual use form does have question 5 answered yes because they propose to generate mouse adapted SARS-CoV-2, but the overall dual use is no and is appropriate. ▪ Clayton Winkler stated that III-E-1 should be added to the Research Product and III-D-3-b should be added to the Eukaryote Cell Section. ▪ Animal studies with mice and hamsters were proposed ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#20-457** with the following minor modifications: 1. Add III-E-1 to the research product section and III-D-3-b for Eukaryote Cell Section. Research using prokaryotic hosts is approved at BSL-2 under section III-D-1-b and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 or BSL-3 under III-D-1-b, III-D-2-a, and III-D-3-b of the NIH Guidelines.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Becky Anderson reviewed the BSO Report
Report:	**Occupational Safety and Health Manager Report/** (b)(6) ▪ (b)(6) had nothing to report.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ The BSL-4 (b)(6); is shutdown this week for annual maintenance. ▪ More groups are starting to study SARS-CoV-2 so we are providing additional BSL-3

	training for them.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ Alida Merritt described the current testing capabilities at Marcus Daly Memorial Hospital as well as turn around times on the various tests.

Other issues	▪ Annual IBC training was provided to the IBC during this meeting. ▪ Becky Anderson summarized testing of positive strand RNA viruses by LV. Biosafety previously required work with RNA of RG3 positive strand RNA viruses to be worked with in separate labs from the main BSL-2 lab. An SOP was developed with PPE, requirements to keep cell culture work out of the dedicated lab, and waste management. LV is busy with SARS-CoV-2 research and the small dedicated labs for RNA work are becoming crowded. They requested to work with the RNA in the main labs without the restrictions listed in the SOP. Biosafety requested testing to determine the amount of infectivity from free RNA to inform a risk assessment. Becky Anderson summarized the testing on Ross River virus (Alphavirus) and MERS-CoV (Coronavirus) and discussed the results. It is clear that the only way to get free RNA into cells was with transfection reagent or by electroporation of the cells. Biosafety and Sue Priola reviewed the data prior to the IBC meeting and allowed LV to begin performing RNA work with positive strand RNA from RG3 viruses in the main labs. Sue Priola questioned the committee if they had any comments or concerns with this change. None of the committee had any concerns.

Next Meeting:

- Date: July 16, 2020
- Place: online via Skype for Business
- Time: 1:00pm

RML Biosafety Committee Meeting
June 18, 2020
Biosafety Officer/Responsible Official Report

1) Requests approved by BSO since last meeting:

a) ***Amend***

i) Feldmann RD-17-410 Amend

(1) Add aerosol route of inoculation for NHPs

ii) Feldmann PRD-17-143 Amend

(1) Add aerosol route of inoculation for NHP

2) ***New requests approved by committee via electronic review:***

a) ***None***

3) ***New requests***

a) *Pathogen Registration Documents*

i) ***New***

(a) *Tirloni (LB)*

(a) *PRD-20-227; Borrelia burgdorferi*

ii) ***Renew***

(a) *None*

iii) ***Amend***

(a) *None*

b) *Registration Documents for Recombinant Nucleic Acid Experiments*

i) ***New***

(a) *None*

ii) ***Renew***

(a) *Feldmann (LV)*

(i) RD-20-432

(b) *Feldmann (LV)*

(i) RD-20-442

(c) *Feldmann (LV)*

(i) RD-20-416

iii) ***Amend***

(a) *Feldmann (LV)*

(i) RD-17-410 Amend

(b) *Feldmann (LV)*

(i) RD-16-440 Amend

c) ***Standard Operating Procedures***

(a) ***None***

4) ***Animal Study Protocols Review***

Title	*Associated PRD*	*Associated RD*	*Reviewer*
Ad26COVS1 vaccine efficacy in the rhesus macaque model	*17-143*	*17-410*	*R. Anderson*
Efficacy Testing of a Plaque-Purified VSV-Nipah Vaccine Stock in African Green Monkeys	*13-91* *18-82*	*15-44*	*M. Brose*
Prophylactic and therapeutic efficacy of CR-1-31-B against SARS-CoV-2 in K18-hACE2 mice	*17-143*	*N/A*	*R. Anderson*
Efficacy of a subcutaneous formulation of remdesivir against SARS-CoV-2 infection in rhesus macaques	*17-143*	*N/A*	*R. Anderson*
Importance of tick salivary proteins in blood feeding and pathogen transmission	*N/A*	*N/A*	*M. Brose*
Evaluation of tick salivary proteins in blood feeding and pathogen transmission	*20-227*	*N/A*	*R. Anderson*
Immune cell-depletion in hACE2 mice challenged with SARS-CoV-2	*17-143*	*N/A*	*M. Brose*
Role of obesity in pulmonary infection with SARS-CoV-2, *Francisella tularensis*, *Bordetella pertussis* in mice	*20-223* *18-71* *17-195*	*N/A*	*M. Brose*

5) ***Biosafety Training Performed – Megan Brose, Rebecca Anderson, Nancy Hoe***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
BSL-3 Laboratory Biosafety	*None*	*None*
BSL-4 Laboratory Biosafety	*None*	*None*
Select Agent Initial Training	*1*	*3*
Select Agent visitor/BSL-3 visitor	*1*	*2*
New Employee Training	*2*	*11*

6) ***Safety Audits and Inspections***

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

a) *Biological Incident Report:*
   i) *None*

7) ***Select Agent Issues***
   a) *None*

8) ***Other Issues –***
   a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 07/16/2020
Meeting Time: 1:01 PM **Adjourned:** 2:16 PM
Due to the COVID19 pandemic, this meeting was conducted online via Skype for Business

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Seth Cooley	☒	☐	Greg Saturday	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Alexandra Scranton	☐	☒
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Brian Vickrey	☐	☒
Alan Applebury	☐	☒	Nancy Hoe	☐	☒	Clayton Winkler	☒	☐
Chris Bosio	☒	☐	Erik Hoover	☐	☒			
Marshall Bloom (EO)	☐	☒	Clay Jarrett	☒	☐			
Megan Brose	☒	☐	Josh Kellar (EO)	☐	☒			
Larry Brouwer	☐	☒	Scott Kobayashi	☒	☐			
Carol Calderwood	☐	☒	Jamie Lovaglio	☒	☐			
Marcie Caldwell (EO)	☐	☒	Andrea Marzi	☒	☐			
Bruce Chesebro (EO)	☐	☒	Alida Merritt	☐	☒			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 7/16/2020 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from** 7/16/2020 Action: Meeting minutes for 7/16/2020 were unanimously approved as written.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amend) ▪ Best (LV) ▪ **PRD#20-228 Amend: SARS-CoV-2** ▪ Becky Anderson presented the risk assessment. The amendment is to add mouse adapted SARS-CoV-2. This strain will be obtained from (b)(6) at UTMB. This adapted strain was modified to enable its use of the mouse ACE2 and allows for the use of a mouse model for studying immune responses to SARS-Cov-2.

	▪ Work with the mouse adapted strain of SARS-CoV-2 is approved at BSL-3. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#20-228 Amend** as written.
Item 2:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Feldmann (LV) ▪ **PRD#20-173: Sendai virus** ▪ Becky Anderson presented the risk assessment. This is a renewal for Sendai virus and there are no changes to the proposed studies. The Feldmann lab will continue to use Sendai virus as a potent activator of innate immune response that lead to production of Type I interferon in tissue culture models. They will also use Sendai virus as a vaccine vector to express genes of interest. The vaccine was generated and prepared by a collaborator so no recombinant work will be performed at RML. ▪ Clayton Winkler asked if we should add III-E-1. Sue Priola stated that it is not necessary since this is a PRD. ▪ Animal studies with hamsters were proposed. ▪ Work with Sendai virus is approved at BSL-2. Action: The committee unanimously approved **PRD#20-173** as written.
Item 3:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Feldmann (LV) ▪ **ST-PRD#20-175: Tick borne Orthomyxoviruses** ▪ Becky Anderson presented the risk assessment. This is a renewal for the Feldmann lab but they have requested storage only. This means that they have the materials and are stored at RML but will not work with them until they have updated the PRD and obtained IBC approval. The benefit to them is that they do not need to have current SOPs for handling virus and will not need to keep renewing the PRD if the material stays in the storage only state. ▪ No animal studies were submitted, reviewed, or approved. ▪ Storage of Tick Borne Orthomyxoviruses is approved at BSL-2. Action: The committee unanimously approved **ST-PRD#20-175** as written.
Item 4:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Feldmann (LV) ▪ **ST-PRD#20-147: Coltivirus** ▪ Becky Anderson presented the risk assessment. This is a renewal for the Feldmann lab but they have requested storage only. This means that they have the materials

	which are stored at RML but will not work with them until they have updated the PRD and obtained IBC approval. The benefit to them is that they do not need to have current SOPs for handling virus and will not need to keep renewing the PRD if the material stays in the storage only state. ▪ Sue Priola noted that in the eukaryote cell section, there is a reference to "new" work. This should be removed as it is misleading when we are approving it for storage. ▪ No animal studies were submitted, reviewed, or approved. ▪ Storage of Coltiviruses is approved at BSL-2. Action: The committee unanimously approved **ST-PRD#20-147** with minor modifications: 1. Remove the "new" reference from the eukaryote cell section.
Item 5:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Best (LV) ▪ **RD#20-456**: *CPER* clone of Powassan virus ▪ Reviewers: Clayton Winkler, Scott Kobayashi ▪ **Summary:** Mapping of Powassan virus resistance to TRIM5 ▪ Clayton Winkler summarized the RD amendment. Clayton Winkler summarized the previous work completed by the Best lab. He stated that the Best lab had an unexpected outcome and that they now want to map the genetic resistance to host TRIM5. The approach to mapping the resistance was discussed and then further described to the committee by Dr. Sonja Best. There was extensive discussion on whether this would be dual use research. Sonja Best informed the committee that TRIM5 is not the only aspect of the virus that makes it virulent. Therefore, this information would only be one part of understanding the virulence of Powassan virus. The committee discussed this further and agreed that the proposed research was not dual use. Sonja Best agreed that she would report to biosafety if any unexpected results were obtained. ▪ Sue Priola asked if the amendment is only asking to make the specific amino acid mutations? Sonja Best stated that it would be nice to have some flexibility. Sonja Best will provide a few sentences to describe the mutations they wish to perform to add to the RD amendment. ▪ Scott Kobayashi had no additional comments or concerns. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#20-456** with the following minor modifications: 1. Add a few sentences describing the types of mutations that the best lab will make.

	Research using eukaryotic cells is approved at BSL-2 and BSL-3 under III-D-1-a and III-D-2-a of the NIH Guidelines.
Item 6:	Registration Documents for Recombinant DNA Experiments (New) ▪ Feldmann (LV) ▪ **RD#20-458**: *Herpesvirus* ▪ Reviewers: Sue Priola, Andrea Marzi ▪ **Summary:** Herpesvirus as a vaccine vector ▪ Sue Priola summarized the RD. The gamma herpes virus will be used to express SARS-CoV-2 genes. It is a good virus for achieving a cellular immune response in epithelial cells so the hope is that it will be effective against SARS-CoV-2 which primarily infects epithelial cells. The vector has a deletion in ORF 73 so that the herpesvirus does not establish latency, allowing the virus to be cleared. The proposed virus is not associated with disease in any species studied. There is an ASP for animal work with hamsters attached. Sue Priola noted that III-E-1 should be added to the RD. She had not dual use concerns with the proposed research. ▪ Andrea Marzi agreed that III-E-1 should be added to the RD. Andrea Marzi also questioned why the animal biosafety level listed ABSL-4? Her concern was that some SARS-CoV-2 studies are being performed at ABSL-3 and this would restrict them. Becky Anderson stated that this should be changed. The animal biosafety level should be listed for the herpesvirus vaccine, NOT the challenge virus. The challenge virus biosafety level will be described in the PRD for that virus. The committee agreed that the biosafety level should be changed to ABSL-2, but the comment section can reflect that the biosafety level for the challenge virus will vary. ▪ Animal studies with hamsters were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved**RD#20-458** with the following minor modifications: 1. Add III-E-1 to the Research Product section. 2. Change the animal biosafety level to ABSL-2. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a and III-E-1 of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a of the NIH Guidelines.
Item 7:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Feldmann (LV) ▪ **ST-RD#20-449**: *Tick borne Orthomyxoviruses* ▪ Reviewers: Clay Jarrett, Bob Heinzen

	▪ **Summary:** Reverse genetics systems of tick-borne Orthomyxoviruses. ▪ Clay Jarrett summarized the RD. He briefly described the previous work but informed the committee that this renewal is for storage only. ▪ Bob Heinzen asked why a storage only PRD needed to be reviewed by the IBC. Becky Anderson stated that the IBC had not delegated the authority to the BSO to approve storage only documents. Sue Priola suggested that the IBC consider doing so and that the charter could be reviewed at the next IBC meeting with updates to give the BSO authority to approve storage only documents. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **ST-RD#20-449** as written. Research using prokaryotic hosts is approved at BSL-2 under section III-D-3-a and III-D-3-b of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 and BSL-3 under III-D-3-a, III-D-3-b, and III-E-1 of the NIH Guidelines.
Item 8:	**Full Committee Review of Bloom Lab Inactivation Data with Paraformaldehyde, Glutaraldehyde, and Formalin** ▪ Sue Priola informed the committee that there is inactivation data to review for the Bloom lab. Included in this month's submission is testing data for inactivation of SARS-CoV-2. The Bloom lab tested the ability of 5% formalin in 1.5% Carboxymethylcellulose in Minimal Essential Media, 2% paraformaldehyde, and 2.5% Glutaraldehyde to inactivate SARS-CoV-2. ▪ Sue Priola summarized the testing results for the inactivation of cells. Sue Priola confirmed with the committee that the samples and titers tested were appropriate, all necessary controls were included and that the procedures matched what is listed in the SOP. ▪ Sue Priola noted the following changes necessary in the SOP to match what was tested in the inactivation validation testing: ▪ Give time in hours instead of stating "overnight" incubation (page 17). ▪ Change MOI range to "0.001 to 0.1" in order to match what was tested (page 16 1.e. & page 18 1.e.). ▪ Change incubation time to 3-4 days instead of 3-5 days (page 15 1.e.). ▪ Specify cell number limit 1x106 as this was what was tested (page 16, Fixation, a; page 18 1.h.). ▪ Formalin fixation time should be changed to 2 hours in order to add a safety margin. ▪ There were no additional comments or concerns with the inactivation data.

	Action: The committee unanimously approved the inactivation data using 5% formalin in 1.5% Carboxymethylcellulose in Minimal Essential Media, 2% paraformaldehyde, and 2.5% Glutaraldehyde to inactivate SARS-CoV-2 as written and SOP changes as listed.
Item 9:	**Standard Operating Procedure: (b)(6) Coronavirus SOP (Update)** ▪ Sue Priola informed the committee that the SOP was updated to reflect the new inactivation procedures that the Bloom lab submitted. The following changes are required to match the inactivation testing: Give time in hours instead of stating "overnight" incubation (page 17). ▪ Change MOI range to "0.001 to 0.1" in order to match what was tested (page 16 1.e. & page 18 1.e.). ▪ Change incubation time to 3-4 days instead of 3-5 days (page 15 1.e.). ▪ Specify cell number limit 1x106 as this was what was tested (page 16, Fixation, a; page 18 1.h.). ▪ Formalin fixation time should be changed to 2 hours in order to add a safety margin. ▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved the (b)(6) **BSL-3 Operations and Safety Procedures (Update)**with the following modifications: 1. Change MOI range to "0.001 to 0.1" in order to match what was tested (page 16 1.e. & page 18 1.e.). 2. Change incubation time to 3-4 days instead of 3-5 days (page 15 1.e.). 3. Specify cell number limit 1x106 as this was what was tested (page 16, Fixation, a; page 18 1.h.). 4. Formalin fixation time should be changed to 2 hours in order to add a safety margin.
Item 10:	**Standard Operating Procedure: (b)(6) BSL-3 OSP, BSL-3-28-14 Personal requirements for working with Yellow fever virus, including vaccination (Update)** ▪ Becky Anderson informed the committee that the Best lab wanted to clarify when non-yellow fever work can occur when there are active cultures in the incubator. Becky Anderson worked with the Best lab to add the paragraph to the SOP to state everything that needs to occur in order to allow non-yellow fever vaccinated staff to enter the lab. ▪ The committee discussed the issue that staff are offered or must decline the yellow fever vaccine if they are going to work with the virus or will be working in the same space. At the present time, there is very limited availability of the vaccine and the nearest location to obtain it is Billings, which most staff do not want to travel to at the present time. These added provisions will make it clear when it is safe and appropriate to continue with other studies in the same space.

	▪ Sue Priola noted that the title should have "Personal" changed to "Personnel" ▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved the **A Block BSL-3 OSP, BSL-3-28-14 Personal requirements for working with Yellow fever virus, including vaccination (Update)** with the following modifications: 1. Change Personal to Personnel in the title.
Item 11:	**Exposure Control Plan (Annual Review)** ▪ Becky Anderson informed the committee that the Exposure Control Plan was due for annual review. Several members of RML safety, biosafety, OMS, and emergency services reviewed the document and proposed very minor changes. The changes are all tracked in the document. ▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved the **Exposure Control Plan (Annual Review)** as written.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Becky Anderson reviewed the BSO Report ▪ Becky Anderson informed the committee of a recent Form 3 submission to CDC DSAT.
Report:	**Occupational Safety and Health Manager Report/**(b)(6) ▪ Nothing to report.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ We are working with ORF to design a retrofit of the ABSL-3 to include trench drains in some animal rooms so we can house NHPs. Will soon be working on the phasing of construction plan.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ None.

Other issues	▪ None

Next Meeting:

- Date: August 20, 2020
- Place: online via Skype for Business
- Time: 1:00 PM

RML Biosafety Committee Meeting
July 16, 2020
Biosafety Officer/Responsible Official Report

1) Requests approved by BSO since last meeting:

a) ***Amend***

i) Marzi RD-15-404 Amend

(1) Add intranasal route of inoculation for NHPs

2) ***New requests approved by committee via electronic review:***

a) ***None***

3) ***New requests***

a) *Pathogen Registration Documents*

i) ***New***

(a) *None*

ii) ***Renew***

(a) *Feldmann (LV)*

(a) *PRD-20-173; Sendai virus*

(b) *Feldmann (LV)*

(a) *ST-PRD-20-175; Orthomyxovirus*

(c) *Feldmann (LV)*

(a) *ST-PRD-20-147; Coltivirus*

iii) ***Amend***

(a) *None*

b) *Registration Documents for Recombinant Nucleic Acid Experiments*

i) ***New***

(a) *Feldmann (LV)*

(i) RD-20-458

ii) ***Renew***

(a) *Feldmann (LV)*

(i) ST-RD-20-449

iii) ***Amend***

(a) *Best (LV)*

(i) RD-20-456 Amend

c) ***Standard Operating Procedures***

(a) (b)(6) ***BSL-3***

(a) *Add inactivation procedures and update PPE removal.*

(b) (b)(6) ***BSL-3 SOP 3-28-14 Personal requirements for working with Yellow Fever virus, including vaccination.***

(a) *Update procedures for working with Yellow Fever virus.*

(c) ***RML Exposure Control Plan***

(a) *Annual Review, minor updates.*

4) ***Animal Study Protocols Review***

Title	*Associated PRD*	*Associated RD*	*Reviewer*
Utilizing the Syrian Hamster Model for Vaccine Efficacy Testing Against SARS-CoV-2	*17-173*	*20-458*	*R. Anderson*
Investigating the efficacy of a live-attenuated Salmonella vaccine against SARS-CoV-2 utilizing the ovalbumin model antigen in mice	*18-44*	*15-108*	*M. Brose*
Efficacy of an Intranasally Delivered Chimpanzee Adenovirus-based Vaccine in the SARS-CoV-2 Rhesus Macaque Model	*17-173*	*17-410*	*R. Anderson*

5) ***Biosafety Training Performed – Megan Brose, Rebecca Anderson, Nancy Hoe***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
BSL-3 Laboratory Biosafety	*4*	*12*
BSL-4 Laboratory Biosafety-Initial	*1*	*1*
BSL-4 Laboratory Biosafety-Refresher	*1*	*1*
Laboratory Biosafety Support Staff	*1*	*1*
Select Agent Initial Training	*1*	*1*
Select Agent visitor/BSL-3 visitor	*1*	*2*
New Employee Training	*1*	*3*

6) ***Safety Audits and Inspections***

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

a) *Biological Incident Report:*
   i) *None*

7) ***Select Agent Issues***

a) *Form 3 submitted 7-1-2020 for a "Release" of a Select Agent. Inactivation performed without a validated method for that specific viral family. Methods used were validated with other viral families.*

8) ***Other Issues –***

RML Biosafety Committee Meeting
July 16, 2020
Biosafety Officer/Responsible Official Report

a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 08/20/2020
Meeting Time: 1:02 PM **Adjourned:** 1:47 PM
Due to the COVID19 pandemic, this meeting was conducted online via Skype for Business

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Seth Cooley	☒	☐	Greg Saturday	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Alexandra Scranton	☐	☒
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Brian Vickrey	☐	☒
Alan Applebury	☐	☒	Nancy Hoe	☐	☒	Clayton Winkler	☒	☐
Chris Bosio	☒	☐	Erik Hoover	☐	☒			
Marshall Bloom (EO)	☐	☒	Clay Jarrett	☒	☐			
Megan Brose	☒	☐	Josh Kellar (EO)	☐	☒			
Larry Brouwer	☐	☒	Scott Kobayashi	☒	☐			
Carol Calderwood	☐	☒	Jamie Lovaglio	☒	☐			
Marcie Caldwell (EO)	☐	☒	Andrea Marzi	☐	☒			
Bruce Chesebro (EO)	☐	☒	Alida Merritt	☐	☒			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 7/16/2020 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from** 7/16/2020 Action: Meeting minutes for 7/16/2020 were unanimously approved as written.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amend) ▪ Saito (LB) ▪ **PRD#20-229: Ehrlichia spp.** (*E. muris; E. muris subsp. eauclarensis; E. chaffeensis; Ixodes ovatus ehrlichia; E. canis*) ▪ Becky Anderson presented the risk assessment. The proposed research is to understand the initial immune response to the tick-borne intracellular pathogens of the Ehrlichia spp. in order to identify determinant factors associated with the development of progressive disease. Ehrlichia infections can cause fever,

	headache, muscle aches, nausea, confusion and possibly rash which is more common in children. There are no vaccines available, however infections are treated with doxycycline. ▪ Work with the listed Ehrlichia spp. is approved at BSL-2. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#20-229** as written.
Item 2:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Saito (LB) ▪ **PRD#20-230: Rickettsia spp.** (*R. parkeri, R. andeanae; R. montanensis, R. bellii, R. rhipicephali, R. canadenesis,* and *R. amblyommatis*) ▪ Becky Anderson presented the risk assessment. The proposed studies are to understand the initial immune response to the tick-borne intracellular pathogens of the Rickettsia spp. in order to identify determinant factors associated with the development of progressive disease. *Rickettsia parkeri* causes rickettsiosis, which is less severe than rocky mountain spotted fever caused by *Rickettsia rickettsii*. Symptoms from *R. parkeri* infection include an ulcerated lesion at the site of tick bite, fever, headache, rash, and muscle aches. Diagnosis of *R. parkeri* rickettsiosis can be difficult to distinguish from rocky mountain spotted fever in the early stage of disease and antibiotic treatment is recommended to be started immediately before a clear diagnosis is made. *R. andeanae, R. montanenesis, R. bellii, R. rhipicephali, R. canadenesis, R. amblyommatis* are not associated with illness in humans. Doxycycline, chloramphenicol and quinolones are the drugs of choice for treatment, there are no vaccines for Rickettsia spp. Infections. ▪ Animal studies with mice were proposed. ▪ Becky Anderson suggested that the following information be added to the Recommendations section. Work with all listed species on the PRD except for *R. parkeri* is approved for work at BSL-2/ABSL-2. If propagating or working with large volumes of these bacterial species, then the work should be performed with BSL-3 practices. Work with *R. parkeri* is approved at BSL-2 with BSL-3 practices with the following precautions: (1) fastidious adherence to proper microbiological techniques,(2) decontaminating all potentially infectious waste, (3) working in a BSC wearing proper PPE- double gloves, eye and face protection, tie-back gown, etc, (4) use of gasketed safety cups for centrifugation procedures, and (5) minimizing the use of sharps. Animal work with *R. parkeri* is approved at ABSL-2. Procedures should be performed in a certified BSC or other primary containment device. Particular care should be taken to safely manage sharps (e. g. at inoculation, necropsy). Action: The committee unanimously approved **PRD#20-230** with the following modifications:

	1. Add the precautions for work with *R. parkeri* to the recommendations section.
Item 3:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Marzi (LV) ▪ **RD#20-406**: *Replication-deficient vesicular stomatitis virus (VSV)* ▪ Reviewers: Clayton Winkler, Chris Bosio ▪ **Summary:** Replication deficient VSV ▪ Clayton Winkler summarized the RD renewal. They will study the role of glycoproteins from different viral families with the VSV system. This is a replication deficient virus, but they do get viral entry. They will use VSV to develop vaccine candidates for various viruses. The system has several safety factors built into it making it safe to work with. The referenced paper in the Research Product section is not attached and should be. Clayton Winkler also stated that there are several vectors attached but that are not referenced in the text and they should be. ▪ Chris Bosio had no additional comments or concerns. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#20-406** with the following minor modifications: 1. Attach the referenced Schnell paper that is mentioned in the Research Product Section. 2. Include text in the RD about the vectors that are attached (pCDNA and pCGC). Research using prokaryotic hosts is approved at BSL-2 under III-D-2-a, III-D-1-a, and III-E-1 of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a and III-D-1-a and III-E-1 of the NIH Guidelines.
Item 4:	**Full Committee Review of Bosio Lab Inactivation Data with 3% Paraformaldehyde, on SARS-CoV-2** ▪ Sue Priola informed the committee that there was inactivation data to review for the Bosio lab. Included in this month's submission is testing data for inactivation of SARS-CoV-2. The Bosio lab tested the ability of 3% paraformaldehyde (PFA) to inactivate SARS-CoV-2. ▪ Sue Priola summarized the testing results for the inactivation of cells. Sue Priola confirmed with the committee that the samples and titers tested were appropriate, all necessary controls were included and that the procedures matched what is listed in the SOP. ▪ Sue Priola noted the following changes necessary in the SOP to match what was tested in the inactivation validation testing: ▪ Adjust the range of titer inactivated to include the data from the cells, not the

	data from the supernatant. ▪ There were no additional comments or concerns with the inactivation data. Action: The committee approved (Chris Bosio abstained) the inactivation data using 3% paraformaldehyde to inactivate SARS-CoV-2 as written and SOP changes as listed.
Item 5:	**Full Committee Review of MCL Inactivation Data with RLT, Formalin, and PFA, and SDS plus heat on Coronaviruses** ▪ Sue Priola informed the committee that there was inactivation data to review for the MCL. Included in this month's submission is testing data for inactivation of Coronaviruses. The MCL tested the ability of RLT, 10% formalin, 2% PFA, and SDS plus heat to inactivate SARS-CoV-2 which was used as a surrogate for Coronaviruses. ▪ Sue Priola summarized the testing results for the inactivation of cells. Sue Priola confirmed with the committee that the samples and titers tested were appropriate, all necessary controls were included and that the procedures matched what is listed in the SOP. ▪ There were no additional comments or concerns with the inactivation data. Action: The committee unanimously approved the inactivation data using of RLT, 10% formalin, 2% PFA, and SDS plus heat to inactivate SARS-CoV-2 as written and SOP changes as listed.
Item 6:	**Standard Operating Procedure: (b)(6) SARS-CoV-2 SOP; SP-COVID-4 3% PFA Inactivation of SARS-CoV-2 in flow cytometry samples (Update)** ▪ Sue Priola informed the committee that the SOP was updated to reflect the new inactivation procedures that the Bosio lab submitted. The following changes are required to match the inactivation testing: ▪ Change the virus titer range in 1.1.2 to the titers from cells instead of the supernatant results. ▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved the (b)(6) **SARS-CoV-2 SOP; SP-COVID-4 3% PFA Inactivation of SARS-CoV-2 in flow cytometry samples (Update)** with the following modifications: 1. Change the virus titer range in 1.1.2 to the titers from cells instead of the supernatant results.
Item 7:	**Standard Operating Procedure: SOP#4-28-31 Removal for Protein Analysis (Update)** ▪ Sue Priola informed the committee that the SOP was updated to reflect the new inactivation procedures that the MCL submitted. ▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved **SOP#4-28-31 Removal for Protein Analysis (Update)** as written.

Item 8:	**Standard Operating Procedure: SOP#4-28-32 Removal for Nucleic Acid Extraction (Update)** ▪ Sue Priola informed the committee that the SOP was updated to reflect the new inactivation procedures that the MCL submitted. ▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved **SOP#4-28-32 Removal for Nucleic Acid Extraction (Update)** as written.
Item 9:	**Standard Operating Procedure: SOP#4-28-33 Removal of Specimens for Fluorescence, Immunofluorescence, Histopathology, Immunohistopathology, and Flow Cytometry (Update)** ▪ Sue Priola informed the committee that the SOP was updated to reflect the new inactivation procedures that the MCL submitted. ▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved **SOP#4-28-33 Removal of Specimens for Fluorescence, Immunofluorescence, Histopathology, Immunohistopathology, and Flow Cytometry (Update)** as written.
Item 10:	**Standard Operating Procedure: (b)(6) *Y. pestis* SOP (Update)** ▪ Becky Anderson informed the committee that the updates to the (b)(6) SOP are minimal. There is a change to the PPE that allows for a gown OR coverall unless the researchers are performing flea work, then they must wear a coverall. This change is to give flexibility to the group particularly if there are PPE shortages. The other change is to allow entry to the Suite without respiratory protection when no *Y. pestis* work is going on. This will be indicated by a sign at the entry door. ▪ There were no comments or concerns with the updated procedures. Action: The committee approved (Chris Bosio and Clay Jarrett abstained) the (b)(6) ***Y. pestis* SOP** as written.
Item 11:	**RML IBC Charter (Update)** Sue Priola summarized the changes to the IBC Charter. The changes are minor and give authority to the BSO to approve storage only PRDs and RDs. There were no comments or concerns with the updated Charter. Action: The committee unanimously approved the **RML IBC Charter (Update)** as written.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Becky Anderson reviewed the BSO Report ▪ Becky Anderson informed the committee that there is a remote CDC DSAT BSL-4 Inspection scheduled for September 8-11th.

Report:	**Occupational Safety and Health Manager Report/** (b)(6) ▪ Nothing to report.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ We are currently planning the Select Agent and BSL-4 refresher trainings that are held annually in September.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ None.

Other issues	▪ None

Next Meeting:

- Date: September 17, 2020
- Place: online via Skype for Business
- Time: 1:00 PM

RML Biosafety Committee Meeting
August 20, 2020
Biosafety Officer/Responsible Official Report

1) ***Requests approved by BSO since last meeting:***
    a) ***Amend***
        (1) *None*
2) ***New requests approved by committee via electronic review:***
    a) ***None***
3) ***New requests***
    a) *Pathogen Registration Documents*
        i) ***New***
            (a) *Saito (LB)*
                (a) *PRD-20-229; Ehrlichia spp.*
            (b) *Saito (LB)*
                (a) *PRD-20-230; Rickettsia spp.*
        ii) ***Renew***
            (a) *None*
        iii) ***Amend***
            (a) *None*
    b) *Registration Documents for Recombinant Nucleic Acid Experiments*
        i) ***New***
            (i) None
        ii) ***Renew***
            (a) *Marzi (LV)*
                (i) RD-20-406
        iii) ***Amend***
            (i) None
    c) *Review of Inactivation Procedures*
        i) *Bosio Lab*
            (a) *3% PFA inactivation of SARS-CoV-2*
        ii) *MCL*
            (a) *RLT, 10% Formalin, 2% PFA on Coronaviruses*
    d) ***Standard Operating Procedures***

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(a) (b)(6) ***BSL-3 SARS-CoV-2 SOP***

(a) *Add inactivation procedures*

(b) ***SOP#4-28-31Removal of Specimens for Protein Analysis***

(a) *Add inactivation procedures*

(c) ***SOP#4-28-32 Removal of Specimens for Nucleic Acid Extraction***

(a) *Add inactivation procedures*

(d) ***SOP#4-28-33 Removal of Specimens for fluorescence, Immunofluorescence, Histopathology, Immunohistopathology, and Flow Cytometry***

(a) *Add inactivation procedures*

(e) (b)(6) ***BSL-3 Yersinia Pestis SOP***

(a) *Update PPE procedures*

4) ***Animal Study Protocols Review***

Title	***Associated PRD***	***Associated RD***	***Reviewer***
Protection against SARS-CoV-2 disease by ChAdOx1 nCoV-19 induced antibodies in mice.	*17-143*	*17-410*	*M. Brose*
Establishment of a model of SARS-CoV-2 intranasal infection in wild type mice	*20-223*	*N/A*	*R. Anderson*
Identifying vaccine-induced correlates of protection following immunization with ChAdOx1 nCoV-19 in a mouse model of SARS-CoV-2 infection	*17-143*	*17-410*	*M. Brose*
Pre-clinical assessment of Nicotinamide Riboside (NR) in treatment of COVID-19 in mice and hamsters	*17-143*	*N/A*	*R. Anderson*
Investigating pathogenesis of MA-CCHFV in mice	*18-92*	*N/A*	*M. Brose*
Rearing and maintenance of an *Ixodes scapularis* tick colony	*N/A*	*N/A*	*R. Anderson*

5) ***Biosafety Training Performed – Megan Brose, Rebecca Anderson, Nancy Hoe***

Type of Training	***Number of Sessions***	***Number of Employees Trained***
BSL-3 Laboratory Biosafety	*2*	*2*
BSL-4 Laboratory Biosafety-Initial	*8*	*4*
BSL-4 Laboratory Biosafety-Refresher	*N/A*	*N/A*
Laboratory Biosafety Support Staff	*N/A*	*N/A*
Select Agent Initial Training	*1*	*2*
Select Agent visitor/BSL-3 visitor	*1*	*1*
New Employee Training	*2*	*3*

6) ***Safety Audits and Inspections***

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

a) *Biological Incident Report:*
   i) *None*

7) ***Select Agent Issues***

a) *Form 3 submitted 7-1-2020 for a "Release" of a Select Agent. Inactivation performed without a validated method for that specific viral family. Methods used were validated with other viral families.*
   i) *This Form 3 was downgraded to an incident only by the Form 3 Team*
b) *Remote BSL-4 CDC DSAT Inspection scheduled for September 8 -11.*

8) ***Other Issues –***

a) *None*

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 09/17/2020
Meeting Time: 1:00 PM **Adjourned:** 2:06 PM
Due to the COVID19 pandemic, this meeting was conducted online via Skype for Business

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Seth Cooley	☒	☐	Greg Saturday	☒	☐
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Alexandra Scranton	☐	☒
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Brian Vickrey	☐	☒
Alan Applebury	☐	☒	Nancy Hoe	☐	☒	Clayton Winkler	☒	☐
Chris Bosio	☒	☐	Erik Hoover	☐	☒			
Marshall Bloom (EO)	☐	☒	Clay Jarrett	☒	☐			
Megan Brose	☐	☒	Josh Kellar (EO)	☐	☒			
Larry Brouwer	☐	☒	Scott Kobayashi	☐	☒			
Carol Calderwood	☐	☒	Jamie Lovaglio	☒	☐			
Marcie Caldwell (EO)	☐	☒	Andrea Marzi	☒	☐			
Bruce Chesebro (EO)	☐	☒	Alida Merritt	☒	☐			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 8/20/2020 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from** 8/20/2020 ▪ Sue Priola noted two items, Chris Bosio abstained from the Bosio protocol approvals and that a redundant III-D-1-a should be removed from Item #3 in the Recombinant DNA Guidelines section. Action: Meeting minutes for 7/16/2020 were unanimously approved with minor modifications: 1. State that Chris Bosio abstained on the inactivation data for the (b)(6) lab. 2. On Item #3 in the Recombinant DNA Guidelines section, remove the extra III-D-1-a from the Marzi RD.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration Documents for Recombinant DNA Experiments (New) ▪ Hackstadt (LB)

	▪ **RD#20-135**: *Expression of SARS-CoV-2 genes in eukaryotic cells* ▪ Reviewers: Andrea Marzi, Chris Bosio ▪ **Summary:** Expression of SARS-CoV-2 genes ▪ Andrea Marzi summarized the RD renewal. This RD is very straightforward. They want to characterize individual SARS-CoV-2 genes. Andrea Marzi noted that the recombinant DNA section should refer to the attached paper. The pCMV-ORF-Flag vector in the text does not match the attached vector map which is for pCMV3-ORF-Flag, the vector map and text should be updated. Andrea Marzi also informed the committee that III-E-1 should be added to the Research Product, Prokaryote Host, and Eukaryote Cell sections. ▪ Sue Priola stated that III-D-2-a should be added to the Research Product, Prokaryote Host, and Eukaryote Cell sections. ▪ Chris Bosio had no additional comments or concerns. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **RD#20-135** with the following minor modifications: 1. Reference the attached paper in the recombinant DNA section. 2. Clarify the pCMV-ORF-Flag or pCMV**<u>3</u>**-ORF-Flag vector 3. Add III-E-1 to Research Product, Prokaryote and Eukaryote cell sections 4. Add III-D-2-a Research Product and Eukaryote cell sections Research using prokaryotic hosts is approved at BSL-2 under III-D-2, III-D-2-a, and III-E-1 of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-2 III-D-2-a and III-E-1 of the NIH Guidelines.
Item 2:	<u>Registration Documents for Recombinant DNA Experiments (Renewal)</u> ▪ Hinnebusch (LB) ▪ **RD#20-320**: *Site Specific mutagenesis of CDC-exempt Y. pestis strains* ▪ Reviewers: Bob Heinzen, Sue Priola ▪ **Summary:** Mutagenesis of *Y. pestis* ▪ Bob Heinzen summarized the RD renewal. This is a long RD that describes the Hinnebusch lab's main genetics system for *Y. pestis* exempt. All the experiments described in this RD are for the avirulent strains. They have paid a lot of attention in this RD to the antibiotics used and all described antibiotics are appropriate. There are three aims to the RD that are described clearly. All the referenced vector maps are attached to the RD. Bob Heinzen stated that there is a description in the DURC section that likely does not need to be included, the same language is in the body of the RD. The committee discussed and agreed that the Hinnebusch lab could decide whether to keep the text in the DURC section since it is redundant.

	▪ Sue Priola asked questions regarding antibiotic use on a few vectors, all were agreed to be fine after discussion with the IBC. Sue Priola questioned the text and vector map use of the terms pDsRed vs pDsRed2. The committee agreed this was not an issue. ▪ There were no additional comments or concerns. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Chris Bosio and Clay Jarrett abstained) **RD#20-320** with the following minor modifications: 1. Ask the Hinnebusch lab if they want to remove the redundant language in the dual use section. Research using prokaryotic hosts is approved at BSL-2 under III-D-2-a, III-D-1-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a of the NIH Guidelines.
Item 3:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Hinnebusch (LB) ▪ **RD#20-322**: *Retroviral Vectors for Transduction of Murine Cells* ▪ Reviewers: Scott Kobayashi, Clayton Winkler ▪ **Summary:** Retroviral vectors to introduce foreign DNA into mouse cells ▪ Clayton Winkler summarized the RD renewal. Clayton Winkler informed the committee that the goal of this RD is to introduce Hoxb and Hoxa9 transcription factors into mouse cells with the retrovirus system. Infection of bone marrow myeloid progenitor cells with these retrovirus constructs results in expression of conditionally active ER-Hoxb8 and ER-Hoxa9 transcription factors. Culture of these transduced cells in the presence of beta-estradiol activates the transcription factors which prevents cells differentiation into neutrophils or macrophages. The cells that will be transfected are 293T cells. Clayton Winkler stated that the map and text do not match for pCMV-Eco vs. pEcoPac—are they the same? He also stated that III-E-1- should be added to the Research Product, Prokaryote and Eukaryote cell sections. III-D-3-a should be added to the Research Product and Eukaryote cell sections. ▪ Sue Priola stated that there were no DURC concerns and the biosafety levels were appropriate. ▪ There were no additional comments or concerns. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#20-322** with the following minor

	modifications: 1. In the Recombinant DNA section, the map and text do not match for pCMV-Eco vs. pEcoPac, clarify which is accurate and ensure they match. 2. Add III-E-1 to Research Product, Prokaryote, Eukaryote cell sections. 3. Add III-D-3-a to Research Product and Eukaryote cell sections. Research using prokaryotic hosts is approved at BSL-2 under III-D-3-a and III-E-1 of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-3-a of the NIH Guidelines.
Item 4:	**Full Committee Review of Bloom Lab Inactivation Data with 5% Formalin in 1.5% CMC, 10% Formalin, 2% Paraformaldehyde, 2.5% Glutaraldehyde 1% SDS and 100˚C heat, and DNA/RNA Shield on SARS-CoV-2** ▪ Sue Priola informed the committee that there is inactivation data to review for the Bloom lab. Included in this month's submission is testing data for inactivation of SARS-CoV-2. The Bloom lab tested the ability of 5% Formalin in 1.5% CMC, 10% Formalin, 2% Paraformaldehyde, 2.5% Glutaraldehyde, 1% SDS and 100°C heat, and DNA/RNA Shield to inactivate SARS-CoV-2. ▪ Sue Priola summarized the testing results for the inactivation of cells. Sue Priola confirmed with the committee that the samples and titers tested were appropriate, all necessary controls were included and that the procedures matched what is listed in the SOP. ▪ Sue Priola asked for the following clarifications to ensure the inactivation data matches the SOP: ▪ In the inactivation data for 2% PFA and 2.5% glutaraldehyde the incubation time was listed as overnight. Please state in hours how long the incubation time was. ▪ There were no additional comments or concerns with the inactivation data. Action: The committee unanimously approved the inactivation data using 1.5% CMC, 10% Formalin, 2% Paraformaldehyde, 2.5% Glutaraldehyde 1% SDS and 100°C heat, and DNA/RNA Shield to inactivate SARS-CoV-2 with the SOP change as listed.
Item 5:	**Full Committee Review of MCL Inactivation Data with Trizol on Coronaviruses** ▪ Sue Priola informed the committee that there is inactivation data to review for the MCL. Included in this month's submission is testing data for inactivation of Coronaviruses. The MCL tested the ability of Trizol to inactivate SARS-CoV-2 which was used as a surrogate for Coronaviruses. ▪ Sue Priola summarized the testing results for the inactivation of cells. Sue Priola confirmed with the committee that the samples and titers tested were appropriate, all necessary controls were included and that the procedures matched what is listed in the SOP. ▪ There were no additional comments or concerns with the inactivation data. Action: The committee unanimously approved the inactivation data using of Trizol to

	inactivate Coronaviruses as written and SOP changes as listed.
Item 6:	**Standard Operating Procedure: (b)(6) Coronavirus SOP; SP-COVID-4, 5, 6, 7 & 8 (Update, New)** ▪ Sue Priola informed the committee that the SOP was updated to reflect the new inactivation procedures that the Bloom lab submitted. The following changes are required to match the inactivation testing: ▪ In SOP, SP-COVID-4, in section 1.f clarify that the final formalin concentration is 5%. ▪ In SOP, SP-COVID-5, In the Fixation section b., clarify that formalin samples can be fixed for 1 hour. ▪ In SOP, SP-COVID-6, In the Fixation section b., clarify that formalin samples can be fixed for 1 hour. ▪ In SOP, SP-COVID-7 Change the cell limit in 1.a from $2x10^6$ to $1x10^6$. ▪ In SOP, SP-COVID-8 Add the MOI limit for cells in 1.a. ▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved the (b)(6) **Coronavirus SOP; SP-COVID-4, 5, 6, 7 & 8 (Update, New)** with the following modifications: 1. In SOP, SP-COVID-4, in section 1.f clarify that the final formalin concentration is 5%. 2. In SOP, SP-COVID-5, In the Fixation section b., clarify that formalin samples can be fixed for 1 hour. 3. In SOP, SP-COVID-6, In the Fixation section b., clarify that formalin samples can be fixed for 1 hour. 4. In SOP, SP-COVID-7 Change the cell limit in 1.a from $2x10^6$ to $1x10^6$. 5. In SOP, SP-COVID-8 Add the MOI limit for cells in 1.a.
Item 7:	**Standard Operating Procedure: SOP#4-28-32 Removal for Nucleic Acid Extraction (Update)** ▪ Sue Priola informed the committee that the SOP was updated to reflect the new inactivation procedures that the MCL submitted. ▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved **SOP#4-28-32 Removal for Nucleic Acid Extraction (Update)** as written.
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Becky Anderson reviewed the BSO Report ▪ Becky Anderson summarized the findings from the remote BSL-4 CDC DSAT Inspection that occurred September 8-11.

Report:	**Occupational Safety and Health Manager Report/(b)(6)** ▪ Nothing to report.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ Not present.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ None.

Other issues	▪ None

Next Meeting:

- Date: October 15, 2020
- Place: online via Skype for Business
- Time: 1:00 PM

RML Biosafety Committee Meeting
September 17, 2020
Biosafety Officer/Responsible Official Report

1) Requests approved by BSO since last meeting:

a) ***None***

2) ***New requests approved by committee via electronic review:***

a) ***None***

3) ***New requests***

a) *Pathogen Registration Documents*

i) ***New***

(a) *None.*

ii) ***Renew***

(a) *None*

iii) ***Amend***

(a) *None*

b) *Registration Documents for Recombinant Nucleic Acid Experiments*

i) ***New***

(i) Hackstadt (LB)

(ii) RD-20-135

ii) ***Renew***

(a) *Hinnebusch (LB)*

(i) RD-20-320

(b) *Hinnebusch (LB)*

(i) RD-20-322

iii) ***Amend***

(i) None

c) *Review of Inactivation Procedures*

i) *Bloom Lab*

(a) *DNA/RNA shield, 10% Formalin, PFA, glutaraldehyde, and 1% SDS and heat inactivation of SARS-CoV-2*

ii) *MCL*

(a) *Trizol on Coronaviruses*

d) ***Standard Operating Procedures***

(a) (b)(6) ***BSL-3 Coronavirus SOP***

(a) *Add inactivation procedures*

(b) ***SOP#4-28-32 Removal of Specimens for Nucleic Acid Extraction***

(a) *Add inactivation procedures*

4) ***Animal Study Protocols Review***

Title	*Associated PRD*	*Associated RD*	*Reviewer*
Targeting RAGE to Treat Acute Respiratory Distress Syndrome (ARDS) Following SARS-CoV-2 infection	*20-223*	*N/A*	*M. Brose*
Collection of arterial blood from anesthetized mice	*N/A*	*N/A*	*M. Brose*
SARS-CoV-2 contact and airborne transmission under different environmental conditions in the Syrian golden hamster model	*17-143*	*N/A*	*B. Anderson*
Aerosol SARS-CoV-2 transmission in the Syrian Golden Hamster	*17-143*	*N/A*	*B. Anderson*
Pre-clinical assessment of gelsolin in treatment of COVID-19 in mice	*17-143*	*N/A*	*B. Anderson*

5) ***Biosafety Training Performed – Megan Brose, Rebecca Anderson, Nancy Hoe***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
BSL-3 Laboratory Biosafety	*N/A*	*N/A*
BSL-4 Laboratory Biosafety-Initial	*1*	*2*
BSL-4 Laboratory Biosafety-Refresher	*1*	*~35*
Laboratory Biosafety Support Staff	*N/A*	*N/A*
Select Agent Initial Training	*1*	*3*
Select Agent visitor/BSL-3 visitor	*1*	*1*
New Employee Training	*1*	*5*

6) ***Safety Audits and Inspections***

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

a) *Biological Incident Report:*
   i) *None*

7) ***Select Agent Issues***

a) *Remote BSL-4 CDC DSAT Inspection was September 8 -11.*

8) ***Other Issues –***

a) *None*

Agenda

RML Biosafety Committee Virtual Meeting
October 15, 2020

I. Old Business
   A. Draft minutes of September 17, 2020 meeting

II. New Business
   A. Committee Business

      1. Inactivation procedure review:
         a. Bosio lab: Inactivation of SARS-CoV-2 tissues with methanol

      2. SOPs:
         a. Draft Bosio ABSL3: methanol inactivation of SARS-CoV-2 tissue
         b. Draft SARS-CoV-2 ABSL4 SOPs:
            i. Flash freezing of organs
            ii. flexiVent
         c. Draft SOP#4-28-63: Rodent Transmission Caging Operation for Aerosol Exposure
         d. BSL-3 Operations and Safety Procedures (OSP): Annual Review
         e. ABSL-3 Operations and Safety Procedures (OSP): Annual Review

   B. BSO/Responsible Official report (Dr. Becky Anderson)

   E. Occupational Safety & Health Manager report (Seth Cooley)

   F. IRF Biosafety Manager Report (Lt. Cmdr. Megan Brose)

   G. Associate Director Report (Dr. Marshall Bloom)

   H. Comments from around the room

Attachments:
1. Draft minutes of September 17, 2020 meeting (1 file)
2. Inactivation studies (1 file)
3. SOPs (4 files)
4. OSPs (2 files)
5. Meeting Agenda (1 file)

NEXT MEETING: November 19, 2020 via Skype

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 10/15/2020
Meeting Time: 1:01 PM **Adjourned:** 1:54 PM
Due to the COVID19 pandemic, this meeting was conducted online via Skype for Business

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Seth Cooley	☐	☒	Greg Saturday	☒	☐
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Alexandra Scranton	☐	☒
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Brian Vickrey	☐	☒
Alan Applebury	☐	☒	Nancy Hoe	☐	☒	Clayton Winkler	☒	☐
Chris Bosio	☐	☒	Erik Hoover	☐	☒			
Marshall Bloom (EO)	☐	☒	Clay Jarrett	☐	☒			
Megan Brose	☒	☐	Josh Kellar (EO)	☐	☒			
Larry Brouwer	☐	☒	Scott Kobayashi	☒	☐			
Carol Calderwood	☐	☒	Jamie Lovaglio	☒	☐			
Marcie Caldwell (EO)	☐	☒	Andrea Marzi	☐	☒			
Bruce Chesebro (EO)	☐	☒	Alida Merritt	☐	☒			

(P=present; A=absent)

Guests: (b)(6)

Minutes: Meeting minutes from 9/17/2020 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 9/17/2020** ▪ Sue Priola noted that on page 2, Item 1 the pCMV vector language was not correct needs to be corrected throughout the section. ▪ On page 3, Item 3, add information that estrogen can be added or removed to alter cell differentiation. ▪ On Page 5, item 6, "hours" needs to be changes to "hour". Action: Meeting minutes for 9/17/2020 were unanimously approved with the following minor modifications: 1. Page 2, Item 1 the pCMV vector language was not correct needs to be corrected throughout the section. 2. Page 3, Item 3, add information that estrogen can be added or removed to alter cell differentiation. 3. On Page 5, item 6, "hours" needs to be changes to "hour".

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	**<u>Full Committee Review of Bosio Lab Inactivation Data with Methanol on SARS-CoV-2</u>** ▪ Sue Priola informed the committee that there was inactivation data to review for the Bosio lab. Included in this month's submission is testing data for inactivation of SARS-CoV-2. The Bosio lab tested the ability of methanol to inactivate SARS-CoV-2 infected rodent tissues. ▪ Sue Priola summarized the testing results for the inactivation of cells. Sue Priola confirmed with the committee that the samples and titers tested were appropriate, all necessary controls were included and that the procedures matched what is listed in the SOP. ▪ Sue Priola noted the following changes necessary in the SOP to match what was tested in the inactivation validation testing: ▪ Get the weight of the lungs used in the inactivation testing. This weight can be added to the SOP for comparison. ▪ There were no additional comments or concerns with the inactivation data. <u>Action:</u> The committee unanimously approved the inactivation data using methanol to inactivate SARS-CoV-2 infected tissues as written and SOP changes as listed.
Item 2:	**Standard Operating Procedure: (b)(6) SARS-CoV-2 SOP (Update)** ▪ Sue Priola informed the committee that the SOP was updated to reflect the new inactivation procedures that the Bosio lab submitted. The following changes are required to match the inactivation testing: ▪ Add the average weight of the lungs tested to the SOP in parenthesis after the 50 mg weight limit ▪ There were no comments or concerns with the updated procedures. <u>Action</u>: The committee unanimously approved the (b)(6) **SARS-CoV-2 SOP (Update)** with the following modifications: 1. Add the average weight of the lungs to the SOP in parenthesis after the 50 mg weight limit.
Item 3:	**Standard Operating Procedure: SARS-CoV-2 Animal SOP_LV (Update)** ▪ Becky Anderson informed the committee that there are two new SOPs to add to the SARS-CoV-2 Animal SOP. The first SOP is SP-COVID-1 titled "Freezing of organs following infection with SARS-CoV-2 in liquid nitrogen." Becky Anderson informed the committee that LV would like to flash freeze organs after removing them from infected animals so they can then transport to their BSL-3

	lab. The second SOP is SP-COVID-2 titled, "Flexivent". This SOP describes the use of a Flexivent unit that measures respirations in rodents. The unit and the rodents will be in a BSC for all procedures. ▪ Sue Priola asked what LV is doing with gloves when they are pulling their hands out of the BSC between using the laptop and working with the animals (b)(6) (b)(6) stated that this is at least a two-person procedure and one individual would run the laptop and the other would focus on animal handling in the BSC. Sue Priola noted that this should be added to the Special Practices section so it is clear that no one is trying to do both parts of the procedure. ▪ Sue Priola noted that on page 11 in 6.2.H. there is a misspelling of "cannula". ▪ Clayton Winkler stated for the freezing of organs SOP, there should be a step added to wipe the tube with 5% microchem prior to placing in the liquid nitrogen. ▪ Both Clayton Winkler and Sue Priola stated that the 50 mL conical should only be closed loosely due to the use of liquid nitrogen for freezing the tubes. ▪ There were no additional comments or concerns with the updated procedures. Action: The committee unanimously approved the: **SARS-CoV-2 Animal SOP_LV** with the following modifications: 1. Add to the special precautions section on page 8 that this procedure will require 2 people. 2. Correct the spelling on page 11 in 6.2.H. of "cannula" 3. Add a step to SP-COVID-1 that tubes are wiped with 5% microchem before placing in liquid nitrogen. 4. Clarify step 8 in SP-COVID-1 that the 50 ml conical will be "loosely" capped.
Item 4:	**Standard Operating Procedure: SOP#4-28-63 rodent Transmission Caging Operation for Aerosol Exposure (New)** ▪ Becky Anderson informed the committee that this was a new SOP from the Munster lab. The lab has custom designed a transmission caging system for hamsters. The design has two cages that are separated by a 1, 3, or 6-foot length of tubing. An infected hamster would be placed in a cage that is connected by tubing to another cage. A vacuum pump would be connected to the uninfected cage and would create directional airflow from the infected hamster cage to the uninfected hamster cage. The vacuum pump controls the air flow and is protected by an in-line HEPA filter. The provided SOP describes the procedures for setup, handling, and decon of the equipment. ▪ Becky Anderson stated that biosafety has not had a chance to do any testing on the system. Megan Brose and Becky Anderson plan to do a water test on the connections to make sure they are leak proof and then plan to set up the entire

	caging system and will test it with a smoke generator and particle counter. The equipment is not fulling constructed so biosafety is waiting to be able to perform the testing. Biosafety can report back to the IBC once this testing has been completed. ▪ Sue Priola questioned how multiple uses would affect the equipment? If it is assembled/disassembled? Is there a way you could do some testing prior to each new experiment to make sure the system is functioning properly with all of the connections sealed? The committee discussed this at length, it was decided that LV could do a soap bubble test prior to each experiment, this information should be added to the SOP. ▪ (b)(6) described the quick connections between the cages and the tubing. Clayton Winkler asked how often they will change the gasket (b)(6) stated that if they test the setup before each experiment, that would tell them when they need to replace the gaskets. ▪ Megan Brose suggested changing the wording in 6.2.A.1. from "First test" to "fluid seal test" and 6.2.A.2 from "Second Test" to "Air seal test". ▪ There was extensive discussion on how the system is designed, how to ensure the caging setup is working as designed and how to perform the validation testing. ▪ The committee decided to table the SOP until biosafety can perform the validation testing. The SOP will be sent out for electronic review with the results from the validation testing. ▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously Tabled the **SOP#4-28-63 rodent Transmission Caging Operation for Aerosol Exposure (New).**
Item 5:	**Standard Operating Procedure: BSL-3 Operations and Safety Procedures (OSP) (Annual Review)** ▪ Becky Anderson informed the committee that the BSL-3 OSP is due for annual review. There are very minor changes in the document. The most notable change is the removal of the word "Tyvek" from the gown/coverall PPE section because Tyvek is not available due to the COVID-19 coronavirus pandemic and staff must wear alternative gowns/coveralls. There were no comments or concerns with the updated procedures. Action: The committee unanimously approved the **BSL-3 OSP (Annual Review)** as written
Item 6:	**Standard Operating Procedure: ABSL-3 Operations and Safety Procedures (OSP) (Annual Review)**

	▪ Becky Anderson informed the committee that the ABSL-3 OSP is also due for annual review. Changes to the ABSL-3 OSP are the same as those in the BSL-3 OSP. ▪ There were no comments or concerns with the updated procedures. Action: The committee unanimously approved the A**BSL-3 OSP (Annual Review)** as written
Report:	**BSO/Responsible Official Report/Nancy Hoe** ▪ Becky Anderson reviewed the BSO Report
Report:	**Occupational Safety and Health Manager Report/Seth Cooley** ▪ Not present.
Report	**IRF Biosafety Manager Report/Megan Brose** ▪ (b)(6); (b)(3):42 Lab in the BSL-4 is currently shutdown ▪ We are wrapping up annual refresher training for Select Agent and BSL-4 training. ▪ We will be doing BSL-3 and Support staff refresher training in November. ▪ There is a table top exercise planned for the BSL-4 CIU transport drill that we perform annually.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ None.

Other issues	▪ None

Next Meeting:

- Date: November 19, 2020
- Place: online via Skype for Business
- Time: 1:00 PM

RML Biosafety Committee Meeting
October 15, 2020
Biosafety Officer/Responsible Official Report

1) Requests approved by BSO since last meeting:

a) ***Amend***

i) Feldmann PRD-18-208

(1) Add USDA permit

ii) Feldmann PRD 19-159

(1) Add USDA permit

iii) Feldmann RD 20-458

(1) Add intranasal route of inoculation for Hamsters

iv) Peterson PRD 19-162

(1) Add HBBF

2) ***New requests approved by committee via electronic review:***

a) ***None***

3) ***New requests***

a) *Pathogen Registration Documents*

i) ***New***

(a) *None.*

ii) ***Renew***

(a) *None*

iii) ***Amend***

(a) *None*

b) *Registration Documents for Recombinant Nucleic Acid Experiments*

i) ***New***

(a) *None*

ii) ***Renew***

(a) *None*

iii) ***Amend***

(i) None

c) *Review of Inactivation Procedures*

i) *Bosio Lab*

(a) *Methanol inactivation of SARS-CoV-2*

d) ***Standard Operating Procedures***

(a) (b)(6) ***SARS-CoV-2 SOP***

(a) *Add inactivation procedures*

(b) ***SARS-CoV-2 Animal SOP_LV***

(a) *Add SOP for Flash freezing of organs*

(b) *Add SOP for use of flexiVent*

(c) ***SOP#4-28-63 Rodent Transmission Caging Operation for Aerosol Exposure***

(d) ***BSL-3 Operations and Safety Procedures***

(e) ***ABSL-3 Operations and Safety Procedures***

4) ***Animal Study Protocols Review***

Title	*Associated PRD*	*Associated RD*	*Reviewer*
Murine pulmonary T cell response to SARS-CoV-2	*20-223*	*N/A*	*M. Brose*
Dynamics of ehrlichial/rickettsial pathogen acquisition by tick feeding, in a murine model, and production of "infected" ticks.	*20-229* *20-230*	*N/A*	*M. Brose*
Mink model development for SARS-CoV-2	*17-143*	*N/A*	*M. Brose*
Immunopathogenesis of ehrlichial and rickettsial diseases using an established murine model of tick transmission	*20-229* *20-230*	*N/A*	*M. Brose*

5) ***Biosafety Training Performed – Megan Brose, Rebecca Anderson, Nancy Hoe***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
BSL-3 Laboratory Biosafety	*1*	*6*
BSL-4 Laboratory Biosafety-Initial	*2*	*2*
BSL-4 Laboratory Biosafety-Refresher	*1*	*7*
Laboratory Biosafety Support Staff	*N/A*	*N/A*
Select Agent Initial Training	*1*	*3*
Select Agent visitor/BSL-3 visitor	*N/A*	*N/A*
New Employee Training	*2*	*10*

6) ***Safety Audits and Inspections***

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

a) *Biological Incident Report:*

i) *None*

7) ***Select Agent Issues***
   a) *None*

8) ***Other Issues –***
   a) *None*

Agenda

RML Biosafety Committee Virtual Meeting
November 19, 2020

I. Old Business
   A. Draft minutes of October 15, 2020 meeting

II. New Business
   A. Committee Business
      1. Recombinant DNA Documents (2)
      2. Pathogen Registration Documents (2)
      3. Inactivation procedure reviews:
         a. MCL: inactivation of tissues with 2% PFA (short fixation)
      4. SOPs:
         a. Draft SOP#4-28-64 Removal of tissues following short fixation for High Content Imaging

   B. BSO/Responsible Official report (Dr. Becky Anderson)

   E. Occupational Safety & Health Manager report (Seth Cooley)

   F. IRF Biosafety Manager Report (Lt. Cmdr. Megan Brose)

   G. Associate Director Report (Dr. Marshall Bloom)

   H. Comments from around the room

Attachments:
1. Draft minutes of October 15, 2020 meeting (1 file)
2. Recombinant DNA documents (2 files)
3. Pathogen Registration Documents (2 files)
4. Inactivation studies (1 file)
5. SOPs (1 file)
6. Meeting Agenda (1 file)

NEXT MEETING: December 17, 2020 via Skype

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 11/19/2020
Meeting Time: 1:01 PM **Adjourned:** 1:37 PM
Due to the COVID19 pandemic, this meeting was conducted online via Skype for Business

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Seth Cooley	☐	☒	Greg Saturday	☒	☐
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Alexandra Scranton	☐	☒
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Brian Vickrey	☐	☒
Alan Applebury	☐	☒	Nancy Hoe	☐	☒	Clayton Winkler	☒	☐
Chris Bosio	☒	☐	Erik Hoover	☐	☒			
Marshall Bloom (EO)	☐	☒	Clay Jarrett	☒	☐			
Megan Brose	☒	☐	Josh Kellar (EO)	☐	☒			
Larry Brouwer	☒	☐	Scott Kobayashi	☒	☐			
Carol Calderwood	☐	☒	Jamie Lovaglio	☒	☐			
Marcie Caldwell (EO)	☐	☒	Andrea Marzi	☒	☐			
Bruce Chesebro (EO)	☐	☒	Alida Merritt	☐	☒			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 10/15/2020 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 10/15/2020** ▪ Sue Priola noted a couple of minor typos. ▪ Bob Heinzen stated that on page 4, line 2, "fulling" should be changed to "fully". Action: Meeting minutes for 9/17/2020 were unanimously approved with the following minor modifications: 1. Correct minor typos from Sue Priola. 2. Change on page 4, line 2, "fulling" should be changed to "fully".

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amend) ▪ Feldmann (LV) ▪ **PRD#17-143 Amend: Coronavirus** ▪ Becky Anderson presented the risk assessment. The amendment is to add ferrets as a new animal model for SARS-CoV-2. Studies will be conducted in the BSL-4 according to the IBC approved *SOP#4-28-38 Husbandry and manipulation of Ferrets and mink in Level 4.* LV has submitted a training ASP for mink so the current SOP can be evaluated to determine if it is accurate. A training period will occur for relevant staff prior to any studies with infectious agent. PPE will include a positive pressure suit and additional protective gloves (leather or sheep skin gloves) over the suit gloves when handling mink. ▪ Work with ferrets and SARS-CoV-2 is approved at ABSL-4. ▪ Animal studies with ferrets were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#17-143 Amend** as written.
Item 2:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amend) ▪ Bloom (LV) ▪ **PRD#19-213 Amend: *Borrelia burgdorferi*** ▪ Becky Anderson presented the risk assessment. The amendment is to add *Borrelia hermsii* to the registration. The Bloom lab wants to expand their studies on the impact of Borrelia species on the physiology and microbiome of ticks to include the relapsing fever agent *B. hermsii* and its tick vector Ornithodorus hermsii. Tick borne relapsing fever is caused by Borrelia spp. (*hermsii, parkerii*, and *turicatae*; most commonly hermsii) and is characterized by recurring febrile episodes that last approximately 3 days and are separated by afebrile periods of 7 days. Each febrile episode ends with symptoms known as a "crisis" where patients develop very high fever and may become delirious, agitated, and tachycardic for a duration of 10 to 30 min. This is then followed by a phase called "flush" where they have drenching sweats and a rapid decrease in body temp. Patients that are untreated experience 1 to 4 episodes of fever. Mortality is estimated at 5-10% for untreated TBRF patients. Mortality rate for persons treated is less than 1%. *B. hermsii* infections can be treated successfully with antibiotics like penicillin and other beta-lactam antimicrobials. The incubation period is 3 to 32 days and the natural route of transmission is by the bite of an infected tick. The primary lab hazards include parenteral contact, accidental sharps injuries, and exposure to aerosols. ▪ Sue Priola questioned if *B. hermsii* would be included in the co-infection studies that were described in the original PRD. Becky Anderson stated that co-infections with *B. hermsii* would be approved with this amendment as adding another agent to the PRD covers them for the previous work described. She also added that the Bloom

	lab is currently not performing any tick studies with Powassan virus. The Bloom lab still needs to develop a biosafety plan for working with ticks in the BSL-3 lab that must be reviewed and approved by the IBC. The committee agreed there were no issues with co-infections with *B. hermsii* and Powassan virus. ▪ Work with *B. hermsii* is approved at BSL-2. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#19-213 Amend** as written.

Item 3:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Feldmann (LV) ▪ **RD#20-412**: Hantavirus ▪ Reviewers: Andrea Marzi, Scott Kobayashi ▪ **Summary:** Hantavirus reverse genetics system. ▪ Andrea Marzi summarized the RD. She informed the committee that this is a renewal with no changes to the RD. The NIH Guidelines listed are appropriate, the vector maps are attached and their DURC form is fine. There is one dual use question marked yes, the question for synthetic biology, which should be marked yes as they are using those techniques for these experiments. ▪ Scott Kobayashi had no additional comments or concerns. ▪ Sue Priola questioned the committee if III-E-1 should be added. Andrea Marzi stated that she did not think that it should be and the committee agreed. ▪ Sue Priola noted that the older version of the PRD was referenced, "12-81" and should be updated to the current year. The information for reassortants should be added from the PRD that is referenced. ▪ Sue Priola also pointed out that the plasmids are not listed in the prokaryote host section and need to be added. ▪ Additionally, Sue Priola oted that the DURC questionnaire had information included in 7C that was a copy paste from other sections in the DURC which was redundant, we can ask the PI if they want to remove the redundant language. ▪ No animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#20-412** with the following minor modifications: 1. Update PRD# for 12-81 and add detail for the proposed reassortant work 2. List the plasmids in the prokaryote section 3. If fine with the PI, Remove DURC answers from questionnaire in question 7C. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-b and III-D-3-b of the NIH Guidelines.
Item 4:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Marzi (LV) ▪ **RD#20-404**: *Vesicular stomatitis virus (VSV)- replication competent* ▪ Reviewers: Sue Priola, Chris Bosio ▪ **Summary:** VSV for the studies of viral protein function and as a vaccine delivery

	system. ▪ Sue Priola summarized the RD. This is an RD renewal with no new work proposed. The renewal does include amendments now rolled into one document. The Marzi lab will use VSV to express foreign genes of interest as well as a platform for vaccines and therapeutics. The NIH Guidelines listed are appropriate and there were no DURC issues ▪ Sue Priola did point out to the committee that pCAGGs should be listed in the prokaryote host section. ▪ Sue Priola also noted that in the prokaryote host section, "Nature of gene sequence . . ." question, please change the reference of the VSV backbone to full length VSV. ▪ Andrea Marzi also informed the committee that she had a hard time adding animal species to the RD. Bats were already approved in a previous amendment, but she could not add them in PI Dashboard, would it be ok if there were still added in this renewal? Becky Anderson informed the committee that in cases where there are a lot of animal species to include, we sometimes allow PI's to group rodents like mice, guinea pigs, and hamsters in the PRD so that can include all relevant animal models. The committee agree that Andrea Marzi could group rodents in PI Dashboard in order to make room to add bats. ▪ Animal studies with guinea pigs, NHPs, hamsters, pigs, mice, and bats were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **RD#20-404** with the following minor modifications: 1. Add pCAGGS to the prokaryote host section. 2. In the prokaryote host section, "Nature of gene sequence . . ." question, change the reference of the VSV backbone to full length VSV. 3. PI to reorganize animal models to consolidate species in PI Dashboard and attach the bat ASP. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a, III-D-1-a and III-E-1 of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a, III-D-2-a, and III-E-1 of the NIH Guidelines.
Item 5:	**<u>Full Committee Review of MCL Lab Inactivation Data with PFA on Coronaviridae</u>** ▪ Sue Priola informed the committee that there was inactivation data to review for the MCL. Included in this month's submission is testing data for inactivation of SARS-CoV-2, a surrogate for the Coronaviridae viral family. The BSL-4 lab tested the ability of PFA at 1, 2, and 4% to inactivate SARS-CoV-2 infected tissues. ▪ Sue Priola summarized the testing results for the inactivation of tissues. Sue Priola confirmed with the committee that the samples and titers tested were appropriate, all necessary controls were included and that the procedures matched what is listed in

	the SOP. ▪ There were no additional comments or concerns with the inactivation data. ▪ Action: The committee unanimously approved the inactivation data using 2% PFA to inactivate SARS-CoV-2 infected tissues as written.
Item 6:	**Standard Operating Procedure: SOP#4-28-64 Removal of Tissues Following Short Fixation for High Content Imaging (New)** ▪ Sue Priola summarized the SOP for the committee and associated inactivation testing data. ▪ Clay Jarrett expressed concern that the title is misleading, stating that "short fixation" time is not short for fixation with PFA. He was concerned the regulatory groups might misunderstand it. Becky Anderson informed the committee that the terms "short fixation" were used to separate this SOP from other SOPs that require a 7-day inactivation rather than 3 days specified in this SOP. The committee agreed this title is appropriate. ▪ Bob Heinzen noted that in Section 7, the statement, "The above described procedure will fully inactivate enveloped RNA viruses" is not appropriate when only one viral family has been tested. The committee agreed that this statement should be removed. ▪ There were no additional comments or concerns with the updated procedures. Action: The committee unanimously approved the: **SOP#4-28-64 Removal of Tissues Following Short Fixation for High Content Imaging (New)** with the following modifications: 1. Delete the following sentence in Section 7, "The above described procedure will fully inactivate enveloped RNA viruses"
Report:	**Biosafety Officer (BSO) Report/Becky Anderson** ▪ Becky Anderson reviewed the BSO Report
Report:	**Occupational Safety and Health Manager Report/Seth Cooley** ▪ Not present.
Report	**IRF Biosafety Manager/Responsible Official Report/Megan Brose** ▪ The BSL-3 (b)(6) annual shutdown will occur November 30th to December 4th. ▪ We will be working to schedule the annual shutdown schedule for the other BSL-3 labs soon. ▪ CDC DSAT notified RML that there will be a remote inspection on 3/15/2021. We expect this to be focused on the BSL-3, but will update everyone as we have more information.

Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ None.

Other issues	▪ None

Next Meeting:

- Date: December 17, 2020
- Place: online via Skype for Business
- Time: 1:00 PM

RML Biosafety Committee Meeting
November 19, 2020
Biosafety Officer Report

1) Requests approved by BSO since last meeting:

a) ***Amend***

i) SOP#4-28-50 Operation of the Environmental Chamber

(1) Include new Environmental Chamber details and pictures

(2) Add procedures for using the hamster transmission caging inside the Environmental Chamber

2) ***New requests approved by committee via electronic review:***

a) ***None***

3) ***New requests***

a) *Pathogen Registration Documents*

i) ***New***

(a) *None*

ii) ***Renew***

(a) *None*

iii) ***Amend***

(a) *Feldmann (LV)*

(a) *PRD-17-143; Coronavirus*

(b) *Bloom (LV)*

(a) *PRD-19-213; B. burgdorferi*

b) *Registration Documents for Recombinant Nucleic Acid Experiments*

i) ***New***

(a) *None*

ii) ***Renew***

(a) *Feldmann (LV)*

(i) RD-20-412

(b) *Marzi (LV)*

(i) RD-20-404

iii) ***Amend***

(a) *None*

c) ***Standard Operating Procedures***

(a) ***SOP#4-28-64 Short PFA Fixation- New***

(a) *Inactivation data supports this new SOP*

RML Biosafety Committee Meeting
November 19, 2020
Biosafety Officer Report

4) ***Animal Study Protocols Review***

Title	*Associated PRD*	*Associated RD*	*Reviewer*
Mink Animal Care and Use Training Program	*N/A*	*N/A*	*M. Brose*
Evaluation of an RNA vaccine against Crimean-Congo hemorrhagic fever in mice	*18-92*	*17-452*	*R. Anderson*
Mechanisms of viral vertical transmission and the effect of glial responses on CNS development in a mouse model of Zika virus infection	*16-184*	*N/A*	*R. Anderson*
TLR agonists as a potential treatment against COVID-19 in mice	*17-143*	*N/A*	*M. Brose*
Dose dependency of aerosol and fomites exposure with SARS-CoV-2 in the Syrian golden hamster	*17-143*	*N/A*	*R. Anderson*

5) ***Biosafety Training Performed – Megan Brose, Rebecca Anderson, Nancy Hoe***

Type of Training	*Number of Sessions*	*Number of Employees Trained*
BSL-3 Laboratory Biosafety	*1*	*4*
BSL-4 Laboratory Biosafety-Initial	*6*	*3*
BSL-4 Laboratory Biosafety-Refresher	*16*	*~29*
Laboratory Biosafety Support Staff-Refresher	*2*	*~60*
Select Agent Initial Training	*1*	*3*
Select Agent visitor/BSL-3 visitor	*1*	*1*
New Employee Training	*2*	*8*

6) ***Safety Audits and Inspections***

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

a) *Biological Incident Report:*
   i) *None*

7) ***Other Issues –***

a) *None*

Agenda

RML Biosafety Committee Virtual Meeting
December 17, 2020

I. Old Business
   A. Draft minutes of November 19, 2020 meeting

II. New Business
   A. Committee Business

      1. Inactivation procedure review:
         a. MCL- Inactivation of Flaviviruses with AVL, RLT, and Trizol
         b. MCL- Inactivation of Filoviruses with PFA
         c. Hinnebusch- Inactivation of Y. pestis with methanol and PFA

      2. SOPs:
         a. Draft SOP#4-28-64: Removal of Tissues following short fixation for High Content Imaging
         b. Draft BSL-3-YP-1: Yersinia pestis Culture and Manipulation methods
         c. MCL Operations and Safety Procedures (OSP): Annual Review

   B. BSO report (Dr. Becky Anderson)

   E. Occupational Safety & Health Manager report (Seth Cooley)

   F. IRFBSM/Responsible Official Report (Lt. Cmdr. Megan Brose)

   G. Associate Director Report (Dr. Marshall Bloom)

   H. Comments from around the room

Attachments:
1. Draft minutes of November 19, 2020 meeting (1 file)
2. Inactivation studies (3 files)
3. SOPs (2 files)
4. OSP (1 files)
5. Meeting Agenda (1 file)

NEXT MEETING: December 17, 2020 via Skype

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 12/17/2020
Meeting Time: 1:02 PM **Adjourned:** 1:38 PM
Due to the COVID19 pandemic, this meeting was conducted online via Skype for Business

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☐	☒	Seth Cooley	☒	☐	Greg Saturday	☒	☐
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Alexandra Scranton	☐	☒
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Brian Vickrey	☐	☒
Alan Applebury	☐	☒	Nancy Hoe	☐	☒	Clayton Winkler	☒	☐
Chris Bosio	☒	☐	Erik Hoover	☒	☐			
Marshall Bloom (EO)	☐	☒	Clay Jarrett	☒	☐			
Megan Brose	☒	☐	Josh Kellar (EO)	☐	☒			
Larry Brouwer	☐	☒	Scott Kobayashi	☒	☐			
Carol Calderwood	☐	☒	Jamie Lovaglio	☒	☐			
Marcie Caldwell (EO)	☐	☒	Andrea Marzi	☒	☐			
Bruce Chesebro (EO)	☐	☒	Alida Merritt	☒	☐			

(P=present; A=absent)

Guests: (b)(6)

Minutes: Meeting minutes from 11/19/2020 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 11/19/2020** ▪ No changes Action: Meeting minutes for 11/19/2020 were unanimously approved as written.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	**Full Committee Review of MCL Lab Inactivation Data with AVL, RLT, Trizol with Flaviruses** ▪ Bob Heinzen informed the committee that there was inactivation data to review for the MCL. In this case, the MCL group wanted to provide the IBC with testing data where the inactivation procedure was not effective, they are not looking for approval with any of the submitted results. (b) (6) summarized the testing procedures for Flavivirus infected cells or tissues with RLT, AVL, and Trizol. She informed the committee that AVL and Trizol were effective in cells and tissues and RLT was effective in tissues but not cells. The committee extensively discussed the differences in results of the inactivation testing including genome size, viral load in tissue vs. cells, and infectivity of bare RNA from Coronaviruses vs. Flaviviruses. ▪ (b) (6) clarified to the committee that all Flaviviruses worked with in the BSL-4 are select agents and are not removed from the BSL-4 by these methods alone. Samples that are to be removed are irradiated under the current validated irradiation protocol for Flaviviruses. (b) (6) informed the committee that at this time the MCL is not looking for approval for any of these inactivation methods with Flaviviruses and they have not submitted a corresponding SOP. In the future they may update SOP#4-28-31 to clarify how Flaviviruses need to be handled to be sure there is no confusion. Action: No action taken. Data provided to committee for informational purposes only.
Item 2:	**Full Committee Review of MCL Lab Inactivation Data with PFA on Filoviridae** ▪ Bob Heinzen informed the committee that there was inactivation data to review for the MCL. Included in this month's submission is testing data for inactivation of Filoviruses using Ebola virus as the surrogate. The BSL-4 lab tested the ability of PFA at 2% to inactivate Ebola virus infected tissues. ▪ Bob Heinzen summarized the testing results for the inactivation of tissues. Bob Heinzen confirmed with the committee that the samples and titers tested were appropriate, all necessary controls were included and that the procedures matched what is listed in the SOP. ▪ There were no additional comments or concerns with the inactivation data. Action: The committee unanimously approved the inactivation data using 2% PFA to inactivate Filoviridae infected tissues as written.
Item 3:	**Standard Operating Procedure: SOP#4-28-64 Removal of Tissues Following Short Fixation for High Content Imaging (Updated)** ▪ Bob Heinzen summarized the SOP for the committee and associated inactivation testing data. ▪ Andrea Marzi stated that she thought the titer seemed low for the mouse lymph nodes. (b) (6) stated the Best lab wanted to test a specific route of inoculation which was the foot pad. The committee discussed that since this SOP is for a specific assay, the table should be updated to also include a route of inoculation

	since this will affect the titer of the tissue in the draining lymph node. ▪ There were no additional comments or concerns with the updated procedures. Action: The committee unanimously approved the**: SOP#4-28-64 Removal of Tissues Following Short Fixation for High Content Imaging (Updated)** with the following modifications: 1. Update table to include route of inoculation.
Item 4:	**Full Committee Review of MCL Lab Inactivation Data with PFA and methanol on *Yersinia pestis*** ▪ Bob Heinzen informed the committee that there was inactivation data to review for the Hinnebusch lab. The Hinnebusch lab tested the ability of 4% PFA and 100% methanol to inactivate *Yersinia pestis* in blood smears. ▪ Bob Heinzen summarized the testing results for the inactivation of tissues. Bob Heinzen confirmed with the committee that the samples and titers tested were appropriate, all necessary controls were included and that the procedures matched what is listed in the SOP. ▪ Bob Heinzen questioned why different strains were used in the testing. Chris Bosio informed the committee that they used some strains that were already growing in the lab and then used Kim6+ GFP because of the antibiotic resistance to reduce background contamination because of the long growing times. The committee did not have any concerns with the strains used. ▪ There were no additional comments or concerns with the inactivation data. Action: The committee approved (Chris Bosio and Clay Jarrett abstained) the inactivation data using 4% PFA and 100% methanol to inactivate *Yersinia pestis* in blood smears as written.
Item 5:	**Standard Operating Procedure: BSL-3-Yp-4 and ABSL3 PY-7 Culture and Manipulation Methods (New)** ▪ Bob Heinzen summarized the SOP for the committee and associated inactivation testing data. ▪ Chris Bosio stated that they want the SOP in both the lab and animal SOPs so that can perform the blood smear inactivation in either location. ▪ Becky Anderson stated that in order to have a margin of safety, the fixation time in the SOP should be changed from 10 minutes to 20 minutes since the Hinnebusch lab only tested 10 minutes. ▪ There were no additional comments or concerns with the updated procedures. Action: The committee approved (Chris Bosio and Clay Jarrett abstained) **BSL-3-Yp-4 and ABSL3 PY-7 Culture and Manipulation Methods (New)** with the following modifications: 1. Change the fixation time from 10 minutes to 20 minutes.

Item 6:	**MCL Operations and Safety Procedures (OSP) -Annual Review** ▪ Becky Anderson summarized the updates to the MCL OSP for the committee. ▪ Jamie Lovaglio asked if on page 64 the reference to daily inventory applied to only rodents or includes NHPs? Megan Brose stated that all select agent infected animals need a daily accounting. The current process in the BSL-4 does capture the appropriate inventory and the committee agreed no changes were necessary to this language. ▪ Jamie Lovaglio also asked if on page 64 the reference to squeeze cage mechanisms can be updated to "only when practical" as some of the smaller NHP species RMVB handles do not use the squeeze cage mechanism. The committee agreed this should be updated. ▪ There were no additional comments or concerns with the updated procedures. Action: The committee unanimously approved the **MCL Operations and Safety Procedures (OSP) -Annual Review** with the following modifications: 1. On page 64, update the language for the squeeze cage mechanisms to state that they are used when practical.
Report:	**Biosafety Officer (BSO) Report/Becky Anderson** ▪ Becky Anderson reviewed the BSO Report
Report:	**Occupational Safety and Health Manager Report/Seth Cooley** ▪ Nothing to report.
Report	**IRF Biosafety Manager/Responsible Official Report/Megan Brose** ▪ There are no select agent issues. ▪ The (b)(6) annual shutdown will be in January. ▪ The (b)(6) is due for it's annual shutdown in January and Megan will work with the Heinzen and Hackstadt lab to arrange dates for that shutdown.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ None.

Other issues	▪ None

Next Meeting:

- Date: January 21, 2021

- Place: online via Skype for Business
- Time: 1:00 PM

RML Biosafety Committee Meeting
December 17, 2020
Biosafety Officer Report

1) Requests approved by BSO since last meeting:

a) ***Amend***

(1) None

2) ***New requests approved by committee via electronic review:***

a) *SOP#4-28-63 Rodent Transmission Caging Operation for Aerosol Exposure-Approved 12-7-2020*

3) ***New requests***

a) *Pathogen Registration Documents*

i) ***New***

(a) *None*

ii) ***Renew***

(a) *None*

iii) ***Amend***

(a) *None*

b) *Registration Documents for Recombinant Nucleic Acid Experiments*

i) ***New***

(i) None

ii) ***Renew***

(i) None

iii) ***Amend***

(i) None

c) *Inactivation Procedure Reviews*

i) *MCL Inactivation of Flaviviruses with RLT, AVL, and Trizol*

ii) *MCL inactivation of Filoviruses with PFA*

iii) *Hinnebusch inactivation of Y. pestis with methanol and PFA*

d) ***Standard Operating Procedures***

(a) ***SOP#4-28-64 Short PFA Fixation***

(a) *Add inactivation procedures*

(b) ***Hinnebusch BSL-3-Yp-1, will be added to*** (b)(6) ***SOP and Plague animal SOP***

(a) *Add inactivation procedures for methanol and PFA*

(b) *Annual Review, minor updates.*

RML Biosafety Committee Meeting
December 17, 2020
Biosafety Officer Report

4) ***Animal Study Protocols Review***

Title	*Associated PRD*	*Associated RD*	*Reviewer*
Does Borrelia burgdorferi infection modify gene expression in Ixodes scapularis nymphs feeding in different hosts	*20-227*	*N/A*	*R. Anderson*
Small Rodent Trapping in Mali	*N/A*	*N/A*	*M. Brose*

5) ***Biosafety Training Performed – Megan Brose, Rebecca Anderson,*** (b)(6)

Type of Training	*Number of Sessions*	*Number of Employees Trained*
BSL-3 Laboratory Biosafety	*2*	*3*
BSL-4 Laboratory Biosafety-Initial	*4*	*3*
BSL-4 Laboratory Biosafety-Refresher	*3*	*6*
Laboratory Biosafety Support Staff-Initial	*1*	*2*
Laboratory Biosafety Support Staff-Refresher	*3*	*38*
Select Agent Initial Training	*1*	*3*
Select Agent visitor/BSL-3 visitor	*0*	*0*
New Employee Training	*2*	*5*

6) ***Safety Audits and Inspections***

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

a) *Biological Incident Report:*
   i) *None*

7) ***Other Issues –***

a) *BMBL 6th Edition Released online. Paperback copies will be distributed to IBC members once they arrive at RML from NIH.*
b) *FOIA requests:*
   i) *Allison Young requested incident reports from RML, Bethesda and IRF Frederick dates 2018 to present. Request received July 2020 and documents submitted August 2020.*
   ii) *U.S. Right to Know requested IBC meeting minutes from 2003 to present. Request received in October 2020 and documents submitted December 2020.*

Agenda

RML Biosafety Committee Virtual Meeting
January 21, 2021

I. Old Business
   A. Draft minutes of December 17, 2020 meeting

II. New Business
   A. Committee Business
      1. Pathogen Registration Documents (4)
      2. Recombinant DNA Documents (7)
      3. SOP Updates:
         a. Draft SOP#4-28-15 Rodent Procedures in biocontainment
         b. Draft SOP#4-28-32 Removal of Specimens for Nucleic Acid Extraction
         c. Draft SOP#4-28-50 Operation of the Environmental Chamber

   B. BSO/Responsible Official report (Dr. Becky Anderson

   E. Occupational Safety & Health Manager report (Seth Cooley)

   F. IRF Biosafety Manager Report (Lt. Cmdr. Megan Brose)

   G. Associate Director Report (Dr. Marshall Bloom)

   H. Comments from around the room

Attachments:
1. Draft minutes of December 17, 2020 meeting (1 file)
2. Pathogen Registration Documents (4 files)
3. Recombinant DNA documents (7 files)
4. SOPs (3 files)
5. Meeting Agenda (1 file)

NEXT MEETING: February 18, 2021 via Skype

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 1/21/2021
Meeting Time: 1:00 PM **Adjourned:** 2:54 PM
Due to the COVID19 pandemic, this meeting was conducted online via Skype for Business

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Seth Cooley	☒	☐	Greg Saturday	☒	☐
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Alexandra Scranton	☐	☒
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Brian Vickrey	☐	☒
Alan Applebury	☐	☒	Nancy Hoe	☐	☒	Clayton Winkler	☒	☐
Chris Bosio	☒	☐	Erik Hoover	☐	☒			
Marshall Bloom (EO)	☐	☒	Clay Jarrett	☒	☐			
Megan Brose	☒	☐	Josh Kellar (EO)	☐	☒			
Larry Brouwer	☒	☐	Scott Kobayashi	☒	☐			
Carol Calderwood	☐	☒	Jamie Lovaglio	☒	☐			
Marcie Caldwell (EO)	☐	☒	Andrea Marzi	☒	☐			
Bruce Chesebro (EO)	☐	☒	Alida Merritt	☐	☒			

(P=present; A=absent)

Guests: (b)(6)

Minutes: Meeting minutes from 12/17/2020 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 12/17/2020** ▪ Bob Heinzen noted that in Item 5, the second bullet, "bloom" should be changed to "blood" Action: Meeting minutes for 12/17/2020 were unanimously approved.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amendment) ▪ Feldmann (LV) ▪ **PRD#17-143 Amend: Coronaviruses** ▪ Becky Anderson presented the risk assessment. The amendment from the Feldmann lab was to include SARS-CoV-2 isolates currently on-site as well as any isolates circulating or emerging within the worldwide population. The LV lab will maintain a list of the isolates obtained and their characteristics for reference for their staff. If there are any isolates determined to have a more severe impact on disease compared to the nCoV-WA1-2020, this will require an amendment to the PRD. Additionally, the Feldmann lab proposed animal studies focusing on the new variants of SARS-CoV-2. Specifically, (b)(6) of LV proposed to perform co-infections of two naturally occurring variants to evaluate the shedding and transmission efficiency between the variants. ▪ (b)(6) informed the committee that the variants are still the same virus and the variants only differ by a small number of nucleotides. He reviewed the characteristics of the current variants that are proposed for the animal study. The current variants, like the UK and the South Africa variant only differ from each other by 11 nucleotides. The committee discussed with (b)(6) the potential for recombination between the UK and the South African variant, but since they are so similar, it is unlikely that they will recombine. (b)(6) also stated that if the UK and South African variant did recombine, they would create a variant that is already circulating. The proposed studies are to look at phenotypes, they are not looking at genome changes or isolating virus. The committee extensively discussed the proposed studies, the potential risks and the potential for the proposed research to be dual use research. The committee determined that the following wording should be added to the recommendations section, "The co-infection studies described in the attached addendum are approved. If any new co-infection studies are proposed with significantly different isolates where there is potential for recombination, IBC approval is required prior to initiation of those studies." ▪ Animal studies with hamsters were proposed. ▪ Work with SARS-CoV-2 variants is approved at BSL-3/ABSL-3. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#17-143 Amend** with the following minor modifications: 1. Add to the recommendations section, "The co-infection studies described in the attached addendum are approved. If any new co-infection studies are proposed with significantly different isolates where there is potential for recombination, IBC approval is required prior to initiation of those studies."

Item 2:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Hinnebusch (LB) ▪ **PRD#21-66: *Yersinia pestis* (exempt)** ▪ Becky Anderson presented the risk assessment. This is a renewal for the Hinnebusch lab. There were no changes to the current PRD. The registration covers exempt strains of *Y. pestis* and animal work with mice. ▪ Animal studies with mice were proposed. ▪ Work with *Y. pestis* (exempt) is approved at BSL-2/ABSL-2. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Clay Jarrett, Chris Bosio abstained) **PRD#21-66** as written.
Item 3:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Hinnebusch (LB) ▪ **PRD#21-164: *Staphylococcus aureus*** ▪ Becky Anderson presented the risk assessment. This is another renewal for the Hinnebusch lab. There were no changes to the current PRD. The registration covers work with *Staphylococcus aureus* including methicillin sensitive strains. The proposed studies are to understand host cell responses to infection and how specific bacterial pathogens evade innate host defenses. ▪ No animal studies were submitted, reviewed, or approved. ▪ Work with *Staphylococcus aureus* is approved at BSL-2. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#21-164** as written.
Item 4:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Munster (LV) ▪ **PRD#21-177: Vaccinia Modified Copenhagen virus** ▪ Becky Anderson presented the risk assessment. This is a renewal for the Munster lab. There were no changes to the current PRD. The registration is for vaccinia virus strain Copenhagen. The Copenhagen virus is proposed to be used as a vector to express proteins of interest listed in the PRD. The ACIP Smallpox Vaccine Recommendations and NIH OMS indicate vaccination for personnel working with the Copenhagen virus, however, NIH OMS waived the requirement for vaccination if all work with Copenhagen virus is conducted in the BSL-4 lab. (b)(6) agreed to keep all stocks and samples in the BSL-4 so there is no vaccine requirement for this work. This information is included in the recommendations section of the PRD.

	▪ Animal studies with mice were proposed. ▪ Work with Copenhagen virus is approved at BSL-4/ABSL-4. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#21-177** as written.

Item 5:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Feldmann (LV) ▪ **RD#19-402 Amend**: Lentiviral vectors ▪ Reviewers: Clayton Winkler, Sue Priola ▪ **Summary:** Expression of viral proteins in target cells with lentiviral vector system ▪ Clayton Winkler summarized the RD amendment. The amendment to this RD is to add four different plasmids that are all commercially available. All the added plasmids are replication incompetent. Clayton Winkler had no concerns with the RD amendment. ▪ Sue Priola informed the committee that III-E-1 should be added to both the Prokaryote Host and Eukaryote Cell sections. Sue Priola also questioned if these were all part of the same system. This should be added to the amendment. ▪ No new animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#19-402 Amend** with the following minor modifications: 1. Add III-E-1 to both the Prokaryote Host and Eukaryote Cell sections. 2. Determine if the new plasmids are part of the same system. Add that information to the RD amendment. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a and III-E-1 of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a, III-D-3-a and III-E-1 of the NIH Guidelines.
Item 6:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Heinzen (LB) ▪ **RD#20-106 Amend**: Genetic Manipulation of *Coxiella burnetii* ▪ Reviewers: Clay Jarrett, Chris Bosio ▪ **Summary:** Determination of molecular mechanisms of intracellular survival of *C. burnetii* ▪ Clay Jarrett summarized the RD amendment. The Heinzen lab's RD is for the genetic manipulation of Coxiella. The amendment is to add SARS-CoV-2 spike protein so they can test it as a vaccine. They will use the same plasmids and antibiotic cassettes that were previously approved. Clay Jarrett questioned if this will be used with Phase I or Phase II of *C. burnetii*. Bob Heinzen stated that it will be used for both. This information should be added to the RD. ▪ Clay Jarrett also asked if this study would fall into dual use question 5 if it could alter the host range. Bob Heinzen stated that there is no chance for that to occur because the spike protein will not be expressed in the normal form. It will be in an inclusion in

	the cytoplasm in the organism and cannot be a ligand for a receptor. The committee agreed there was no dual use concern. ▪ Chris Bosio had no additional comments or concerns. ▪ No new animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Bob Heinzen abstained) **RD#20-106 Amend** with the following minor modifications: 1. Specify that both Phase I and Phase II will be used. Research using prokaryotic hosts is approved at BSL-2 or BSL-3 (depending on the bacteria used) under section III-D-1-a and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 or BSL-3 (depending on the bacteria used) under III-D-1-a of the NIH Guidelines.

Item 7:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Best (LV) ▪ **RD#20-457 Amend**: Pathogenesis of SARS-CoV-2 ▪ Reviewers: Andrea Marzi, Sue Priola ▪ **Summary:** Pathogenesis of SARS-CoV-2 ▪ Andrea Marzi summarized the RD amendment. Andrea Marzi informed the committee that the RD describes generating strains of the new isolates of SARS-CoV-2. Most of these isolates was described earlier in the IBC meeting with the Feldmann PRD. These isolates will be studied in cell culture or in the mouse model. Andrea Marzi suggested that this could be written a little broader to cover the newly arriving isolates. There are dual use questions marked yes, number 5 and B. These are appropriate and not considered dual use research of concern. ▪ Sue Priola stated that there should language added to the RD which matches that added to the PRD from the Feldmann lab. Clayton Winkler asked why they will use ORF6, could SARS-CoV-2 be more virulent when it is deleted? (b)(6) informed the committee that it's only known function is an interferon antagonist, so it is not expected to become more virulent. ▪ Sue Priola noted that the Best PRD for SARS-CoV-2 should be updated to include information regarding the isolates. ▪ No new animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#20-457 Amend** with the following minor modifications: 1. Add matching language from the Feldmann lab PRD. 2. Request the Best lab to update their PRD for the SARS-CoV-2 isolates Research using eukaryotic cells is approved at BSL-3 under III-D-1-b, III-D-2-a, and III-D-3-b of the NIH Guidelines.
Item 8:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Best (LV) ▪ **RD#21-448**: Vesicular Stomatitis Virus ▪ Reviewers: Sue Priola, Andrea Marzi ▪ **Summary:** Innate immune response assessment with VSV ▪ Sue Priola summarized the RD renewal. Sue Priola informed the committee that this was a renewal of the Best VSV renewal. There are no changes to the RD. The Best lab uses VSV as a tool to study the innate immune response. There were no concerns with

	the RD. ▪ Andrea Marzi had no additional comments or concerns. ▪ No new animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#21-448** as written. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a and III-D-2-a of the NIH Guidelines.

Item 9:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Hinnebusch (LB) ▪ **RD#21-321**: *Yersinia pseudotuberculosis* ▪ Reviewers: Bob Heinzen, Scott Kobayashi ▪ **Summary:** Evaluation of molecular mechanisms of transmission to fleas ▪ Bob Heinzen summarized the RD renewal. This RD is for genetic manipulation of *Y. pseudotuberculosis* to determine why there is less severe disease compared to *Y. pestis*. They will generate defined mutant strains, complement the mutant strains, generate recombinant proteins, and perform *in vitro* assays and infect fleas with the engineered strains. NIH Guidelines are appropriate and there are no dual use concerns. ▪ Sue Priola noted that in the Prokaryote Host section, nature of the gene sequence question, the section was missing *Y. psueotuberculosis*. ▪ No new animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Clay Jarrett and Chris Bosio abstained) **RD#21-321** with minor modifications: 1. Add *Y. pseudotuberculosis* to the Prokaryote Host section, nature of the gene sequence question. Research using prokaryotic hosts is approved at BSL-2 under section III-D-1-a and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a of the NIH Guidelines.
Item 10:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Hinnebusch (LB) ▪ **RD#21-322**: Retroviral vectors to introduce foreign DNA into mouse cells ▪ Reviewers: Scott Kobayashi, Bob Heinzen ▪ **Summary:** Retroviral vectors to introduce foreign DNA into mouse cells ▪ Scott Kobayashi summarized the RD renewal. Scott Kobayashi informed the committee that this is a renewal with no changes for the Hinnebusch lab. The RD describes using murine retroviral vectors to generate immortalized cell lines that can be differentiated into neutrophils and macrophages. ▪ Bob Heinzen questioned the use of the NIH Guidelines in the RD. The committee agreed that the Research Product section should have an N/A inserted. In both the Prokaryote and Eukaryote cell section, the headings for the NIH Guidelines sections should be removed. ▪ No new animal studies were submitted, reviewed, or approved.

	▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Clay Jarrett and Chris Bosio abstained) **RD#21-322** with minor modifications: 1. Update the NIH Guidelines sections. The Research Product section should have N/A. In both the Prokaryote Host and Eukaryote cell section, headings for the NIH Guidelines sections should be removed. Research using prokaryotic hosts is approved at BSL-2 under section II-A-3 of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under II-A-3 of the NIH Guidelines.

Item 11:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Munster (LV) ▪ **RD#21-441**: Baculovirus system ▪ Reviewers: Chris Bosio, Clay Jarrett ▪ **Summary:** Baculovirus expression system for viral proteins ▪ Chris Bosio summarized the RD renewal. This is a renewal with no new work proposed. The baculovirus expression system will be used to express viral proteins. This is a commercial system. They will purify the proteins for downstream use. There are ASPs attached for mice and rabbits for antibody generation. Chris Bosio asked if III-E-1 should be added. The committee agreed that it could be added to the Prokaryote Host section and the Eukaryote cell section. ▪ Clay Jarrett had no additional comments or concerns. ▪ Animal studies with mice and rabbits were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#21-441** with minor modifications: 1. Add III-E-1 to the Prokaryote Host section and the Eukaryote cell section. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a and III-E-1 of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-3-e, III-D-1-a, and III-E-1 of the NIH Guidelines.
Item 12:	**Standard Operating Procedure: SOP#4-28-16 Rodent Procedures in Level 4 Containment (Updated)** ▪ Becky Anderson summarized the SOP for the committee. The update is to combine multiple rodent SOPs into one SOP. This is an ongoing effort to make each animal SOP one document. With this approval, the following SOPs will be inactivated: SOP#4-28-41 and SOP#4-28-48. ▪ The committee discussed the following changes to the SOP: o In the Animal Husbandry section on page 2, third bullet, delete the entire sentence. o Page 2, 7th bullet, delete "mastomys" o Page 3 in A.1.b state that the clinical observation will be done according to the corresponding ASP. o Page 2 add language for the disinfection of gloves and tongs to the husbandry precautions section. o Page 3 verify the number of cages that can be dumped into one bag.

	▪ There were no additional comments or concerns with the updated procedures. Action: The committee unanimously approved the**: SOP#4-28-16 Rodent Procedures in Level 4 Containment (Updated)** with the following modifications: 1. In the Animal Husbandry section on page 2, third bullet, delete the entire sentence. 2. Page 2, 7th bullet, delete "mastomys" 3. Page 3 in A.1.b state that the clinical observation will be done according to the corresponding ASP. 4. Page 2 add language for the disinfection of gloves and tongs to the husbandry precautions section. 5. Page 3 verify the number of cages that can be dumped into one bag.
Item 13:	**Standard Operating Procedure: SOP#4-28-32 Removal of Specimens for Nucleic Acid Extraction (Updated)** ▪ Becky Anderson summarized the SOP for the committee. The update is to clarify procedures for handling select agent strains of Coronaviruses and Flaviviruses. There are no new inactivation procedures added, this is just rewording to ensure the process is as clear as possible. ▪ Sue Priola stated that "either" should be removed from q.1 on page 5. ▪ There were no additional comments or concerns with the updated procedures. Action: The committee unanimously approved the**: SOP#4-28-32 Removal of Specimens for Nucleic Acid Extraction (Updated)** with the following modifications: 1. Remove "either" from q.1 on page 5.
Item 14:	**Standard Operating Procedure: SOP#4-28-50 Operation of the Environmental Chamber (Update)** ▪ Becky Anderson summarized the SOP for the committee. The SOP was updated to add procedures for the environmental chamber without animals. The Munster lab plans to use their Goldberg drum inside the environmental chamber so they can test a wider range of temperature and humidity. ▪ Jamie Lovaglio pointed out the following corrections: a. Page 4, Manipulation procedures of non-animal studies, g. should have "prior to leaving the procedure corridor" deleted. b. Page 2, Feed and water section, b. Should state that "Feed and water level. . . " c. Page 2, there should be a picture included of the ferret caging. d. Page 3, refer to the species specific SOP for escaped animal procedures and

	cleaning procedures. e. Section 4 page 1, copy animal information from SOP#4-28-16. ▪ There were no additional comments or concerns with the updated procedures. Action: The committee unanimously approved **SOP#4-28-50 Operation of the Environmental Chamber (Update)** with the following modifications: 1. Page 4, Manipulation procedures of non-animal studies, g. should have "prior to leaving the procedure corridor" deleted. 2. Page 2, Feed and water section, b. Should state that "Feed and water level. . . " 3. Page 2, there should be a picture included of the ferret caging. 4. Page 3, refer to the species specific SOP for escaped animal procedures and cleaning procedures. 5. Section 4 page 1, copy animal information from SOP#4-28-16.
Report:	**Biosafety Officer (BSO) Report/Becky Anderson** ▪ Becky Anderson reviewed the BSO Report
Report:	**Occupational Safety and Health Manager Report/Seth Cooley** ▪ Nothing to report.
Report	**IRF Biosafety Manager/Responsible Official Report/Megan Brose** ▪ No select agent issues to report – just a reminder that we are still on schedule for select agent renewal inspection during the week of March 15. We haven't received any additional details. ▪ Annual shutdowns are coming up: ○ BSL-3 (b)(6); (b)(3):42 U.S.C. 262a(h) (Public Heatlh Security and lab starts next week (Jan 25-29) ○ BSL-3 lab is Feb 8-12 ○ BSL-4 lab is Feb 23 – Mar 11 ○ BSL-3 lab is Mar 15 – 24 ○ BSL-4 lab and animal suites are Mar 23 – Apr 8 ▪ COVID Vaccine Planning ○ Not a lot of new information from what Marshall sent out to staff on Tuesday ○ Marshall organized a Town Hall meeting to review all of that next Tuesday ○ We have to get our vaccines from the state, as NIH didn't get a direct allotment. ○ We have been successfully enrolled as a COVID vaccine provider with state ○ Just waiting for them to send us a shipment and we have no idea when that will be ○ We are planning our clinic setup here in the seminar A room in the meantime and will be ready to administer it whenever it is that we do get a shipment
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ None.

Other issues	▪ None

Next Meeting:

- Date: February 18, 2021
- Place: online via Skype for Business
- Time: 1:00 PM

RML Biosafety Committee Meeting
January 21, 2021
Biosafety Officer Report

1) Requests approved by BSO since last meeting:

a) ***Amend***

(1) None

2) ***New requests approved by committee via electronic review:***

a) *None*

3) ***New requests***

a) *Pathogen Registration Documents*

i) ***New***

(a) *None*

ii) ***Renew***

(a) *Hinnebusch (LB)*

(i) PRD 21-66

(b) *Hinnebusch (LB)*

(a) *PRD 21-164*

(c) *Munster (LV)*

(a) *PRD 21-177*

iii) ***Amend***

(a) *Feldmann (LV)*

(a) *PRD 17-143*

b) *Registration Documents for Recombinant Nucleic Acid Experiments*

i) ***New***

(a) *None*

ii) ***Renew***

(a) *Best (LV)*

(a) *RD 21-488*

(b) *Hinnebusch (LB)*

(a)

iii) ***Amend***

(a) *Feldmann (LV)*

(a) *RD 19-402*

(b) *Heinzen (LB)*

(a) *RD 20-106*

(c) *Best (LV)*

(a) *RD 20-457*

(d) *Hinnebusch (LB)*

(a) *RD 21-321*

(e) *Hinnebusch (LB)*

(a) *RD 21-322*

(f) *Munster (LV)*

(a) *RD 21-441*

c) *Inactivation Procedure Reviews*

i) *None*

d) ***Standard Operating Procedures***

(a) ***SOP#4-28-16 Rodent Procedures in biocontainment***

(a) *Combine SOP#4-28-16, 4-28-41, 4-28-48*

(b) ***SOP#4-28-32 Removal of Specimens for Nucleic Acid Extraction***

(a) *Clarify language in table for Flaviviruses and Coronaviruses*

(c) ***SOP#4-28-50 Operation of the Environmental Chamber***

(a) *Add language to work to perform wok with non-animal studies in the environmental chamber, such as Goldberg drum*

4) ***Animal Study Protocols Review***

Title	***Associated PRD***	***Associated RD***	***Reviewer***
Investigating the Mastomys natalensis as a possible disease model, reservoir and amplifying host of SARS-CoV-2	*17-143*	*N/A*	*R. Anderson*
Assessment of UV-C as a countermeasure for aerosol transmission of SARS-CoV-2	*17-143*	*N/A*	*R. Anderson*
Determine the role of Ebola virus matrix protein VP40 as a virulence factor in inflammatory activation and pathogenesis	*18-90*	*14-407*	*R. Anderson*
Defining Time to Immunity of the GMP-Produced VSV-Nipah Vaccine in African Green Monkeys	*18-91*	*20-404*	*M. Brose*
Assessing disease kinetics and severity of mutated SARS-CoV-2 variants in the African green monkey	*17-143*	*N/A*	*R. Anderson*
Does prior antigenic immunity impact the protective efficacy of VSV based vaccines in mice.	*18-82*	*20-404*	*R. Anderson*
Efficacy testing of new phenol based disinfectants against infectious prions; bioassays in mice.	*16-190 20-166*	*N/A*	*M. Brose*

RML Biosafety Committee Meeting
January 21, 2021
Biosafety Officer Report

5) ***Biosafety Training Performed – Megan Brose, Rebecca Anderson,*** (b)(6)

Type of Training	***Number of Sessions***	***Number of Employees Trained***
BSL-3 Laboratory Biosafety	*1*	*2*
BSL-4 Laboratory Biosafety-Initial	*2*	*2*
BSL-4 Laboratory Biosafety-Refresher	*7*	*7*
Laboratory Biosafety Support Staff-Initial	*1*	*2*
Laboratory Biosafety Support Staff-Refresher	*0*	*0*
Select Agent Initial Training	*1*	*3*
Select Agent visitor/BSL-3 visitor	*1*	*2*
New Employee Training	*2*	*3*

6) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
a) *Biological Incident Report:*
   i) *None*

7) ***Other Issues –***
   i) *None*

Agenda

RML Biosafety Committee Virtual Meeting
February 18, 2021

I. Old Business
   A. Draft minutes of January 21, 2021 meeting

II. New Business
   A. Committee Business
      1. Pathogen Registration Documents (1)
      2. Recombinant DNA Documents (1)
      3. Inactivation Validation Study
         a. MCL: PFA inactivation of high titer CoV infected tissue
      4. SOP Updates:
         a. Draft SOP#4-28-64: Removal of high titer CoV tissues following short fixation for High Content Imaging
         b. Draft SOP#4-28-53: Husbandry and Manipulation of Rabbits combined SOP
         c. Draft SOP#4-28-17: NHP Procedures in BSL-4 combined SOP

   B. BSO/Responsible Official report (Dr. Becky Anderson)

   E. Occupational Safety & Health Manager report (Seth Cooley)

   F. IRF Biosafety Manager Report (Lt. Cmdr. Megan Brose)

   G. Associate Director Report (Dr. Marshall Bloom)

   H. Comments from around the room

Attachments:
1. Draft minutes of January 21, 2021 meeting (1 file)
2. Pathogen Registration Documents (1 file)
3. Recombinant DNA documents (1 file)
4. Inactivation validation study (1 file)
5. SOPs (3 files)
6. Meeting Agenda (1 file)

NEXT MEETING: March 18, 2021 via Skype

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 2/18/2021
Meeting Time: 1:00 PM **Adjourned:** 1:20 PM
Due to the COVID19 pandemic, this meeting was conducted online via Skype for Business

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Seth Cooley	☒	☐	Greg Saturday	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Alexandra Scranton	☐	☒
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Brian Vickrey	☐	☒
Alan Applebury	☐	☒	Nancy Hoe	☐	☒	Clayton Winkler	☒	☐
Chris Bosio	☒	☐	Erik Hoover	☒	☐			
Marshall Bloom (EO)	☐	☒	Clay Jarrett	☐	☒			
Megan Brose	☐	☒	Josh Kellar (EO)	☐	☒			
Larry Brouwer	☐	☒	Scott Kobayashi	☒	☐			
Carol Calderwood	☐	☒	Jamie Lovaglio	☒	☐			
Marcie Caldwell (EO)	☐	☒	Andrea Marzi	☒	☐			
Bruce Chesebro (EO)	☐	☒	Alida Merritt	☒	☐			

(P=present; A=absent)

Guests: (b)(6)
(b)(6)

Minutes: Meeting minutes from 1/21/2021 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 1/21/2021** ▪ Bob Heinzen pointed out a minor typo in Item 6. Action: Meeting minutes for 1/21/2021 were unanimously approved.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New) ▪ Marzi (LV) ▪ **PRD#21-231: Flaviviruses (Zika, Spondweni, Kedougou, Bagaza virus)** ▪ Becky Anderson presented the risk assessment. The PRD is to elucidate mechanisms of mosquito-borne Flavivirus pathogenesis for the purpose of evaluating medical counter measures. This PRD covers four Flaviviruses: ▪ Zika virus- the most common symptoms of Zika virus infection are fever, rash, headache, joint pain, and conjunctivitis. Symptoms are usually mild lasting for several days to a week. Zika virus usually remains in the blood of an infected person for about a week but it can be found longer in some people. Zika virus is transmitted by mosquitos. Zika virus infection in women has been associated with microcephaly, a birth defect in which a developing baby's brain fails to grow to its usual size. The Zika outbreak was also associated with an increase in Guillian-Barre syndrome. ▪ Spondweni virus-infection is characterized by fever, chills, headache, malaise, nausea, nose bleeds, and in one case rash. Transmitted by mosquitos. ▪ Bagaza virus- (also called Israel turkey meningoencephalomyeltis virus ITV)- Serologic evidence suggests that the virus may infect humans but its pathogenicity in humans is unclear. This virus is better known for causing high mortality in wild birds (India, Israel, and S. Africa). ▪ Kedougou virus-not much is known about human infections with Kedougou. There is one documented case in Africa, but no details available. It is classified as a member of the Dengue virus group. ▪ Animal studies with NHPs, mice, hamsters, and guinea pigs were proposed. ▪ Work with the listed Flaviviruses is approved at BSL-2/ABSL-2 with the following precautions for Zika virus: Care should be taken to minimize worker exposure to aerosols, such as working in a certified Class II BSC at all times and using gasketed bucket covers when centrifuging infectious material. Gasketed bucket covers or sealed rotors must only be loaded/unloaded in a BSC. It is recommended if possible that work with Zika virus be performed in a small or dedicated lab away from the main lab areas. Women of childbearing years must be advised of the risks of working with this agent, please consult with OMS. Animal studies with rodents will be performed in the Human Pathogen Wing of (b)(6) or in the BSL-4. All manipulations must be performed in a BSC. A sign at the suite door will indicate when Zika procedures are in progress. PPE includes: Lab coat, gloves, surgical mask. Husbandry practices will include spraying used cages with disinfectant, autoclaving, and then dumping the used bedding or if disposable caging is used, cages will be bagged and then incinerated. Hazard awareness training must be provided to all individuals listed on the PRD, animal care staff, and staff working in shared lab/animal spaces. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.

	Action: The committee approved (Andrea Marzi abstained) **PRD#21-231** as written.

Item 2:	Registration Documents for Recombinant DNA Experiments (New) ▪ Heinzen (LB) ▪ **RD#21-109**: Lentiviral and Sleeping Beauty transposon systems ▪ Reviewers: Sue Priola, Andrea Marzi ▪ **Summary:** Generation of stable transgenic cells lines ▪ Sue Priola summarized the RD. The RD is straightforward and describes establishing a stable transgenic cell line so the Heinzen lab can use it to determine protein function. The Heinen lab will use either a lentiviral system or the Sleeping Beauty transposon system. Once the stable transgenic cell lines expressing *C. burnetti* or mammalian cell proteins are generated, they will be used to define *C. burnetii* type IV effector functions and the mammalian proteins that impact *C. burnetii* infection. The Sleeping Beauty system is a 2-plasmid system. The proposed lentiviral system is a commercially available system and is safe. The listed NIH Guidelines are appropriate and there were no dual use issues. ▪ Andrea Marzi noted a few typos in the text that need to be corrected. She also noted that the duration of the project should be changed to "indefinite" so there is no time limit on the study. Andrea Marzi also informed the committee that the research product section did not include a description of the Sleeping Beauty system. Bob Heinzen will write a few more sentences to add to that section. ▪ No new animal studies were submitted, reviewed, or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Bob Heinzen abstained) **RD#21-109** with the following minor modifications: 1. Fix minor typos. 2. Change the duration of the project from 5 years to indefinite. 3. Add detail to the Research Product section for the Sleeping Beauty System. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-3-a of the NIH Guidelines.
Item 3:	**Full Committee Review of MCL Inactivation Data with PFA on Coronaviruses** ▪ Sue Priola informed the committee that there is inactivation data to review for the MCL. Included in this month's submission is testing data for inactivation of Coronaviruses. The MCL tested the ability of 1% and 2% PFA to inactivate SARS-CoV-2 which was used as a surrogate for Coronaviruses. This is a repeat of previous inactivation testing so they could increase the approval viral titer for inactivation. ▪ Sue Priola summarized the testing results for the inactivation of cells. Sue Priola confirmed with the committee that the samples and titers tested were appropriate, all necessary controls were included and that the procedures matched what is listed in

	the SOP. ▪ There were no additional comments or concerns with the inactivation data. Action: The committee unanimously approved the inactivation data using of 2% PFA for 72 hours to inactivate Coronaviruses as written.
Item 4:	**Standard Operating Procedure: SOP#4-28-16 Removal of Tissues Following Short Fixation for High Content Imaging (Updated)** ▪ Sue Priola summarized the changes to the SOP for the committee. The update is to the table of approved inactivation methods. The only change is the approved titer for Coronavirus infected mouse lungs. ▪ There were no additional comments or concerns with the updated procedures. Action: The committee unanimously approved the: **SOP#4-28-16 Removal of Tissues Following Short Fixation for High Content Imaging (Updated)** as written.
Report:	**Biosafety Officer (BSO) Report/Becky Anderson** ▪ Becky Anderson reviewed the BSO Report ▪ Becky Anderson reminded the committee that there is a CDC DSAT Inspection scheduled for the week of March 15th, the same week as the IBC meeting. We will cancel the March IBC meeting and resume in April.
Report:	**Occupational Safety and Health Manager Report/Seth Cooley** ▪ Nothing to report.
Report	**IRF Biosafety Manager/Responsible Official Report/Megan Brose** ▪ Not present
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ None.

Other issues	▪ None

Next Meeting:

- Date: April 15, 2021
- Place: online via Skype for Business
- Time: 1:00 PM

RML Biosafety Committee Meeting
April 15, 2021
Biosafety Officer Report

1) Requests approved by BSO since last meeting:

a) ***Amend***

(1) Feldmann RD 17-143

(a) Add IT and IV route of administration for mink

2) ***New requests approved by committee via electronic review:***

a) *Bloom PRD 20-224 Amend*

i) *Add strains for Coronavirus*

b) *Draft SARS-CoV-2_Bosio SOP for Pulse Oximeter-New SOP*

c) *Draft 4-28-38 Ferret and Mink Procedures in Biocontainment-updated for mink procedures*

3) ***New requests***

a) *Pathogen Registration Documents*

i) ***New***

(a) *None*

ii) ***Renew***

(a) *Bosio (LB)*

(i) PRD 21-156

(b) *Bosio (LB)*

(i) PRD 21-179

(c) *Bosio (LB)*

(i) PRD 21-183

(d) *De Leo (LB)*

(i) PRD 21-180

(e) *Hinnebusch (LB)*

(i) PRD 21-174

(f) *Priola (LPVD)*

(i) PRD 21-178

iii) ***Amend***

(a) *None*

b) *Registration Documents for Recombinant Nucleic Acid Experiments*

i) ***New***

(a) *None*

ii) ***Renew***

(a) *Best (LV)*

(i) RD 21-449

(b) *De Leo (LB)*

(i) RD 21-313

iii) ***Amend***

(a) *Feldmann (LV)*

(i) RD 17-431

(b) *Martens (RTB)*

(i) RD 19-550

c) *Inactivation Procedure Reviews*

i) *MCL formalin inactivation of Coronavirus*

(a) *Test large tissue type*

d) ***Standard Operating Procedures***

(a) SOP#4-28-33 Removal of Specimens for Fluorescence, Immunofluorescence, Histopathology, Immunohistopathology, and Flow Cytometry
(a) *Add new tissue type to list of approved inactivation procedures*
(b) *BSL-3* (b)(6) *Tick Biosafety Plan*

4) ***Animal Study Protocols Review***

Title	***Associated PRD***	***Associated RD***	***Reviewer***
Efficacy of current vaccines and modifications to current vaccines to protect against divergent strains of SARS-CoV-2 in the hamster model	*17-143*	*17-410*	*M. Brose*
Vaccine potential of Coxiella burnetii Dugway strains in Guinea pigs	*20-43* *18-70*	*20-106*	(b)(6);
Generation of prion infected brain material from various mouse and prion strains for experimental use	*18-51* *16-191*	*12-211*	*R. Anderson*
Immune responses to VSV-LASV vaccination in CD-1 mice	*18-82*	*20-404*	(b)(6); (b)(3):42
Training in the use of the intravital microscope using mice	*N/A*	*N/A*	*R. Anderson*
Continued evaluation of a DNA vaccine for CCHFV in cynomolgus macaques	*18-92*	*17-431*	*M. Brose*
Evaluation of a PPMO Inhibitor of Lassa Virus Infection and Disease in a Guinea pig Model	*18-94*	*N/A*	*R. Anderson*

RML Biosafety Committee Meeting
April 15, 2021
Biosafety Officer Report

5) ***Biosafety Training Performed – Megan Brose, Rebecca Anderson,*** (b)(6)

Type of Training	***Number of Sessions***	***Number of Employees Trained***
BSL-3 Laboratory Biosafety	*2*	*4*
BSL-4 Laboratory Biosafety-Initial	*12*	*5*
BSL-4 Laboratory Biosafety-Refresher	*1*	*1*
Laboratory Biosafety Support Staff-Initial	*N/A*	*N/A*
Laboratory Biosafety Support Staff-Refresher	*N/A*	*N/A*
Select Agent Initial Training	*1*	*2*
Select Agent visitor/BSL-3 /BSL-4 visitor	*3*	*5*
New Employee Training	*2*	*5*

6) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
a) *Biological Incident Report:*
   i) *None*

7) ***Other Issues –***
   i) *None*

Agenda

RML Biosafety Committee Virtual Meeting
April 15, 2021

I. Old Business
   A. Draft minutes of February 18, 2021 meeting

II. New Business
   A. Committee Business
      1. Pathogen Registration Documents (6)
      2. Recombinant DNA Documents (4)
      3. Inactivation Validation Study
         a. MCL inactivation of coronavirus infected nasal tissue
      4. SOPs:
         a. SOP#4-28-33 Removal of Specimens for Fluorescence, Immunofluorescence, Histopathology, Immunohistopathology, and Flow Cytometry
         b. Draft BSL-3 (b)(6) Tick Biosafety Plan

   B. BSO/Responsible Official report (Dr. Becky Anderson)

   E. Occupational Safety & Health Manager report (Seth Cooley)

   F. IRF Biosafety Manager Report (Lt. Cmdr. Megan Brose)

   G. Associate Director Report (Dr. Marshall Bloom)

   H. Comments from around the room

Attachments:
1. Draft minutes of February 18, 2021meeting (1 file)
2. Pathogen Registration Documents (6 files)
3. Recombinant DNA documents (4 files)
4. Inactivation validation study (1 file)
5. SOPs (2 files)
6. Meeting Agenda (1 file)

NEXT MEETING: May 20, 2021 via Skype

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 4/15/2021
Meeting Time: 1:00 PM **Adjourned:** 2:08 PM
Due to the COVID19 pandemic, this meeting was conducted online via Skype for Business

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Seth Cooley	☒	☐	Greg Saturday	☒	☐
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Alexandra Scranton	☐	☒
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Brian Vickrey	☐	☒
Alan Applebury	☐	☒	Nancy Hoe	☐	☒	Clayton Winkler	☒	☐
Chris Bosio	☒	☐	Erik Hoover	☒	☐			
Marshall Bloom (EO)	☐	☒	Clay Jarrett	☒	☐			
Megan Brose	☒	☐	Josh Kellar (EO)	☐	☒			
Larry Brouwer	☐	☒	Scott Kobayashi	☒	☐			
Carol Calderwood	☐	☒	Jamie Lovaglio	☒	☐			
Marcie Caldwell (EO)	☒	☒	Andrea Marzi	☒	☐			
Bruce Chesebro (EO)	☐	☒	Alida Merritt	☒	☐			

(P=present; A=absent)

Guests: (b)(6)
(b)(6)

Minutes: Meeting minutes from 2/18/2021 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 2/18/2021** Action: Meeting minutes for 2/18/2021 were unanimously approved.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Bosio (LB) ▪ **PRD#21-156: Lymphocytic choriomeningitis virus (LCMV)** ▪ Becky Anderson presented the risk assessment. This is a renewal for the Bosio lab. There were no changes to the current PRD. The registration covers work with LCMV and animal work with mice. ▪ Animal studies with mice were proposed.

	▪ Work with LCMV is approved at BSL-2/ABSL-2 with the following precautions: ○ All work with infectious material is conducted in a biosafety cabinet, centrifugation of infectious materials must be carried out in sealed safety cups or removable rotors that can be loaded and unloaded in a biosafety cabinet. ○ ABSL-2 with additional practices: LCMV will be transported from the lab to the vivarium in a sealed primary container that is placed in a leak proof secondary container. Mice are to be housed in micro-isolator caging. All procedures involving the administration of LCMV to mice must be conducted in a Class II BSC in the procedure room. Minimum PPE requirement when handling animals exposed to LCMV: mucous membrane protection (surgical mask and eye protection), double gloves. **Any additional significant aerosol generating procedures will require the use of N95 respirators. ○ All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 375-9600. Women who are pregnant or are thinking of becoming pregnant are encouraged to notify the Laboratory Supervisor and the RML OMS Nurse. This is in order to assure that they are aware of any potential risks to themselves or the fetus and to determine if any additional risk reduction measures should be taken. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Chris Bosio abstained) **PRD#21-156** as written.
Item 2:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Bosio (LB) ▪ **PRD#21-179: Pichinde virus** ▪ (b)(6) presented the risk assessment. This is a renewal for the Bosio lab. There were no changes to the current PRD. The registration covers work with Pichinde virus and animal work with mice. ▪ Animal studies with mice were proposed. ▪ Work with Pichinde virus is approved at BSL-2/ABSL-2. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Chris Bosio abstained) **PRD#21-179** as written.
Item 3:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Bosio (LB)

	▪ **PRD#21-183: West Nile virus** ▪ (b)(6) presented the risk assessment. This is a renewal for the Bosio lab. There were no changes to the current PRD. The registration covers work with West Nile virus and animal work with mice. ▪ Animal studies with mice were proposed. ▪ Work with West Nile virus is approved at BSL-3/ABSL-3. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Chris Bosio abstained) **PRD#21-183** as written.
Item 4:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ De Leo (LB) ▪ **PRD#21-180: *Klebsiella pneumoniae*** ▪ Becky Anderson presented the risk assessment. This is a renewal for the De Leo lab. There were no changes to the current PRD. The registration covers work with *Klebsiella pneumoniae* and animal work with mice and NHP. ▪ Sue Priola noted that "amendment" is in the PRD in a few sections from copying/pasting from a previous amendment into the PRD. The word "amendment" should be deleted. ▪ Animal studies with mice and NHP were proposed. ▪ Work with *Klebsiella pneumoniae* is approved at BSL-2/ABSL-2 and immunocompromised individuals must be warned of the risks of working with *Klebsiella pneumoniae*. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Scott Kobayashi abstained) **PRD#21-180** with the following modifications: 1. Remove "amendment" wording in PRD in multiple sections.
Item 5:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Hinnebusch (LB) ▪ **PRD#21-174: Diphtheria toxin** ▪ Becky Anderson presented the risk assessment. This is a renewal for the Hinnebusch lab. There were no changes to the current PRD. The registration covers work with Diphtheria toxin and animal work with mice. ▪ Animal studies with mice were proposed. ▪ Work with Diphtheria toxin is approved at BSL-2/ABSL-2. The following additional precautions are included in the recommendations section: Preparative work with the toxin should be done in a ducted BSC or chemical fume hood at BSL-2 with

	proper PPE (lab coat/gloves). Refer to the BMBL Appendix I for more details on toxins. A recent DTP vaccination is recommended. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Clay Jarrett and Chris Bosio abstained) **PRD#21-174** as written.
Item 6:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Priola (LPVD) ▪ **PRD#21-178: Bovine spongiform encephalopathy (BSE)** ▪ Becky Anderson presented the risk assessment. This is a renewal for the Priola lab. There were no changes to the current PRD. The registration covers work with BSE. ▪ No animal studies were submitted, reviewed or approved. ▪ Work with BSE is approved at BSL-2. The following precautions were also added to the PRD: o The lab is a restricted access lab, gown and gloves are required and a face mask should be worn, use of a respirator is optional. o (b)(6) houses the mass spec where samples containing BSE will be analyzed. These samples will be prepared in (b)(6) and placed in vials with a rubber stopper. Sample must be transported between labs in a durable leak proof container. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Sue Priola abstained) **PRD#21-178** as written.
Item 7:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Feldmann (LV) ▪ **RD#17-431 Amend: Molecular characterization of viral proteins of pathogenic RNA viruses** ▪ Reviewers: Sue Priola, Chris Bosio ▪ Summary: Amendment to add non-human primate studies. ▪ Sue Priola summarized the RD. The RD describes methods for characterizing the roles that viral proteins play in the viral replication cycle and pathogenesis using both in vivo and in vitro systems. The amendment is to add animal studies with non-human primates. ▪ Chris Bosio had no additional comments or concerns. ▪ Animal studies with NHP were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal.

	Action: The committee unanimously approved **RD#17-431 Amend** as written. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-2-a and III-E-1 of the NIH Guidelines
Item 8:	Registration Documents for Recombinant DNA Experiments (Amendment) ▪ Martens (RTB) ▪ **RD#19-550: *Roseomonas mucosa* RNA-Seq of strains carrying wild-type or knockout Hybrid Histidine Kinase Gene** ▪ Reviewers: Scott Kobayashi, Clay Jarrett ▪ Summary: ▪ Scott Kobayashi summarized the RD. The original RD described procedures to knock out genes in *Roseomonas mucosa*, a gram-negative skin microbiota. They previously did targeted deletions for their studies. In the amendment they are adding molecular work for screening purposes where they will use the Himar system and suicide plasmids. The amendment includes all the appropriate information, the proposed antibiotics are included and there are no changes to the dual use questions. ▪ Clay Jarrett questioned if we are concerned about the use of gentamycin. (b)(6) stated that the wrong map was included, there will not be any gentamycin resistance in these studies. ▪ Andrea Marzi stated that the wording in the amendment should be updated to state that the sequences will be cloned into the plasmids that are attached. ▪ No new animal studies were submitted, reviewed or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#19-550** with minor modifications: 1. Update the amendment with correct vector maps. 2. Clarify that sequences will be cloned into plasmids that are attached to the RD. Research using prokaryotic hosts is approved at BSL-2 under section III-E of the NIH Guidelines.
Item 9:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Best (LV) ▪ **RD#21-449: Reverse genetics of Zika virus** ▪ Reviewers: Andrea Marzi, Sue Priola ▪ Summary: Reverse genetics system for Zika virus ▪ Andrea Marzi summarized the RD. This RD renewal describes the development of a reverse genetics system for Zika virus and other Flaviviruses. There are no changes to

	this RD renewal. There is a reference to the Zika virus PRD and the number should be updated. Also, the Research Product section should also have III-D-1-a added. ▪ Sue Priola questioned the percent of the source genome number listed. It currently says 100% but should state a range. ▪ No animal studies were submitted, reviewed or approved. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#21-449** with minor modifications: 1. Update the PRD number for Zika virus. 2. In the Prokaryote Host section, update the percent source genome from 100% to a range. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-3-a of the NIH Guidelines.
Item 10:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ De Leo (LB) ▪ **RD#21-313: Understanding Pathogen-PMN Interactions** ▪ Reviewers: Bob Heinzen, Chris Bosio ▪ Summary: Elucidating mechanisms of bacterial pathogenesis ▪ Bob Heinzen summarized the RD. This is a renewal for the de Leo lab and there are no changes to the registration. They will purify acceptable amounts of toxin, they have summarized the vectors and antibiotics, all are appropriate. The NIH Guidelines listed are appropriate and there are no dual use issues. ▪ Sue Priola questioned the antibiotics for the usage of tetracycline and whether that was used for treatment clinically. Scott Kobayashi stated that this was previously reviewed by (b) (6) and he determined that tetracycline was not a frontline treatment. Scott also stated that he needed to double check some of the vectors that are attached and verify the antibiotics used. ▪ Chris Bosio had no additional comments or concerns. ▪ Animal studies with rabbits and mice were proposed. ▪ The committee discussed the dual-use potential of these experiments as described above. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#21-313** with minor modifications: 1. Verify the attached vectors and antibiotic usage. Research using prokaryotic hosts is approved at BSL-2 under section III-D-1-a and III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under III-D-1-a of the NIH Guidelines.

Item 11:	**Full Committee Review of MCL Inactivation of Coronavirus infected NHP nasal tissue** ▪ Sue Priola informed the committee that there is inactivation data to review for the MCL. Included in this month's submission is testing data for inactivation of Coronaviruses. The MCL tested the ability of 10% formalin to inactivate SARS-CoV-2 in nasal and bone structure of the face and skull of non-human primates (SARS-CoV-2 was used as a surrogate for Coronaviruses). ▪ Sue Priola summarized the testing results for the inactivation of tissues and bones. Sue Priola confirmed with the committee that the samples and titers tested were appropriate, all necessary controls were included and that the procedures matched what is listed in the SOP. ▪ There were no additional comments or concerns with the inactivation data. Action: The committee unanimously approved the inactivation data of Coronavirus infected NHP nasal tissue as written.
Item 12:	**Standard Operating Procedure: SOP#4-28-33 Removal of Specimens for Fluorescence, Immunofluorescence, Histopathology, Immunohistopathology, and Flow Cytometry (Update)** ▪ Sue Priola summarized the SOP for the committee. The updates are to include the inactivation procedures that the were submitted. ▪ Sue Priola questioned the titers listed in the validation testing and the SOP. She requested that they be updated to match, whichever numbers are the correct ones. Action: The committee unanimously approved the: **SOP#4-28-33 Removal of Specimens for Fluorescence, Immunofluorescence, Histopathology, Immunohistopathology, and Flow Cytometry (Updated)** as written.
Item 13:	**Standard Operating Procedure: Draft BSL-3 (b)(6) Tick Biosafety Plan (NEW)** ▪ Becky Anderson summarized the new BSL-3 tick biosafety plan. This plan is for new work in the Bloom lab so they can start studies with ticks and Powassan virus. ▪ Becky Anderson informed the committee that biosafety would do a walk thru of the space prior to the new studies being started to ensure the space is appropriately set up. ▪ Becky noted that a few of (b)(6) comments had not been sent to the Bloom lab to be addressed so those still need to be followed up on. ▪ Sue Priola asked if page numbers could be added. ▪ There were no additional comments or concerns. Action: The committee unanimously approved the: **Draft BSL-3 (b)(6) Tick Biosafety Plan (NEW)** with the following minor modifications: 1. Address the doffing of two pairs of gloves with the outer pair taped to gown. 2. Add page numbers.

Report:	**Biosafety Officer (BSO) Report/Becky Anderson** ▪ Becky Anderson reviewed the BSO Report.

Report:	**Occupational Safety and Health Manager Report/Seth Cooley** ▪ Nothing to report.
Report	**IRF Biosafety Manager/Responsible Official Report/Megan Brose** ▪ Informed the committee that the Select Agent inspection is schedule for April 26 thru May 7. The first week will be a remote review of the documents by the inspectors and the second week will include onsite walk thru of lab and animal spaces. ▪ BSL-4 (b)(6); (b)(3):42 U.S.C. 262a(h) shutdown is almost complete. ▪ BSL-3 annual shutdown is complete. ▪ RML vaccine clinics for RML staff are complete. Anyone that was not covered by the vaccine clinic can now get vaccine at MDMH.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present.
Around the room	▪ None
Other issues	▪ None

Next Meeting:

- Date: May 20, 2021
- Place: online via Skype for Business
- Time: 1:00 PM

RML Biosafety Committee Meeting
April 15, 2021
Biosafety Officer Report

1) Requests approved by BSO since last meeting:

a) ***Amend***

(1) Feldmann RD 17-143

(a) Add IT and IV route of administration for mink

2) ***New requests approved by committee via electronic review:***

a) *Bloom PRD 20-224 Amend*

i) *Add strains for Coronavirus*

b) *Draft SARS-CoV-2_Bosio SOP for Pulse Oximeter-New SOP*

c) *Draft 4-28-38 Ferret and Mink Procedures in Biocontainment-updated for mink procedures*

3) ***New requests***

a) *Pathogen Registration Documents*

i) ***New***

(a) *None*

ii) ***Renew***

(a) *Bosio (LB)*

(i) PRD 21-156

(b) *Bosio (LB)*

(i) PRD 21-179

(c) *Bosio (LB)*

(i) PRD 21-183

(d) *De Leo (LB)*

(i) PRD 21-180

(e) *Hinnebusch (LB)*

(i) PRD 21-174

(f) *Priola (LPVD)*

(i) PRD 21-178

iii) ***Amend***

(a) *None*

b) *Registration Documents for Recombinant Nucleic Acid Experiments*

i) ***New***

(a) *None*

ii) ***Renew***

(a) *Best (LV)*

(i) RD 21-449

(b) *De Leo (LB)*

(i) RD 21-313

iii) ***Amend***

(a) *Feldmann (LV)*

(i) RD 17-431

(b) *Martens (RTB)*

(i) RD 19-550

c) *Inactivation Procedure Reviews*

i) *MCL formalin inactivation of Coronavirus*

(a) *Test large tissue type*

d) ***Standard Operating Procedures***

(a) SOP#4-28-33 Removal of Specimens for Fluorescence, Immunofluorescence, Histopathology, Immunohistopathology, and Flow Cytometry
(a) *Add new tissue type to list of approved inactivation procedures*
(b) *BSL-3* (b)(6) *Tick Biosafety Plan*

4) ***Animal Study Protocols Review***

Title	***Associated PRD***	***Associated RD***	***Reviewer***
Efficacy of current vaccines and modifications to current vaccines to protect against divergent strains of SARS-CoV-2 in the hamster model	*17-143*	*17-410*	*M. Brose*
Vaccine potential of Coxiella burnetii Dugway strains in Guinea pigs	*20-43* *18-70*	*20-106*	(b)(6); (b)(3):42
Generation of prion infected brain material from various mouse and prion strains for experimental use	*18-51* *16-191*	*12-211*	*R. Anderson*
Immune responses to VSV-LASV vaccination in CD-1 mice	*18-82*	*20-404*	(b)(6);
Training in the use of the intravital microscope using mice	*N/A*	*N/A*	*R. Anderson*
Continued evaluation of a DNA vaccine for CCHFV in cynomolgus macaques	*18-92*	*17-431*	*M. Brose*
Evaluation of a PPMO Inhibitor of Lassa Virus Infection and Disease in a Guinea pig Model	*18-94*	*N/A*	*R. Anderson*

RML Biosafety Committee Meeting
April 15, 2021
Biosafety Officer Report

5) ***Biosafety Training Performed – Megan Brose, Rebecca Anderson,*** (b)(6)

Type of Training	*Number of Sessions*	*Number of Employees Trained*
BSL-3 Laboratory Biosafety	*2*	*4*
BSL-4 Laboratory Biosafety-Initial	*12*	*5*
BSL-4 Laboratory Biosafety-Refresher	*1*	*1*
Laboratory Biosafety Support Staff-Initial	*N/A*	*N/A*
Laboratory Biosafety Support Staff-Refresher	*N/A*	*N/A*
Select Agent Initial Training	*1*	*2*
Select Agent visitor/BSL-3 /BSL-4 visitor	*3*	*5*
New Employee Training	*2*	*5*

6) ***Safety Audits and Inspections***

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

a) *Biological Incident Report:*
   i) *None*

7) ***Other Issues –***
   i) *None*

Agenda

RML Biosafety Committee Virtual Meeting
May 20, 2021

I. Old Business
   A. Draft minutes of April 15, 2021 meeting

II. New Business
   A. Committee Business
      1. Pathogen Registration Documents (9)
      2. Recombinant DNA Documents (4)
      3. SOPs:
         a. Draft SOP#4-28-16: Rodent Biocontainment Procedures - add plethysmography
         b. Draft SOP#4-28-63: Rodent Transmission Caging Operation for Aerosol Exposure- Add UV box

   B. BSO/Responsible Official report (Dr. Becky Anderson)

   E. Occupational Safety & Health Manager report (Seth Cooley)

   F. IRF Biosafety Manager Report (Lt. Cmdr. Megan Brose)

   G. Associate Director Report (Dr. Marshall Bloom)

   H. Comments from around the room

Attachments:
1. Draft minutes of April 15, 2021 meeting (1 file)
2. Pathogen Registration Documents (9 files)
3. Recombinant DNA documents (4 files)
4. SOPs (2 files)
5. Meeting Agenda (1 file)

NEXT MEETING: June 17, 2021 via Skype

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 5/20/2021
Meeting Time: 1:00 PM **Adjourned:** 2:23 PM
Due to the COVID19 pandemic, this meeting was conducted online via Skype for Business

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Seth Cooley	☒	☐	Alexandra Scranton	☐	☒
Bob Heinzen, Vice Chair	☐	☒	Frank DeLeo (EO)	☐	☒	Brian Vickrey	☐	☒
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Clayton Winkler	☒	☐
Alan Applebury	☐	☒	Erik Hoover	☒	☐			
Chris Bosio	☒	☐	Clay Jarrett	☒	☐			
Marshall Bloom (EO)	☐	☒	Josh Kellar (EO)	☐	☒			
Megan Brose	☒	☐	Scott Kobayashi	☒	☐			
Larry Brouwer	☐	☒	Jamie Lovaglio	☒	☐			
Carol Calderwood	☐	☒	Andrea Marzi	☒	☐			
Marcie Caldwell (EO)	☐	☒	Alida Merritt	☒	☐			
Bruce Chesebro (EO)	☐	☒	Greg Saturday	☒	☐			

(P=present; A=absent)

Guests: (b)(6)
(b)(6)

Minutes: Meeting minutes from 4/15/2021 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 4/15/2021** Action: Meeting minutes for 4/15/2021 were unanimously approved with minor changes. 1. Change Clayton Winkler to absent. 2. On page 6 for the De Leo RD, state that Scott Kobayashi abstained.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Hasenkrug (LPVD) ▪ **PRD#21-169: Staphylococcal enterotoxin B (SEB) (exempt)** ▪ (b)(6) presented the risk assessment. This is a renewal for the Hasenkrug lab and the only change was to update the exempt quantity of SEB to 100 mg in accordance with the regulation. This registration covers work with SEB. ▪ No animal studies were submitted, reviewed or approved. ▪ Work with Staphylococcal enterotoxin B (SEB) is approved at BSL-2. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#21-169** as written.

Item 2:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal)</u> ▪ Hasenkrug (LPVD) ▪ **PRD#21-185: Lactate Dehydrogenase-elevating virus** ▪ (b)(6) presented the risk assessment. This is a renewal for the Hasenkrug lab. There were no changes to the current PRD. The registration covers work with Lactate Dehydrogenase-elevating virus and animal work with mice. ▪ Clayton Winkler noted that the ASP title was entered in twice, this should be updated. ▪ Clayton Winkler also noted that the check box indicating all individuals have taken animal care training was not checked. This should be followed up on. ▪ Animal studies with mice were proposed. ▪ Work with Lactate Dehydrogenase-elevating virus is approved at BSL-1/ABSL-1. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee unanimously approved **PRD#21-185** with the following minor modifications: 1. The check box indicating all individuals have taken animal care training was not checked. Check with the PI to ensure training has been completed and update the registration. 2. <u>Delete the redundant ASP title in the animal section.</u>
Item 3:	<u>Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal)</u> ▪ Hasenkrug (LPVD) ▪ **PRD#21-186: Zika virus** ▪ Becky Anderson presented the risk assessment. This is a renewal for the Hasenkrug lab. There were no changes to the current PRD. The registration covers work with Zika virus and animal work with mice. ▪ Animal studies with mice were proposed. ▪ Work with Zika virus is approved at BSL-2/ABSL-2 with the following precautions: o Care should be taken to minimize worker exposure to aerosols, such as working in a certified Class II BSC at all times and using gasketed bucket covers when centrifugating infectious material. Gasketed bucket covers or sealed rotors must only be loaded/unloaded in a BSC. It is recommended if possible that work with Zika virus be performed in a small or dedicated lab away from the main lab areas. Women of child bearing years must be advised of the risk of working with this agent, please consult with OMS. o Animal studies with rodents will be performed in the Human Pathogen Wing of Building 13 in (b)(6) or in (b)(6). Both areas are restricted access. All manipulations must be performed in a BSC. A sign at the suite door will indicate when Zika procedures are in progress. PPE includes: Lab coat, gloves, surgical mask. Husbandry practices will include spraying used cages and disinfectant, autoclaving, and then dumping the used bedding or if disposable caging is used, cages will be bagged and then incinerated. o The PI is responsible for providing hazard awareness training to all individuals listed on the PRD, animal care staff, and staff working in shared lab/animal spaces. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.

	Action: The committee unanimously approved **PRD#21-186** as written.
Item 4:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Hasenkrug (LPVD) ▪ **PRD#21-187: Murine gammaretroviruses** ▪ (b)(6) presented the risk assessment. This is a renewal for the Hasenkrug lab. There were no changes to the current PRD. This registration covers work with Murine gammaretroviruses and animal work with mice. ▪ Animal studies with mice were proposed. ▪ Work with murine gammaretroviruses is approved at BSL-1/ABSL-1. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#21-187** as written.
Item 5:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Bloom (LV) ▪ **PRD#21-181: Zika virus** ▪ Becky Anderson presented the risk assessment. This is renewal for the Bloom lab. There were no changes to the current PRD. This registration covers work with Zika virus. ▪ No animal studies were submitted, reviewed or approved ▪ Work with Zika virus is approved at BSL-2 with the following precautions: ○ Care should be taken to minimize worker exposure to aerosols, such as working in a certified Class II BSC at all times and using gasketed bucket covers when centrifugating infectious material. Gasketed bucket covers or sealed rotors must only be loaded/unloaded in a BSC. It is recommended if possible that work with Zika virus be performed in a small or dedicated lab away from the main lab areas. Women of child bearing years must be advised of the risk of working with this agent, please consult with OMS. ○ The PI is responsible for providing hazard awareness training to all individuals listed on the PRD, animal care staff, and staff working in shared lab/animal spaces. ▪ Sue Priola noted that they need to add the list of Zika strains. ▪ Clayton Winkler stated that the mammalian and tick cell lines should be listed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved **PRD#21-181** with the following modifications: 1. Under the Pathogen section, list Zika strains they have in the lab. 1. List mammalian and tick cell lines they will be using in the Pathogen section.
Item 6:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Hackstadt (LB) ▪ **PRD#21-165: *Yersinia pseudotuberculosis*** ▪ Becky Anderson presented the risk assessment. This is a renewal for the Hackstadt lab. There were no changes to the PRD. The registration covers work with *Yersinia pseudotuberculosis*. ▪ Becky Anderson noted that the RD number in the registration needs to be updated to the correct year.

	▪ No animal studies were submitted, reviewed or approved. ▪ Work with *Yersinia pseudotuberculosis* is approved at BSL-2. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved **PRD#21-165** with the following modifications: 1. Update the RD number in registration from RD-14-128 to RD-20-128.
Item 7:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Race (LPVD) ▪ **PRD#21-171: Transmissible spongiform encephalopathies (TSE)** ▪ Becky Anderson presented the risk assessment. This is a renewal for the Race lab. There were no changes to the PRD. This registration covers non-human primate samples that were infected with Chronic Wasting Disease. ▪ Becky Anderson stated the NHP blood and body fluid language needs to be added to the recommendations section. ▪ No animal studies were submitted, reviewed or approved. ▪ Work with TSE is approved at BSL-2. ▪ The committee discussed the dual-use potential of these experiments. DURC questions 5 and 6 were both checked yes by the PI. The committee discussed the responses and did not have any concerns with the studies registered. Action: The committee approved **PRD#21-171** with the following modifications: **1.** Update BSO recommendations with NHP BBF language.
Item 8:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Bosio (LB) ▪ **PRD#21-157: *Listeria monocytogenes*** ▪ Becky Anderson presented the risk assessment. This is a renewal for the Bosio lab. There were no changes to the current PRD. The registration covers work with *Listeria monocytogenes* and animal work with mice ▪ Animal studies with mice were proposed. ▪ Work with *Listeria monocytogenes* is approved at BSL-2/ABSL-2 with the following precautions: o Women who are pregnant or are thinking of becoming pregnant are encouraged to notify the Laboratory Supervisor and the RML OMS Nurses. This is in order to assure they are aware of any potential risks to themselves or the fetus and to determine if any additional risk reduction measures should be taken. o Immunocompromised persons should be made aware of the risks of working with this material. RML OMS Nurses can help to determine if any additional risk reduction measures should be taken. o All work with infectious material is conducted in a biosafety cabinet, centrifugation of infectious materials must be carried out in sealed safety cups or removeable rotors that can be loaded and unloaded in a biosafety cabinet. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee (Chris Bosio abstained) approved **PRD#21-157** as written.

Item 9:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New) ▪ Best (LV) ▪ **PRD#21-232: Human blood and body fluids (HBBF)** ▪ Becky Anderson presented the risk assessment. This is a new registration for the Best lab. They proposed to work with primary human cell and organoid systems using inducible pluripotent stem cells (iPSCs) to understand how immune signals are propagated in tissues. This registration covers work with HBBF. ▪ Sue Priola noted that the precautions for aerosols should be added to the recommendations section. ▪ No animal studies were submitted, reviewed or approved. ▪ Work with HBBF is approved BSL-2 with the following precautions: o All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurses at 375-9600. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved **PRD#21-232** with the following modification: 1. Include that all aerosol generating procedures will be done in the BSC in the BSO recommendations.
Item 10:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Bosio (LB) ▪ **RD#21-127: Lentivirus** ▪ Reviewers: Andrea Marzi, Sue Priola ▪ Summary: Use of replication deficient lentiviral reporter vectors ▪ Andrea Marzi summarized the RD. This RD renewal describes methods to use a replication deficient lentiviral vector system to generate stable cells lines that have a luciferase reporter gene. There are no changes to this RD renewal. The AMJ cells should be removed from the prokaryotic section and moved to the eukaryotic section as they are a mouse cell line. Andrea Marzi also stated that since they are not performing the prokaryote work, that section can be left blank and refer to the attached product insert from the commercial vendor. ▪ Sue Priola agreed with the change in AMJ cells from prokaryotic to eukaryotic section and the removal of information in the prokaryote section. ▪ No animal studies were submitted, reviewed or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee (Chris Bosio abstained) approved **RD#21-127** with minor modifications: 1. Prokaryotic section should be removed 2. Move AMJ cells to the Eukaryote Cell section. Research using eukaryotic cells is approved at BSL-2 under section III-D-3-a and III-D-1-a of the NIH Guidelines.
Item 11:	Registration Documents for Recombinant DNA Experiments (Renewal)

	▪ Bloom (LV) ▪ **RD#21-445: Lentivirus** ▪ Reviewers: Clayton Winkler, Sue Priola ▪ Summary: Analysis of molecular signaling pathways in Tickborne Flavivirus persistence ▪ Clayton Winkler summarized the RD. This RD renewal describes the use of lentiviral vector systems to knock out or overexpress certain genes in cells to elucidate the role of certain signaling pathways in the initiation and persistence of Tick-borne Flavivirus persistence. Clayton Winkler noted that GFP should be included under research products and as a foreign gene in the Eukaryote Cell section. It was noted that pGEX vector map was not included in the submission and the Akt1 shRNA attachment was included twice. ▪ Sue Priola indicated that III-D-2-a should be included under the prokaryotic section of this RD. ▪ No animal studies were submitted, reviewed or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved **RD#21-445** with minor modifications 1. Include "through an addendum" language for the information in the synopsis section. 2. Include GFP under the Research Product section 3. Attach the pGEX vector map 4. Add GFP as foreign gene in the Eukaryote Cell section 5. Remove one of the Akt1 shRNA attachments 6. Add NIH Guideline III-D-1-a and III-D-2-a to Prokaryote Host section Research using prokaryotic hosts is approved at BSL-2 under section III-D-1-a and III-D-2-a of the NIH Guidelines. Research using eukaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines.
Item 12:	<u>Registration Documents for Recombinant DNA Experiments (Renewal)</u> ▪ Hackstadt (LB) ▪ **RD#21-119:** ▪ Reviewers: Scott Kobayashi, Clay Jarrett ▪ Summary: Genetically modify *Chlamydiae trachomatis* and *C. caviae* to determine any effects on virulence ▪ Scott Kobayashi summarize the RD. This RD renewal is for the shuttle plasmid vector system for *Chlamydia*. The Hackstadt lab wants to introduce various tags for protein fusion markers. The committee discussed the usage of antibiotics with Chlamydia. The registration was not clear on what *C. trachomatis* serovars were being used, so the committee could not clearly determine if the proposed antibiotics for selection were appropriate. The committee decided to table the RD until the serovars could be clarified. Scott Kobayashi would like blood and body fluids language added to the recommendations section. ▪ Clay Jarrett asked for clarification of the statement "reintroduce chlamydial genes to compliment deficient strains". Usually, registrations say they will correct defects in strains. There should be a few sentences that clarify what genes are being used. This is listed in both the synopsis section and the Prokaryote Host section.

	▪ No animal studies were submitted, reviewed or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee TABLED **RD#21-119** pending more information regarding the Chlamydia serovars used and these antibiotic resistance markers. The committee agreed that if there were no concerns with the proposed usage of antibiotic resistance markers with the serovars, the committee could electronically review the registration.
Item 13:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Hackstadt (LB) ▪ **RD#21-126:** ▪ Reviewers: Chris Bosio, Scott Kobayashi ▪ Summary: Development of expression vectors for *Chlamydia trachomatis* ▪ Chris Bosio summarized the RD. This renewal RD describes developing expression vectors for *Chlamydia trachomatis*. They are using it to express reporter genes and non-virulence related genes from Chlamydia. The RD does have correspondence from the RAC attached. The RD describes the use of a particular serovar hybrid, *Chlamydia trachomatis* strain RD-Ls3. Consultation with the RAC approved the use of beta lactamase resistance genes in this strain in 2013. ▪ Scott Kobayashi had no additional comments or concerns. ▪ Sue Priola noted that the Prokaryotic Host section for the vector plasmid DNA indicated to see the attached list but did not give a list of specific plasmids. Include a list of plasmids to confirm that all are attached. ▪ No animal studies submitted, reviewed or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved **RD#21-126** with minor modifications: 1. Under prokaryotic host section list all applicable plasmids being used. Research using prokaryotic hosts is approved at BSL-2 under section III-D-1-a and III-D-2-a of the NIH Guidelines. Research using eukaryotic hosts is approved at BSL-2 with BSL-3 precautions under section III-D-1-a of the NIH Guidelines.
Item 14:	**Standard Operating Procedure: SOP#4-28-16 Rodent Procedures in Biocontainment (Update)** ▪ Becky Anderson summarized the SOP for the committee. The updates are to include procedures for rodent plethysmography. ▪ There we no comments or concerns from the committee. Action: The committee unanimously approved the: **SOP#4-28-16 Rodent Procedures in Biocontainment (Update)** as written.
Item 15:	**Standard Operating Procedure: SOP#4-28-63 Rodent Transmission Caging Operation for Aerosol Exposure (Update)** ▪ Becky Anderson summarized the SOP for the committee. The updates are to include new transmission tubing to allow for testing UV disinfection with a UV box and quartz tubes to allow for UV penetration. The new unit was tested by safety with particulate readings and a positive pressure test, the unit passed all tests. The

	update also added procedures and precautions for UV protection and what to do in the event of a break of the quartz tube in BSL-4. ▪ Sue Priola asked if the connections to the cages were polypropylene, as this is sensitive to damage from UV. Bob Fischer indicated that the polypropylene connections were sufficiently protected from UV exposure by distance and a PVC barrier. Action: The committee unanimously approved the: **SOP#4-28-63 Rodent Transmission Caging Operation for Aerosol Exposure (Update)** as written.
Report:	**Biosafety Officer (BSO) Report/Becky Anderson** ▪ Becky Anderson reviewed the BSO Report. ▪ She informed the committee that the NIH is working on updates to the NHP Bite, Scratch, Splash, Exposure Guidelines. The most significant change will be that the kits in labs will need to include valacyclovir. Becky Anderson is working with PI's to get the number of kits that will need valacyclovir. NIH will be providing the drug for the labs.
Report:	**Occupational Safety and Health Manager Report/Seth Cooley** ▪ Nothing to report
Report	**IRF Biosafety Manager/Responsible Official Report/Megan Brose** ▪ The Select Agent renewal inspection for BSL-3 and BSL-4 was April 26-May 5 with a hybrid remote approach and preliminary findings are: o A few discrepancies were found from handwritten report to data-based entries with HEPA filter certifications o One BSC was 2 months past annual inspection due date, likely due to animals being present in the room o Inactivation certificates must include PI written name and signature o Inactivation certificates should only have one inactivation method on a single inactivation certificate o Found single container of 70% Ethanol that was unlabeled with no expiration date ▪ Form 3 submitted: during the inspection in BSL-4 one inspector had a very small hole in their suit at the edge of exhaust vent. The suit had successfully passed an integrity test the day before. ▪ Amendment submitted to DSAT for CCHF and RVFV for animals not in containment cages or biobubbles. These pathogens are not expected to be transmitted by infectious aerosols and this proposed change is in line with the updates to the BMBL 6th edition.
Report	**Associate Director Report/Marshall Bloom** ▪ Not present
Around the room	▪ None

Other issues	▪ None

Next Meeting:

- Date: June 17, 2021
- Place: online via Skype for Business
- Time: 1:00 PM

RML Biosafety Committee Meeting
May 20, 2021
Biosafety Officer Report

1) ***Requests approved by BSO since last meeting:***
   a) ***Amend***
      (1) *None*
2) ***New requests approved by committee via electronic review:***
   a) *Inactivation Procedure Review:*
      i) *Bosio lab 10% formalin fixation of SARS-CoV-2 mouse tissues*
   b) *Standard Operating Procedures:*
      i) *Bosio lab SARS-CoV-2 Animal SOP-updated to include 10% formalin fixation*
3) ***New requests***
   a) *Pathogen Registration Documents*
      i) ***New***
         (a) *Best (LV) PRD 21-232*
      ii) ***Renew***
         (a) *Hasenkrug (LPVD) PRD 21-169*
         (b) *Hasenkrug (LPVD) PRD 21-185*
         (c) *Hasenkrug (LPVD) PRD 21-187*
         (d) *Hasenkrug (LPVD) PRD 21-186*
         (e) *Bloom (LV) PRD 21-181*
         (f) *Hackstadt (LB) PRD 21-165*
         (g) *Race PRD (LPVD) PRD 21-171*
         (h) *Bosio PRD (LB) PRD 21-157*
      iii) ***Amend***
         (a) *None*
   b) *Registration Documents for Recombinant Nucleic Acid Experiments*
      i) ***New***
         (a) *None*
      ii) ***Renew***
         (a) *Bosio RD 21-127*
         (b) *Bloom RD 21-445*
         (c) *Hackstadt RD 21-119*
         (d) *Hackstadt RD 21-126*

iii) ***Amend***

(a) *None*

c) ***Inactivation Procedure Reviews***

i) *None*

d) ***Standard Operating Procedures***

(a) ***SOP#4-28-16 Rodent Procedures in biocontainment***

(a) *Add procedures for plethysmography*

(b) ***SOP#4-28-63 Rodent Transmission Caging Operation for Aerosol Exposure***

(a) *Add procedures for new UV box*

4) ***Animal Study Protocols Review***

Title	***Associated PRD***	***Associated RD***	***Reviewer***
Determination of the role of interferon resistance in SARS-CoV-2 evolution of variants	*17-143*	*N/A*	(b)(6)
Use of bivalent nanobodies to reduce SARS-CoV-2 infection in Syrian Hamsters and ACE2 Tg mice	*17-143*	*N/A*	
Initial assessment of virulence of Salmonella mutants in mice	*18-44*	*15-108*	
Role of inflammasome and IL-1 family of cytokines in early infection by tick transmission in mouse infection model.	*20-229* *20-230*	*N/A*	*B. Anderson*
Transmission efficiency of SARS-CoV-2 variant P.1	*17-143*	*N/A*	*M. Brose*
Efficacy of Mosaic-8 nanoparticle vaccine against SARS-CoV-2 or SARS-CoV in the mouse model	*17-143* *17-145*	*N/A*	*B. Anderson*
Experimental SARS-CoV-2 infection in Artibeus jamaicensis bats	*17-143*	*N/A*	*M. Brose*

RML Biosafety Committee Meeting
May 20, 2021
Biosafety Officer Report

5) ***Biosafety Training Performed – Megan Brose, Rebecca Anderson,*** (b)(6)

Type of Training	***Number of Sessions***	***Number of Employees Trained***
BSL-3 Laboratory Biosafety	*2*	*3*
BSL-4 Laboratory Biosafety-Initial	*3*	*2*
BSL-4 Laboratory Biosafety-Refresher	*N/A*	*N/A*
Laboratory Biosafety Support Staff-Initial	*1*	*1*
Laboratory Biosafety Support Staff-Refresher	*N/A*	*N/A*
Select Agent Initial Training	*1*	*1*
Select Agent visitor/BSL-4 visitor	*1*	*4*
New Employee Training	*2*	*2*

6) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
a) *Biological Incident Report:*
   i) *None*

7) ***Other Issues –***
   i) *None*

Agenda

RML Biosafety Committee Virtual Meeting
June 17, 2021

I. Old Business
   A. Draft minutes of May 20, 2021 meeting

II. New Business
   A. Committee Business
      1. Pathogen Registration Documents (4)
      2. Recombinant DNA Documents (5)
      3. Inactivation Validation Study
         a. Heat inactivation of Coronavirus infected sera or plasma
      4. SOPs:
         a. Draft SOP# BSL-3-28-16: Inactivation of COVID19 Patient Sera or Plasma Samples
         b. Draft BSL-2 SOP Inactivation of COVID19 Patient Sera or Plasma Samples (same as above but for BSL-2)

   B. BSO/Responsible Official report (Dr. Becky Anderson)

   E. Occupational Safety & Health Manager report (Seth Cooley)

   F. IRF Biosafety Manager Report (Lt. Cmdr. Megan Brose)

   G. Associate Director Report (Dr. Marshall Bloom)

   H. Comments from around the room

Attachments:
1. Draft minutes of May 20, 2021 meeting (1 file)
2. Pathogen Registration Documents (4 files)
3. Recombinant DNA documents (5 files)
4. Inactivation Validation study (1 file)
5. SOPs (2 files)
6. Meeting Agenda (1 file)

NEXT MEETING: July 15, 2021 via Skype

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 6/17/2021
Meeting Time: 1:00 PM **Adjourned:** 2:21PM
Due to the COVID19 pandemic, this meeting was conducted online via Skype for Business

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Seth Cooley	☒	☐	Alexandra Scranton	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Brian Vickrey	☐	☒
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Clayton Winkler	☒	☐
Alan Applebury	☐	☒	Erik Hoover	☐	☒			
Chris Bosio	☐	☒	Clay Jarrett	☒	☐			
Marshall Bloom (EO)	☐	☒	Josh Kellar (EO)	☐	☒			
Megan Brose	☐	☒	Scott Kobayashi	☒	☐			
Larry Brouwer	☒	☐	Jamie Lovaglio	☒	☐			
Carol Calderwood	☐	☒	Andrea Marzi	☒	☐			
Marcie Caldwell (EO)	☐	☒	Alida Merritt	☐	☒			
Bruce Chesebro (EO)	☐	☒	Greg Saturday	☐	☒			

(P=present; A=absent)

Guests: (b)(6)
(b)(6)

Minutes: Meeting minutes from 5/20/2021 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 5/20/2021** Action: Meeting minutes for 5/20/2021 were unanimously approved with minor changes. 1. Sue Priola noted that in item 5, there are actions listed but does not include the discussion of who recommended the change. Originally Sue Priola commented that a list of strains should be included and Clayton Winkler noted that the cell lines should be included.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New) ▪ Groshong (LB) ▪ **PRD#21-233: *Borrelia spp.* (pathogenic)** ▪ Becky Anderson presented the risk assessment. This is a new registration for the Groshong lab. The proposed studies are to dissect the nutritional pathways of *Borrelia*. The registration covers work with pathogenic *Borrelia spp.* and animal work with mice and rats. ▪ Animal studies with mice and rats were proposed. ▪ Work with *Borrelia spp.* is approved at BSL-2/ABSL-2.

	▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved **PRD#21-233** as written.
Item 2:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New) ▪ De Wit (LV) ▪ **PRD#21-235: NHP tissues, blood, and body fluids** ▪ Becky Anderson presented the risk assessment. This is a new registration for the De Wit Lab. They plan to develop organoids and will use them to assess viral replication kinetics and host response. The registration covers work with NHP blood, body fluid or tissues. ▪ Becky Anderson noted to add in the BSO recommendations that PPE can be reduced to lab coat and gloves once the samples have tested negative for Herpes B virus. ▪ No animal studies were submitted, reviewed or approved. ▪ Work with NHP blood, body fluid or tissues is approved at BSL-2 with the following additional precautions: o Personnel should be advised of the potential risks with Herpes B virus when handling this materials. Potential exposures to this material must be reported immediately to OMS 406-375-9600 (business hours) or 301-496-1211 (on-call OMS healthcare provider). o A bite, scratch, splash, exposure kit and a 1-2-3 poster must be located in the laboratory where the work is performed. o Required PPE for work with NHP derived organoids includes: double gloves, face mask, face shield, shoe covers, and disposable gown. o The PI, Lab Chief, and RML Biosafety will be informed of any samples that test positive for Herpes B virus and the destruction of such samples ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved **PRD#21-235** with the following modifications: 1. Add to BSO recommendations that PPE can be reduced to lab coat and gloves after samples have tested negative for Herpes B virus.
Item 3:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amend) ▪ Feldmann (LV) ▪ **PRD#18-91: Henipavirus** ▪ Becky Anderson presented the risk assessment. This is an amendment for the Feldmann lab to lower the biosafety level for Cedar virus. Previously little information was available about Cedar virus and it showed similarities to Hendra and Nipah viruses. Per that information, the biosafety level was set at BSL-4. More information is now available regarding Cedar virus and there is evidence that it is not pathogenic to humans. Cedar virus is missing key proteins needed for virulence. ▪ Becky Anderson proposed restricting live samples of Cedar virus being removed from BSL-4 and would instead request that new stocks be obtained and worked with at BSL-3. ▪ No animal studies were submitted, reviewed or approved. ▪ Work with Cedar virus is approved at BSL-3/ABSL-3.

	▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved **PRD#18-91** amendment with minor modifications. 1. Restrict live Cedar virus samples being removed from the BSL-4 and request new stocks be obtained to start work at BSL-3.
Item 4:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renewal) ▪ Feldmann (LV) ▪ **PRD#21-188: Plasmodium spp.** ▪ Becky Anderson presented the risk assessment. This is a renewal for the Feldmann lab. There were no changes to the current PRD. This registration covers work with *Plasmodium spp.* and animal work with mice. ▪ Animal studies with mice were proposed. ▪ Work with *Plasmodium spp.* is approved at BSL-2/ABSL-2. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved **PRD#21-188** as written.
Item 5:	Registration Documents for Recombinant DNA Experiments (New) ▪ Groshong (LB) ▪ **RD#21-134: *Borrelia burgdorferi*** ▪ Reviewers: Scott Kobayashi, Clay Jarrett ▪ Summary: Defining the nutritional requirements for *Borrelia burgdorferi* throughout the enzootic cycle ▪ Scott Kobayashi summarized the RD. This RD describes methods to investigate nutrient uptake of *Borrelia burgdorferi*. Experiments will also be performed in *E. coli*. The lab will acquire DNA from other pathogens to amplify genes of interest. Proteins of interest will be expressed in *E. coli* and *Borrelia spp*. Antibiotics used for selection were listed. All vector maps were listed. ▪ Scott Kobayashi noted that pMC2498 contains AmpR gene for betalactamase, and this is a frontline antibiotic for *Borrelia* infections. Further clarification is needed regarding if this gene has been deleted in the plasmid. ▪ Sue Priola noted that the abbreviations listed in the RD section could be written out to aid in understanding which antibiotics are used for treatment. It was also noted that *E. coli* should be listed under prokaryotic hosts. ▪ Animal studies with mice and rats were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved **RD#21-134** with minor modifications and excluding the use of pMC2498 in *Borrelia spp*.: 1. Clarify pMC2498 plasmid containing AmpR use with *Borrelia*. Becky Anderson will work with Ashley Groshong to either replace the plasmid or include its use with a different antibiotic for selection. 2. List *E. coli* under prokaryotic hosts.

	Research using prokaryotic cells is approved at BSL-2 under section III-D-1-a and III-D-2-a of the NIH Guidelines. Animal work is approved at ABSL-2 under section III-D-1-a of the NIH Guidelines.
Item 6:	<u>Registration Documents for Recombinant DNA Experiments (Renewal)</u> ▪ Feldmann (LV) ▪ **RD#21-413: Henipavirus** ▪ Reviewers: Sue Priola, Clayton Winkler ▪ Summary: Henipavirus reverse genetics, minigenomes and trVLP studies. ▪ Sue Priola summarized the RD. This RD renewal describes methods to create minigenomes, reverse genetics system, and virus-like particles for Hendra, Nipah and Cedar viruses to study replication kinetics and function. Full-length clones will be created. *E. coli* will be used as a prokaryotic host. There are no changes to this RD renewal. ▪ Sue Priola noted that vectors pSMART and pRF240 should be added to the list of plasmids used. ▪ Sue Priola questioned the percent source genome. It currently states up to 100% and can be updated to state up to 66% or 100%. ▪ Clayton Winkler noted that helper virus was mentioned in this RD but does not have any additional information regarding its use. ▪ Andrea Marzi commented that helper viruses were a historic option but are not currently being used. ▪ No animal studies were submitted, reviewed or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved **RD#21-413** with minor modifications: 1. Add pSMart and pRF240 to list of plasmids used under the prokaryote host section 2. Update percent source genome listed 3. Delete any reference to helper virus Research using prokaryotic cells is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-4 for Hendra and Nipah viruses and BSL-3 for Cedar virus under section III-D-2-a, III-D-3-a, III-D-3-c, and III-E-1 of the NIH Guidelines.
Item 7:	<u>Registration Documents for Recombinant DNA Experiments (Renewal)</u> ▪ Feldmann (LV) ▪ **RD#21-418: Crimean-Congo Hemorrhagic Fever Virus (CCHFV)** ▪ Reviewers: Chris Bosio, Clay Jarrett ▪ Summary: Reverse genetics, minigenome systems, and VLP studies with CCHFV ▪ Clay Jarrett summarized the RD. This RD renewal describes the use of CCHFV to generate minigenome systems, virus-like particles, and full-length clones. Clay Jarrett noted that the plasmids in figures 3 and 4 were difficult to see. The committee agreed the figures should be updated. ▪ Sue Priola questioned the percent source genome. It currently states up to 100% and can be updated to state up to 66% or 100%. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.

	Action: The committee approved **RD#21-418** with minor modifications: 1. Update percent source genome listed 2. Upload higher quality image of the plasmids in Figure 3 and 4 Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic hosts is approved at BSL-4 under sections III-D-2-a, III-D-1-c, III-D-3-c, and III-E-1 of the NIH Guidelines. Animal studies were approved at ABSL-4 under section III-D-1-c of the NIH Guidelines.
Item 8:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Feldmann (LV) ▪ **RD#21-433: 1918 Pandemic Influenza virus (any portion)** ▪ Reviewers: Andrea Marzi, Sue Priola ▪ Summary: Perform pathogenesis studies using pandemic 1918 Influenza virus A. ▪ Andrea Marzi summarized the RD. This RD renewal describes recovery of 1918 Influenza virus A for pathogenesis studies through reverse genetic techniques. E. coli will be used to amplify and propagate the plasmids. These plasmids will then be used to transfect eukaryotic cells. There are no changes to this RD renewal. ▪ Andrea Marzi noted that Figure 2 only contains 6 segments and not the 9 shown in Figure 3. Also, it was requested to delete III-D-1-a as it does not apply. ▪ Sue Priola noted that we should add III-E-1 to the research products and the percent source genome currently states up to 100% and can be updated to up to 66% or 100%. ▪ Animal studies with ferrets and mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved **RD#21-433** with minor modifications 1. Update Figure 2 to include 9 segments 2. Delete III-D-1-a as it is not applicable in eukaryotic cells and research products 3. Add NIH Guideline III-E-1 to research products section 4. Update percent source genome to “up to 66% or 100%” Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a and III-E-1 of the NIH Guidelines. Research using eukaryotic hosts is approved at BSL-4 under section III-D-7-c of the NIH Guidelines. Animal work is approved at ABSL-4 under section III-D-7-c.
Item 9:	Registration Documents for Recombinant DNA Experiments (Renewal) ▪ Feldmann (LV) ▪ **RD#21-436: Arenaviruses** ▪ Reviewers: Clayton Winkler, Chris Bosio ▪ Summary: Arenavirus reverse genetics, minigenome systems and trVLPs. ▪ Clayton Winkler summarized the RD. This RD renewal describes the development of minigenomes, trVLPs, and chimeric or recombinant viruses using an established reverse genetics procedure for Arenaviruses (Lassa, Junin, Machupo, Guanarito, Sabia, Lujo, Mobala, Chapare, Tacaribe, Pichinde, and Ippy viruses). The Feldmann lab will be using cell culture and animal models. Biosafety level will be based on the parent arenavirus and the chimeric virus biosafety level will follow the virus with

	the highest biosafety level in the chimera. NIH Guidelines were applicable. All plasmid maps present. ▪ Clayton Winkler noted that the percent source genome currently states up to 100% and can be updated to up to 66% or 100%. ▪ Clayton Winkler noted that helper virus was mentioned under the eukaryotic section and to remove if not being used. ▪ Clayton Winkler requested that the answer to section 3 of the dual use questionnaire be moved to section 1 as it is more applicable. The committee agreed to this change. ▪ Animal work with NHPs and guinea pigs were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved **RD#21-436** with minor modifications: 1. Update percent source genome listed to "up to 66% or 100%" 2. Remove references to the use of helper viruses. 3. Move Dual Use questionnaire answer from #3 to question #1 as it is more applicable. Research using prokaryotic hosts is approved at BSL-2 under section III-D-2-a of the NIH guidelines. Research using eukaryotic hosts is approved at BSL-2 to BSL-4 under section III-D-2-a, III-D-1-a, III-D-1-b, III-D-1-c, III-D-3-a, III-D-3-b, III-D-3-c, and III-E-1 of the NIH Guidelines. Animal work is approved at ABSL-2 to ABSL-4 under section III-D-1-a, III-D-1-b, and III-D-1-c of the NIH Guidelines.
Item 10:	**Full Committee Review of BSL-3 Heat Inactivation Data of Coronavirus infected sera or plasma** ▪ Sue Priola informed the committee that there is inactivation data to review for the BSL-3. Included in this month's submission is testing data for heat inactivation of Coronaviruses. The ability of heat to inactivate SARS-CoV-2 in serum and plasma samples was tested. ▪ Sue Priola summarized the testing results for the inactivation of serum and plasma. Sue Priola confirmed with the committee that the titers tested were appropriate and all necessary controls were included. ▪ There were no additional comments or concerns with the inactivation data. Action: The committee unanimously approved the inactivation data of Coronavirus infected serum or plasma as written.
Item 11:	**Standard Operating Procedure: SOP# BSL-3-28-16 Inactivation of COVID19 Patient Sera or Plasma Samples (New)** ▪ Sue Priola summarized the SOP for the committee. This SOP is to heat inactivate COVID19 patient sera or plasma samples in the BSL-3. ▪ Sue Priola recommended doubling the inactivation time from 30 minutes to 60 minutes as an added safety factor in the procedure. Action: The committee unanimously approved the: **SOP# BSL-3-28-16 Inactivation of COVID19 Patient Sera or Plasma Samples (New)** with minor modifications. 1. Double the time for heat inactivation from 30 minutes to 60 minutes.

Item 12:	**Standard Operating Procedure: BSL-2 Inactivation of COVID19 Patient Sera or Plasma Samples (New)** ▪ Sue Priola summarized the SOP for the committee and noted that we do not usually review SOPs for work conducted at BSL-2. This SOP is a companion SOP to the work being done in BSL-3 depending on how the samples arrive. ▪ Sue Priola recommended doubling the inactivation time from 30 minutes to 60 minutes as an added safety factor in the procedure. ▪ Clayton Winkler noted that the lettering systems used for each step was incorrect and should be updated. Action: The committee unanimously approved the: **BSL-2 Inactivation of COVID19 Patient Sera or Plasma Samples (New)** with minor modifications. 1. Double the time for heat inactivation from 30 minutes to 60 minutes. 2. Update lettering system for consistency.
Report:	**Biosafety Officer (BSO) Report/Becky Anderson** ▪ Becky Anderson reviewed the BSO Report. ▪ Reviewed two incident reports with the committee. The first incident was a small splash to the cheek of an individual. The splash was wash buffer from a membrane that contained CJD. The second incident was a small splash of mouse normalized scrapie to a pant leg below lab coat. ▪ (b)(6) reviewed an incident report. The incident was a bite from an uninfected mink.
Report:	**Occupational Safety and Health Manager Report/Seth Cooley** • Nothing to report
Report	**IRF Biosafety Manager/Responsible Official Report/Megan Brose** • Not present
Report	**Associate Director Report/Marshall Bloom** • Not present
Around the room	• None

Other issues	▪ None

Next Meeting:

- Date: July 15, 2021
- Place: online via Skype for Business
- Time: 1:00 PM

RML Biosafety Committee Meeting
June 17, 2021
Biosafety Officer Report

1) ***Requests approved by BSO since last meeting:***
    i) ***None***
2) ***New requests approved by committee via electronic review:***
    i) *Hackstadt RD 21-119*
        (a) *Reviewed to ensure antibiotic usage was appropriate.*
3) ***New requests***
    a) *Pathogen Registration Documents*
        i) ***New***
            (a) *Groshong (LB) PRD 21-233*
            (b) *De Wit (LB) PRD 21-235*
        ii) ***Renew***
            (a) *Feldmann (LV) PRD 21-188*
        iii) ***Amend***
            (a) *Feldmann (LV) PRD 18-91*
    b) *Registration Documents for Recombinant Nucleic Acid Experiments*
        i) ***New***
            (a) *Groshong (LB) RD 21-134*
        ii) ***Renew***
            (a) *Feldmann (LV) RD 21-413*
            (b) *Feldmann (LV) RD 21-418*
            (c) *Feldmann (LV) RD 21-433*
            (d) *Feldmann (LV) RD 21-436*
        iii) ***Amend***
            (a) *None*
    c) ***Inactivation Procedure Reviews***
        i) *Building 28 BSL-3: Heat inactivation of Coronavirus infected human sera or plasma*
    d) ***Standard Operating Procedures***
            (a) *SOP#BSL-3-28-16 Inactivation of COVID19 Patient Sera or Plasma Samples (NEW)*
            (b) *BSL-2 SOP Inactivation of COVID19 Patient Sera or Plasma Samples (NEW)*
4) ***Animal Study Protocols Review***

RML Biosafety Committee Meeting
June 17, 2021
Biosafety Officer Report

Title	*Associated PRD*	*Associated RD*	*Reviewer*
Investigating Phenotypic Range of Highly Pathogenic Crimean-Congo Hemorrhagic Fever virus in CC Mice	*18-92*	*N/A*	(b)(6)
Influence of mosquito salivary gland proteins on California Serogroup viral pathogenesis in mice	*18-103*	*N/A*	
Pathogenesis of CCHFV in livestock	*18-92*	*N/A*	
Surveillance for zoonotic pathogens in wildlife reservoirs in the Republic of Congo	*19-158*	*N/A*	
Global Surveillance of Wildlife to Determine Potential Risk of Zoonotic Spillover	*19-158*	*N/A*	

5) ***Biosafety Training Performed – Megan Brose, Rebecca Anderson,*** (b)(6)

Type of Training	*Number of Sessions*	*Number of Employees Trained*
BSL-3 Laboratory Biosafety	*2*	*2*
BSL-3/4 Laboratory Biosafety-Initial	*7*	*3*
BSL-4 Laboratory Biosafety-Refresher	*N/A*	*N/A*
Laboratory Biosafety Support Staff-Initial	*1*	*1*
Laboratory Biosafety Support Staff-Refresher	*N/A*	*N/A*
Select Agent Initial Training	*N/A*	*N/A*
Select Agent visitor/BSL-4 visitor	*2*	*2*
New Employee Training	*2*	*3*

6) ***Safety Audits and Inspections***

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

a) *Biological Incident Report:*
   i) *Three incidents to update the committee on.*

7) ***Other Issues –***
   i) *None*

Agenda

RML Biosafety Committee Virtual Meeting
July 15, 2021

I. Old Business
   A. Draft minutes of June 17, 2021meeting

II. New Business
   A. Committee Business
      1. Pathogen Registration Documents (2)
      2. Recombinant DNA Documents (1)
      3. Inactivation Validation Study
         a. Inactivation of SchuS4 using Qiagen AVL
      4. SOPs:
         a. Draft SOP# BSL[(b)(6)] Inactivation of SchuS4 using Qiagen AVL
         b. Draft SOP#4-28-17 NHP Procedures in Level 4
         c. Draft Exposure Control Plan-Annual Review

   B. Annual IBC Training

   C. BSO report (Dr. Becky Anderson)

   E. Occupational Safety & Health Manager report (Seth Cooley)

   F. IRF Biosafety Manager/RO Report (Lt. Cmdr. Megan Brose)

   G. Associate Director Report (Dr. Marshall Bloom)

   H. Comments from around the room

Attachments:
1. Draft minutes of June 17, 2021 meeting (1 file)
2. Pathogen Registration Documents (2 files)
3. Recombinant DNA documents (1 files)
4. Inactivation Validation study (1 file)
5. SOPs (2 files)
6. Meeting Agenda (1 file)

NEXT MEETING: August 19, 2021 via Skype

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 7/15/2021
Meeting Time: 1:00 PM **Adjourned:** 1:49 PM
Due to the COVID19 pandemic, this meeting was conducted online via Skype for Business

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Seth Cooley	☒	☐	Alexandra Scranton	☐	☒
Bob Heinzen, Vice Chair	☐	☒	Frank DeLeo (EO)	☐	☒	Brian Vickrey	☐	☒
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Clayton Winkler	☒	☐
Alan Applebury	☐	☒	Erik Hoover	☒	☐			
Chris Bosio	☐	☒	Clay Jarrett	☒	☐			
Marshall Bloom (EO)	☐	☒	Josh Kellar (EO)	☐	☒			
Megan Brose	☒	☐	Scott Kobayashi	☒	☐			
Larry Brouwer	☐	☒	Jamie Lovaglio	☒	☐			
Carol Calderwood	☐	☒	Andrea Marzi	☒	☐			
Marcie Caldwell (EO)	☐	☒	Alida Merritt	☐	☒			
Bruce Chesebro (EO)	☐	☒	Greg Saturday	☒	☐			

(P=present; A=absent)

Guests: (b)(6)

(b)(6)

Minutes: Meeting minutes from 6/17/2021 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 6/17/2021** Action: Meeting minutes for 6/17/2021 were unanimously approved with minor changes. 1. Sue Priola noted a few minor typos to be corrected.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amend) ▪ Feldmann (LV) ▪ **PRD#18-92 Amend: Bunyaviridae** ▪ Becky Anderson presented the risk assessment. The amendment is to add sheep to the PRD. There is an SOP already in place for sheep and goats. The sheep will be housed in caging with a solid bottom to protect the floors and walls. We already have CDC DSAT approval to work with sheep and CCHFV. ▪ Sue Priola questioned if they were adapting CCHFV to sheep or if this was an experimental model. Becky Anderson stated that sheep are already a susceptible species, the studies are to just use sheep as an experimental model. ▪ Animal studies with sheep were proposed. ▪ Work with Bunyaviridae is approved at ABSL-4.

	▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved **PRD#18-92 Amend** as written.
Item 2:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amend) ▪ Bloom (LV) ▪ **PRD#20-224 Amend: Coronavirus** ▪ Becky Anderson presented the risk assessment. The amendment to the PRD is to add bovine coronavirus strain Mebus and bovine syncytial virus. Neither of these are known to cause any human illnesses. ▪ No animal studies were submitted, reviewed or proposed. ▪ Work with bovine coronavirus strain Mebus and Bovine syncytial virus is approved at BSL-2. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved **PRD#20-224 Amend** as written.
Item 3:	Registration Documents for Recombinant DNA Experiments (Amend) ▪ Feldmann (LV) ▪ **RD#21-418 Amend: Crimean-Congo Hemorrhagic Fever Virus (CCHFV)** ▪ Reviewers: Chris Bosio and Sue Priola ▪ Summary: Reverse genetics system for CCHFV ▪ Chris Bosio was not present, Sue Priola summarized the RD amendment instead. The RD describes developing reverse genetics for CCHFV. The amendment is to add pCDNA 3.1 to the RD as an alternate to pCAGGS vector. Plasmids are very similar in antibiotic resistance markers. Sue Priola had no dual use concern with the amendment. ▪ No animal studies were submitted, reviewed or proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved **RD#21-418 Amend** as written. Research using prokaryotic cells is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-4 under section III-D-2-a, III-D-3-a, III-D-3-c, and III-E-1 of the NIH Guidelines.
Item 4:	**Full Committee Review of BSL-3 AVL Inactivation Data of *Francisella tularensis* SchuS4** ▪ Sue Priola informed the committee that there is inactivation data to review for the Bosio lab. Included in this month's submission is testing data for AVL inactivation of SchuS4. The ability of AVL to inactivate SchuS4 was tested. ▪ Sue Priola summarized the testing results for the inactivation of SchuS4. Sue Priola confirmed with the committee that the titers tested were appropriate and all necessary controls were included. ▪ There were no additional comments or concerns with the inactivation data. Action: The committee unanimously approved the inactivation data of SchuS4 as written.
Item 5:	**Standard Operating Procedure: SOP# BSL-3-C-8 AVL Inactivation of SchuS4 (New)**

	▪ Sue Priola summarized the SOP for the committee. This SOP is to use AVL to inactivate SchuS4. ▪ Sue Priola noted that the volumes in the SOP are different from the validation study. She voiced concern that the volumes need to match. The committee agreed that the SOP should be tabled until the volumes for the SOP and validation testing can be straightened out. ▪ Sue Priola asked to clarify if this titer is in cfu/mL. Becky Anderson confirmed that this is correct. ▪ Andrea Marzi asked if the max titer needs to be specified in the SOP. The committee agreed this should be added. ▪ Becky Anderson will confirm with the laboratory about the revisions. The SOP will be tabled and the IBC will review electronically once the SOP is revised. Action: The committee TABLED: **SOP# BSL-3-C-8 AVL Inactivation of SchuS4 (New).**
Item 6:	**Standard Operating Procedure: SOP# 4-28-17 Nonhuman Primate Procedures in Level 4 Biocontainment (Update)** ▪ Becky Anderson summarized the SOP for the committee. This SOP is a consolidation of information from four SOPs (4-28-17, 4-28-18, 4-28-22, and 4-28-49). These other SOPs will be inactivated after approval of this SOP. ▪ Jamie Lovaglio commented under inoculation to add intracranial inoculations which are described in the ASP and inhalation inoculation which will be covered in a separate SOP. ▪ Sue Priola noted under section G for euthanasia, "generally" is listed for how we follow the RML ACUC euthanasia guidelines. Jamie Lovaglio noted that there may be exceptions to the guidelines and we should leave "generally" ▪ Andrea Marzi asked if we have CDC DSAT approval to do intracranial inoculations. Becky Anderson noted that the inoculations listed in the SOP are for everything performed in the BSL-4. Approvals for routes of inoculation are agent specific. Action: The committee unanimously approved the: **SOP# 4-28-17 Nonhuman Primate Procedures in Level 4 Biocontainment (Update)** with minor modifications: 1. Add intracranial inoculations 2. Add inhalation inoculation
Item 7:	**Exposure Control Plan (Annual Review)** ▪ Becky Anderson informed the committee that the Exposure Control Plan was due for annual review. Several members of RML safety, biosafety, OMS and emergency services reviewed the document and proposed minor changes. The changes are all tracked in the document. ▪ Sue Priola noted a few minor typos. ▪ (b)(6) summarized for the IBC, the review of safer sharps devices that were tested this year. The review evaluated various types of box cutters. Action: The committee unanimously approved the Exposure Control Plan (Annual Review) with minor modifications. 1. Sue Priola noted a few typos that would be addressed
Report:	**Biosafety Officer (BSO) Report/Becky Anderson** ▪ Becky Anderson gave annual IBC training.

	▪ Becky Anderson reviewed the BSO Report.
Report:	**Occupational Safety and Health Manager Report/Seth Cooley** • Nothing to report
Report	**IRF Biosafety Manager/Responsible Official Report/Megan Brose** • BSL-3/4 CDC DSAT inspection report was received. We are finalizing responses and will be submitting next week. • BSL-4 (b)(6); shut down is wrapping up
Report	**Associate Director Report/Marshall Bloom** • Not present
Around the room	• None

Other issues	▪ None

Next Meeting:

- Date: August 19, 2021
- Place: online via Skype for Business
- Time: 1:00 PM

RML Biosafety Committee Meeting
July 15, 2021
Biosafety Officer Report

1) Requests approved by BSO since last meeting:

i) None

2) ***New requests approved by committee via electronic review:***

i) *None*

3) ***New requests***

a) *Pathogen Registration Documents*

i) ***New***

(a) *None*

ii) ***Renew***

(a) *None*

iii) ***Amend***

(a) *Feldmann (LV) PRD 18-92 Amend*

(b) *Bloom (LV) PRD 20-224 Amend*

b) *Registration Documents for Recombinant Nucleic Acid Experiments*

i) ***New***

(a) *None*

ii) ***Renew***

(a) *None*

iii) ***Amend***

(a) *Feldmann (LV) RD 21-418 Amend*

c) ***Inactivation Procedure Reviews***

i) *Bosio- Inactivation of SchuS4 using Qiagen AVL*

d) ***Standard Operating Procedures***

(a) ***Draft Suite C BSL-3-C-8 Inactivation of SchuS4***

(i) New inactivation procedures

(b) ***SOP#4-28-17 Nonhuman primate Procedures in Level 4 biocontainment***

(a) *Combine SOP#4-28-17, 4-28-18, 4-28-22, 4-28-49*

4) ***Animal Study Protocols Review***

RML Biosafety Committee Meeting
July 15, 2021
Biosafety Officer Report

Title	Associated PRD	Associated RD	Reviewer
Borrelia burgdorferi nutrient acquisition throughout the enzootic cycle	*21-233*	*21-134*	*R. Anderson*
Borrelia burgdorferi nutrient acquisition within the mammalian host environment	*21-233*	*21-134*	*R. Anderson*
Generation of antisera from purified recombinant protein in mice and rats	*N/A*	*21-134*	(b)(6)
Studying chronic shedding and transmission of Salmonella in mice	*18-44*	*15-108*	
Role of subcapsular sinus macrophages in bubonic plague pathogenesis	*18-04*	*15-303*	*R. Anderson*
Role of the F1 capsular antigen in facilitating mammal to flea transmission of Yersinia pestis	*18-04*	*15-303*	*M. Brose*
Efficacy of DNA-encoded Monoclonal Antibody Cocktail against SARS-CoV-2 infection in Rhesus Macaques	*17-143*	*N/A*	(b)(6)

5) ***Biosafety Training Performed – Megan Brose, Rebecca Anderson,*** (b)(6)

Type of Training	Number of Sessions	Number of Employees Trained
BSL-3 Laboratory Biosafety	*N/A*	*N/A*
BSL-4 Laboratory Biosafety-Initial	*N/A*	*N/A*
BSL-4 Laboratory Biosafety-Refresher	*N/A*	*N/A*
Laboratory Biosafety Support Staff-Initial	*N/A*	*N/A*
Laboratory Biosafety Support Staff-Refresher	*N/A*	*N/A*
Select Agent Initial Training	*N/A*	*N/A*
Select Agent visitor/BSL-4 visitor	*2*	*2*
New Employee Training	*N/A*	*N/A*

6) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
a) *Biological Incident Report:*
i) *None*

7) ***Other Issues –***
i) *None*

Agenda

RML Biosafety Committee Virtual Meeting
September 16, 2021

I. Old Business
   A. Draft minutes of July 15, 2021 meeting

II. New Business
   A. Committee Business
      1. Pathogen Registration Documents (1)
      2. Recombinant DNA Documents (5)
      3. SOPs:
         a. Draft SOP#28-16: Oral drug delivery to rodents in biocontainment
         b. Draft4-28-43: Aerosol Exposure System-add mink
         c. Draft BSL-3 OSP- Annual review
         d. Draft ABSL-3 OSP- Annual review

   B. BSO report (Dr. Becky Anderson)

   E. Occupational Safety & Health Manager report (Seth Cooley)

   F. IRFBSM/Responsible Official Report (Lt. Cmdr. Megan Brose)

   G. Associate Director Report (Dr. Marshall Bloom)

   H. Comments from around the room

Attachments:
1. Draft minutes of July 15, 2021 meeting (1 file)
2. Pathogen Registration Documents (1 file)
3. Recombinant DNA documents (5 files)
4. SOPs (4 files)
5. Meeting Agenda (1 file)

NEXT MEETING: October 21, 2021 via Skype

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 9/16/2021
Meeting Time: 1:00 PM **Adjourned:** 2:34 PM
Due to the COVID19 pandemic, this meeting was conducted online via Zoom

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Seth Cooley	☒	☐	Alexandra Scranton	☐	☒
Bob Heinzen, Vice Chair	☐	☒	Frank DeLeo (EO)	☐	☒	Brian Vickrey	☐	☒
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Clayton Winkler	☒	☐
Alan Applebury	☐	☒	Erik Hoover	☒	☐			
Chris Bosio	☒	☐	Clay Jarrett	☒	☐			
Marshall Bloom (EO)	☒	☐	Josh Kellar (EO)	☐	☒			
Megan Brose	☒	☐	Scott Kobayashi	☒	☐			
Larry Brouwer	☐	☒	Jamie Lovaglio	☒	☐			
Carol Calderwood	☐	☒	Andrea Marzi	☒	☐			
Marcie Caldwell (EO)	☐	☒	Alida Merritt	☐	☒			
Bruce Chesebro (EO)	☐	☒	Greg Saturday	☐	☒			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 7/16/2021 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 7/16/2021** Action: Meeting minutes for 7/16/2021 were unanimously approved as written.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (New) ▪ Groshong (LB) ▪ **PRD#21-236: Human Blood and Body Fluid (HBBF)** ▪ Becky Anderson presented the risk assessment. The Groshong lab will obtain human clinical samples to improve methods for detection of *Borrelia burgdorferi* in human samples. These samples are obtained from patients and may also have *Borrelia burgdorferi* in the samples, this lab is already registered for *Borrelia*. Becky Anderson discussed possible bloodborne pathogens that could be present in the samples including Hep B, HIV and Hep C. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact OMS at 406-375-9600.

	▪ No animal studies were submitted, reviewed or approved. ▪ Work with HBBF is approved at BSL-2. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. ▪ Sue Priola noted to add "of detection" following improved methods and noted a typo of RT-RT-PCR in the synopsis. Action: The committee unanimously approved **PRD#21-136** with minor modifications. 1. Include the language "of detection" in the synopsis. 2. Correct RT-RT-PCR typo.
Item 2:	Registration Documents for Recombinant DNA Experiments (New) ▪ Bosio (LB) ▪ **RD#21-136: *Bordetella pertussis*** ▪ Reviewers: Scott Kobayashi and Clay Jarrett ▪ Summary: Generate recombinant *Bordetella pertussis* strains to track antigen specific responses. ▪ Scott Kobayashi summarized the RD. Two Bordetella genes, bsp22c and bscF, will be tagged with LCMV GP 61-80 and cloned into the pUCS12 plasmid. This plasmid will be put in *E. coli* RHO3 to perform conjugation into *Bordetella pertussis*. TNS3 is used to provide the transposon machinery to insert the DNA into a specific site in *Bordetella pertussis*. The tagged Bordetella will then be used to track T-cell populations. These two Bordetella genes are found in the type 3 secretion system. Additional information should be included on what the LCMV peptide is doing or expected to do, in targeting of T cells. More information about Bordetella D20 strain should be included. Antibiotics proposed are not used for treatment and the NIH Guidelines listed were appropriate. ▪ Clay Jarrett noted that, in general, additional information could be added to the registration to aid in understanding. Additional information is needed on the biological origin of the recombinant materials. IDT DNA is listed for this section, but it is not specified what the lab will be receiving from IDT DNA. Sue Priola agreed that additional information was needed. ▪ Clay Jarrett noted that Dual Use question #2 was answered no. He asked the committee if targeting T cells would disrupt immunity or effectiveness of an immunization. ▪ Becky Anderson discussed that the recombinant Bordetella would track T-cell response and would not be expected to alter the immune response. The committee agreed. ▪ Sue Priola noted that there are currently no cell lines listed under the eukaryotic cells, but animal cells were listed elsewhere in the registration. Animal cells should be included in the eukaryotic cells section. ▪ No animal studies were submitted, reviewed or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved (Chris Bosio abstained) **RD#21-136 with modifications:** 1. Add additional information on the LCMV GP61-80 peptide. 2. Describe the RHO3 conjugal transfer system. 3. Describe the transposon system.

	4. Include information that this is a clinical strain of *Bordetella pertussis*. 5. Add information regarding experiments with animal cells in the eukaryotic cell section. 6. Include additional information on what materials are being received from IDT DNA. Research using prokaryotic cells is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under section III-D-2-a NIH Guidelines.
Item 3:	<u>Registration Documents for Recombinant DNA Experiments (Amend)</u> ▪ Groshong (LB) ▪ **RD#21-134 Amend: *Borrelia burgdorferi*** ▪ Reviewers: Chris Bosio and Clay Jarrett ▪ Summary: *Borrelia burgdorferi* nutrient acquisition throughout the enzootic cycle: updating plasmids with ampicillin resistance to plasmids with kanamycin resistance. ▪ Chris Bosio summarized the RD. This amendment is to switch from ampicillin resistance to Kanamycin resistance genes in the plasmids. That is the only change in the protocol. Plasmid maps are attached. ▪ Clay Jarrett noted that the plasmids were attached. No Dual Use questionnaire or NIH Guideline updates are necessary. ▪ Sue Priola asked if the pUC19 plasmid map was included. Becky Anderson noted that due to the file type it may not be showing properly, and she could change this file type. ▪ No new animal studies were submitted, reviewed or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. <u>Action:</u> The committee approved **RD#21-134 Amend** as written. Research using prokaryotic cells is approved at BSL-2 under section III-D-1-a and III-D-2-a of the NIH Guidelines.
Item 4:	<u>Registration Documents for Recombinant DNA Experiments (Amend)</u> ▪ Steele-Mortimer (LB) ▪ **RD#19-126 Amend: Salmonella Cancer Vaccine** ▪ Reviewers: Clayton Winkler and Scott Kobayashi ▪ Summary: Developing recombinant attenuated *Salmonella typhimurium* vaccine (RASV) as a platform for developing therapeutic vaccines and as a delivery system for therapeutic molecules. ▪ Clayton Winkler summarized the RD amendment. This amendment is to expand the existing RD for the Salmonella vaccine platform to include Recombinant Salmonella Therapeutic (RST) strains. This will be used as a drug delivery system specifically targeting tumors. Fluorescent indicators will be used to confirm localization. The therapeutic delivery plasmid has two bacterial genes to stabilize it without the use of antibiotics. The lab will use an attenuated strain to start but will make wild type strains as well. NIH Guidelines and biosafety level were applicable. No dual use concerns were raised. ▪ Scott Kobayashi had no additional comments or concerns.

	▪ Sue Priola inquired about the ampicillin resistance gene. The committee asked that a statement of what antibiotics are used clinically for Salmonella infection be included. ▪ No new animal studies were submitted, reviewed or approved. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved **RD#19-126 Amend with minor modifications**. 1. Included what antibiotics are used clinically for treatment of Salmonella. Research using prokaryotic cells is approved at BSL-2 under section III-D-1-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under section III-D-1-a of the NIH Guidelines.
Item 5:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Feldmann (LV) ▪ **RD#21-407: Filovirus** ▪ Reviewers: Andrea Marzi and Sue Priola ▪ Summary: Reverse genetics, minigenome, and trVLP work for Filoviruses. ▪ Andrea Marzi summarized the RD. This is a renewal combining all recombinant filovirus work in a single RD. All work has been previously approved except 1) Bundibugyo will be included in the minigenome system work, 2) Inclusion of monoclonal antibody sequences expressed as additional ORF from the full-length clone will be added to the list of foreign non-coding sequences used, and 3) Inclusion of human and non-human primate blood and serum usage. The Feldmann lab is proposing to do reverse genetics, minigenome and trVLP experiments for filoviruses. Minigenome systems are used for working with portions of the filovirus genome, specifically less than 2/3 of the genome. Full length clone work is only performed in a specific BSL-2 facility where plasmids are manipulated in bacteria and no eukaryotic cell culture is performed. Virus recovery is then performed at BSL-4. The technetium receptor is listed under research products, and Andrea was unsure if it used or should be removed from the registration. The committee agreed to remove technetium receptor from the registration. All plasmids listed have associated vector maps attached. Animal work was proposed, and the ASP is attached. For the dual use questionnaire, as noted, none of the mutations are expected to be more infectious than the donor virus. The NIH Guidelines listed are appropriate. ▪ Sue Priola agreed that the NIH Guidelines and dual use questions were answered appropriately. ▪ Becky Anderson commented that animal species are specifically approved for particular projects, rather than overall filovirus work and asked the committee to comment. Sue Priola and Andrea Marzi agreed that the current way it is written is acceptable. ▪ Animal studies with mice, guinea pigs, hamsters, and NHP were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved **RD#21-407** with minor modifications: 1. Remove reference to technetium receptor under research products.

	Research using prokaryotic cells is approved at BSL-2 under section III-D-1-a, III-D-2-a, III-D-2-b, and III-E-1 of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-4 under section III-D-1-a, III-D-1-c, and III-E-1 of the NIH Guidelines.
Item 6:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Feldmann (LV) ▪ **RD#21-440: Coronavirus** ▪ Reviewers: Sue Priola and Clayton Winkler ▪ Summary: Development and use of reverse genetics systems for coronaviruses. ▪ Sue Priola summarized the RD. This is a renewal and combines the previously approved coronavirus work in a single RD. This RD covers reverse genetic systems for bacterial and yeast artificial chromosomes. Each plasmid contains less than 2/3 of the viral genome. Recombinant viruses are used *in vitro, in vivo* and to study viral entry and pathogenesis. In the synopsis, it states that this registration includes all known Coronaviruses in the subfamily Coronaviridae that infect humans, this should be updated to include a list of specific viruses. Chimeric viruses will be generated utilizing multiple coronaviruses. Some chimeric viruses and bat coronaviruses will be obtained from a colleague at UNC Chapel Hill. The Dual Use Question #1 should address why making recombinants will not provide a dual use concern. Vector maps were present. pCC1BAC-his3 BAC is not listed in the RD, but the map was attached. ▪ Clayton Winkler agreed that Dual Use question #1 should be addressed. Becky Anderson concurred. ▪ Clayton Winkler asked if NIH Guideline III-D-2-b was applicable to this research. (b)(6) noted that it is not applicable because it is multisegmented and not located on the same plasmid. (b)(6) noted that no new information was added to this registration. ▪ Sue Priola asked to include if a specific chimera is discovered to be more fit for transmission or had increased pathogenicity than the parent viruses, then that information should be brought back to the IBC. ▪ Becky Anderson proposed removing the bat coronaviruses from this registration and creating a separate RD with this information. Sue Priola suggested that IBC may want a description of the chimeras being made instead of a blanket approval. More specific detail on the proposed chimeric viruses with human and bat coronaviruses may be needed. ▪ Animal studies with mice, NHP and bats were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee TABLED **RD#21-440** pending additional information on the proposed chimeric viruses, listing the specific Coronaviruses that will be worked with, and the removal of the bat coronaviruses from this registration. The committee will review the registration at a later date.
Item 7:	**Standard Operating Procedure: SOP# 4-28-16 Rodent Procedures in Biocontainment (Update)** ▪ Becky Anderson summarized the SOP for the committee. This update is to include oral drug delivery and oral gavage to non-anesthetized rodents. Rodents will be manually restrained utilizing bite resistant gloves or physically restrained utilizing a

	wrap that swaddles the rodent. Syringes (without the needle) will be used to feed the rodent. Rodents will be adequately restrained with these two techniques. ▪ Clayton Winkler asked if oral gavage could be performed while animals were not anesthetized. Jamie Lovaglio confirmed that this was correct. ▪ Alex Scranton emailed additional comments. One comment was that the protocol states that mastomys must be housed in two specific rooms and are restricted to those two rooms listed. Becky Anderson confirmed that is correct. The second comment was to clarify language in Section B7 and B8 regarding which cage will be decontaminated. ▪ There were no additional comments or concerns with the updated procedures. Action: The committee unanimously approved: **SOP# 4-28-16 Rodent Procedures in Biocontainment (Update)** with minor modifications: 1. Clarify cage decontamination language in Section B7 and B8.
Item 8:	**Standard Operating Procedure: SOP# 4-28-43 Aerosol Exposure System Operation (Update)** ▪ Becky Anderson summarized the SOP for the committee. The update to this SOP is to add mink to the Aerosol Exposure System. Provisions are already in place for whole body exposure of other species. ▪ Jamie Lovaglio noted that Tyvek sleeves listed in the protocol may be difficult to obtain and suggested broadening the language. Becky Anderson commented that the SOP could state moisture resistant instead of specifying Tyvek. ▪ Jamie Lovaglio noted that some of the SOPs listed at the end of the document are no longer relevant or active. ▪ There were no additional comments or concerns with the updated procedures. Action: The committee unanimously approved: **SOP# 4-28-43 Aerosol Exposure System Operation (Update)** with minor modifications: 1. Update Tyvek sleeve to moisture resistant sleeve. 2. Update SOPs that are referenced.
Item 9:	**BSL-3 Operations and Safety Procedures (OSP) - Annual Review** ▪ Becky Anderson summarized the changes to the BSL-3 OSP. Updates included: 1) Updated the abbreviations list and the abbreviations used throughout the document. 2) Updated BMBL reference to 6th edition. 3) Added to list of requirements for BSL-3 facility design requirements. 4) Clarified reporting of incidents in BSL-3-25-4. ▪ Sue Priola asked about the removal of the paragraph on pg. 40 regarding processing attenuated strains in the BSL-3 until additional identification is made. Becky Anderson noted that this requirement is now listed in the BSL-3 Rickettsia SOP only. ▪ Clayton Winkler asked about the additional statement on pg. 35 that laboratory airflow does not reverse at the containment barrier under failure conditions. Becky Anderson noted that this is standard language from the CDC DSAT checklist and is verified annually. ▪ There were no additional comments or concerns with the updated procedures. Action: The committee unanimously approved the BSL-3 OSP (Annual Review) as written.
Item 10:	**ABSL-3 Operations and Safety Procedures (OSP) - Annual Review**

	▪ Becky Anderson summarized the updates to the ABSL-3 OSP. Updates included: 1) Add acronym list and clean up the acronyms used throughout the document. 2) Clarify room cleaning frequency by RMVB. 3) Updated BMBL reference to 6th edition. 4) Added to list of requirements for ABSL-3 facility design requirements. ▪ There were no additional comments or concerns with the updated procedures. Action: The committee unanimously approved the ABSL-3 OSP (Annual Review) as written.
Report:	**Biosafety Officer (BSO) Report/Becky Anderson** ▪ Becky Anderson reviewed the BSO Report. ▪ Two incidents were reviewed with the committee. ▪ Becky Anderson reviewed the first incident. There was a needlestick following flushing femurs of uninfected mice. ▪ Megan Brose reviewed the second incident. There was a splash to the eye and face from washing histology slides, one of which contained CJD.
Report:	**Occupational Safety and Health Manager Report/Seth Cooley** • Nothing to report
Report	**IRF Biosafety Manager/Responsible Official Report/Megan Brose** • Form 3 submitted: a BSC unexpectedly shutoff in the ABSL-3 shortly after researchers were handling *Coxiella burnetii* infected guinea pigs. The final cage had been closed but the inside of the BSC had not yet been decontaminated.
Report	**Associate Director Report/Marshall Bloom** • Not present
Around the room	• None

Other issues	▪ None

Next Meeting:

- Date: October 21, 2021
- Place: online via Skype for Business
- Time: 1:00 PM

RML Biosafety Committee Meeting
September 16, 2021
Biosafety Officer Report

1) Requests approved by BSO since last meeting:

i) Feldmann (LV) PRD 17-143 Amend

(1) Add aerosol route of inoculation for mink

ii) Feldmann (LV) RD 20-442 Amend

(1) Add permit

iii) Feldmann PRD 18-90 Amend

(1) Add intravaginal route of inoculation for NHP

2) ***New requests approved by committee via electronic review:***

i) *SOP#4-28-33* Removal of Specimens for Fluorescence, Immunofluorescence, Histopathology, Immunohistopathology, and Flow Cytometry

(a) *Add inactivation of Coronavirus infected mink nasal structure with 10% formalin for 30 days*

3) ***New requests***

a) *Pathogen Registration Documents*

i) ***New***

(a) *Groshong (LB) PRD 21-236*

ii) ***Renew***

(a) *None*

iii) ***Amend***

(a) *None*

b) *Registration Documents for Recombinant Nucleic Acid Experiments*

i) ***New***

(a) *Bosio (LB) RD 21-136*

ii) ***Renew***

(a) *Feldmann (LV) RD 21-407 (combines -407, -417, -426, -427, -450)*

(b) *Feldmann (LV) RD 21-440*

iii) ***Amend***

(a) *Groshong RD 21-134*

(b) *Steele-Mortimer RD 19-126*

c) ***Inactivation Procedure Reviews***

i) *None*

d) ***Standard Operating Procedures***

(a) ***SOP#4-28-16 Rodent Procedures in Level 4 biocontainment***

(a) *Add procedures for oral delivery of drugs on physically or mechanically restrained rodents*

(b) *SOP#4-28-43 Aerosol Exposure System Operation*

(a) *Add mink to animals inoculated with aerosol exposure system*

(c) *BSL-3 Operations and Safety Procedures*

(a) *Annual Review*

(d) *ABSL-3 Operations and Safety Procedures*

(a) *Annual Review*

4) ***Animal Study Protocols Review***

Title	***Associated PRD***	***Associated RD***	***Reviewer***
Evaluation of ARN-75039 an as entry inhibitor of Lassa virus in the Guinea pig model of disease	*18-94*	*N/A*	(b)(6); (b)(3):42
Refinement of a SARS-CoV-2 Mink Severe Disease Model	*17-143*	*N/A*	*R. Anderson*
Transmission and evolution of SARS-CoV-2 in immunocompromised Syrian golden hamster model	*17-143*	*N/A*	*R. Anderson*
Assessing the role of antiviral immunity in COVID-19 lung injury and potential for therapeutic targeting in mice.	*17-143*	*N/A*	(b)(6)
Ornithodoros tick colony feeding and maintenance on mice	*N/A*	*N/A*	(b)(6)
Infectious Cycle of Relapsing Fever Spirochetes in Mice	*20-03*	*20-319*	
Comparison of epithelial response to influenza A virus infection in organoid cultures and C57BL/6J mice	*17-132*	*N/A*	*R. Anderson*
Development of an animal model to study Nipah virus neurological disease in Syrian hamsters	*18-91*	*N/A*	(b)(6); (b)(3):42
The effect of Pikachurin knockout on prion-induced photoreceptor degeneration	*16-190*	*N/A*	*R. Anderson*
Evaluating the longevity of pulmonary pathology after SARS-CoV-2 infection in the mouse	*20-223*	*N/A*	(b)(6); (b)(3):42 U.S.C. 262a(h) (Public Health
Defining the contribution of patrolling monocytes to Francisella tularensis dissemination in the mouse	*18-73* *18-71*	*N/A*	

RML Biosafety Committee Meeting
September 16, 2021
Biosafety Officer Report

5) ***Biosafety Training Performed – Megan Brose, Rebecca Anderson,*** (b)(6)

Type of Training	***Number of Sessions***	***Number of Employees Trained***
BSL-3 Laboratory Biosafety	*3*	*7*
BSL-4 Laboratory Biosafety-Initial	*2*	*2*
BSL-4 Laboratory Biosafety-Refresher	*N/A*	*N/A*
Laboratory Biosafety Support Staff-Initial	*1*	*1*
Laboratory Biosafety Support Staff-Refresher	*N/A*	*N/A*
Select Agent Initial Training	*1*	*1*
Select Agent visitor/BSL-3/4 visitor	*1*	*2*
New Employee Training	*4*	*7*
Full length Clone lab-Annual Refresher	*1*	*2*

6) ***Safety Audits and Inspections***
Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)
   a) *Biological Incident Report:*
      i) *Update on recent incidents*

7) ***Other Issues –***
      i) *None*

Agenda

RML Biosafety Committee Virtual Meeting
October 21, 2021

I. Old Business
   A. Draft minutes of September 16, 2021 meeting

II. New Business
   A. Committee Business
      1. Pathogen Registration Documents (3)
      2. Recombinant DNA Documents (2)
      3. Inactivation Validation Study
         a. MeOH inactivation of SchuS4 in Murine Tissues
      4. SOPs:
         a. Draft BSL-3 SOP BSL3-C-8: Addition of methanol inactivation of SchuS4 in murine tissues
         b. Draft Tularemia animal SOP: Addition of methanol inactivation of SchuS4 in murine tissues

   B. BSO/Responsible Official report (Dr. Becky Anderson)

   E. Occupational Safety & Health Manager report (Seth Cooley)

   F. IRF Biosafety Manager Report (Lt. Cmdr. Megan Brose)

   G. Associate Director Report (Dr. Marshall Bloom)

   H. Comments from around the room

Attachments:
1. Draft minutes of September 16, 2021 meeting (1 file)
2. Pathogen Registration Documents (3 files)
3. Recombinant DNA Documents (2 files)
4. Inactivation validation study (1 file)
5. SOPs (2 files)
6. Meeting Agenda (1 file)

NEXT MEETING: November 18, 2021 via Skype

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 10/21/2021
Meeting Time: 1:00 PM **Adjourned:** 1:58 PM
Due to the COVID-19 pandemic, this meeting was conducted online via Zoom

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☒	☐	Seth Cooley	☒	☐	Alexandra Scranton	☐	☒
Bob Heinzen, Vice Chair	☒	☐	Frank DeLeo (EO)	☐	☒	Brian Vickrey	☐	☒
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Clayton Winkler	☒	☐
Alan Applebury	☐	☒	Erik Hoover	☒	☐			
Chris Bosio	☐	☒	Clay Jarrett	☒	☐			
Marshall Bloom (EO)	☐	☒	Josh Kellar (EO)	☐	☒			
Megan Brose	☐	☒	Scott Kobayashi	☒	☐			
Larry Brouwer	☒	☐	Jamie Lovaglio	☐	☒			
Carol Calderwood	☐	☒	Andrea Marzi	☒	☐			
Marcie Caldwell (EO)	☐	☒	Alida Merritt	☒	☐			
Bruce Chesebro (EO)	☐	☒	Greg Saturday	☒	☐			

(P=present; A=absent)

Guests (b)(6)

(b)(6)

Minutes: Meeting minutes from 9/16/2021 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 9/16/2021** Action: Meeting minutes for 9/16/2021 were unanimously approved as written.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amend) ▪ Heinzen (LB) ▪ **PRD#20-43: *Coxiella burnetii*; add mice** ▪ Becky Anderson presented the risk assessment. This is an amendment to their current PRD to work with mice. They have approval to work with guinea pigs already. All SOPs are already in place for work with mice. ▪ Animal studies with mice were proposed. ▪ Work with *Coxiella burnetii* is approved at ABSL-3. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved **PRD#20-43 amendment** as written.

Item 2:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amend) ▪ Feldmann (LV) ▪ **PRD#17-173: Coronavirus; hamster transmission studies** ▪ Becky Anderson presented the risk assessment. This animal study proposal describes transmission of SARS-CoV-2 with immunocompromised hamsters. The first study is to evaluate shedding of SARS-CoV-2 in immunocompetent vs immunocompromised hamsters. The second study is to serially passage SARS-CoV-2 through immunocompromised or immunocompetent hamsters with aerosol inoculation route. This was brought to the IBC for a Dual Use review. ▪ (b)(6) explained the study. They are trying to model what is happening in immunocompromised individuals. This study is based on an immunocompromised patient that was studied and the SARS-CoV-2 virus population was expanded in that individual. They are trying to understand if SARS-CoV-2 infection favors immunocompromised status in infection kinetics. Also, they are looking to determine evolutionary bottlenecks of SARS-CoV-2 in combination with an immunocompromised status. Evolution of the virus will be assessed during serial passage. For analysis, RT-PCR and deep sequencing will be performed. They will not be isolating the virus or performing additional characterization. ▪ Sue Priola asked if these mutations will be deposited in a database. (b)(6) (b)(6) indicated that this sequence would be made available, but that information may not be helpful in determining which mutations were selected for. ▪ Sue Priola asked about the differences between control immunocompetent vs immunocompromised serial transmission. (b)(6) indicated that in either group, it is not expected that single variants would emerge. ▪ Larry Brouwer asked which strain or variants would be used for this study. (b)(6) (b)(6) indicated that any of the circulating variants would be expected to be used, in particular the Delta variant. ▪ Sue Priola asked if a more transmissible variant is expected. (b)(6) indicated that a more transmissible variant is not expected from these studies, and the genetic information is not typically useful for creating a more transmissible variant. ▪ (b)(6) indicated that SARS-CoV-2 is already aerosol transmissible. ▪ Sue Priola asked if there would be increased pathology in the hamsters following serial passaging. (b)(6) indicated that under direct inoculation there is mild to moderate pathology, and during aerosol transmission there is little pathology noted. This could be based on the dose of virus by the inoculation routes. ▪ Clayton Winkler asked about a cited paper regarding RAG2-/- hamsters that appeared to have increased pathogenicity. (b)(6) indicated that genetic may be linked to the pathogenicity. Clayton Winkler asked about the choice of cyclophosphamide to induce immunocompromised state. (b)(6) indicated that this is used to induce the immunocompromised state and does not directly replicate the immunocompromised patient referenced above. Clayton Winkler asked if genetic knockout could be used instead of cyclophosphamide. (b)(6) (b)(6) indicated that they are trying to study the transmission of the virus instead of the hamster genetics. ▪ Becky Anderson asked if they are expecting to get short reads and not a different variant, then what information will they gain by performing the study. (b)(6) (b)(6) indicated that this would give them more information on what drives

	transmission of the virus. It will also help answer the question, do immunocompromised people drive the transmission cycle. ▪ Becky Anderson asked if there is a possibility to drive it to a more transmissible variant. (b)(6) indicated that this is unlikely. They would only know this information if the virus was subsequently isolated, which they will not be doing. They are not doing large scale population genetics with many animals, and instead looking at transmission and evolution on a small scale. The virus already transmits well, so it is unlikely to increase transmissibility. ▪ Clayton Winkler noted that Dual Use question #3 is currently indicated as "No" but would like additional comments on the answer. ▪ Sue Priola commented that the committee should consider public perception of the experiment. ▪ Becky Anderson informed the committee on what the options to proceed are. Option 1: This experiment could be elevated for NIH Dual Use Research Committee (DURCOM) review with a Dual Use Research Mitigation Plan analysis. Sue Priola noted that this should be something we considered. Becky Anderson recommended this review process. Clayton Winkler, (b)(6) Alida Merrit, Scott Kobayashi, Andrea Marzi, and Bob Heinzen agreed with additional review. The committee agreed with the additional review by the DURCOM. Action: The committee TABLED **PRD#17-173 amendment** pending DURCOM review.
Item 3:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amend) ▪ Bosio (LB) ▪ **PRD#20-222: HBBF; add NHP blood and body fluids** ▪ Becky Anderson presented the risk assessment. Amendment to existing HBBF COVID-19 positive patients and is amending to receive NHP COVID-19 samples. Samples will be irradiated prior to work. Recommendations included: ○ All NHP samples from SARS-CoV-2 infected animals will be irradiated prior to work. Work with non-human primate blood, body fluids, cells and tissues is approved at BSL-2 with all work being restricted to being performed within a biological safety cabinet (BSC). After irradiation of samples, downstream processing can occur at BSL-2 with standard precautions. ○ Personnel should be advised of the potential risks with monkey B virus when handling non-human primate material. Potential exposures to this material must be reported immediately to OMS at 406-375-9600 (business hours) or 301-496-1211 (on-call OMS healthcare provider). A 1-2-3 poster must be displayed in the lab. Follow the Bite, Scratch, Splash, Exposure Guidelines for NHP samples in the following link: https://oacu.oir.nih.gov/system/files/media/file/2021-06/oacu_bsse_guidelines.pdf ▪ No animal studies were submitted, reviewed or approved. ▪ Work with NHP BBF is approved at BSL-2. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved **PRD#20-222 amendment** as written.

Item 4:	Registration Documents for Recombinant DNA Experiments (Amend) ▪ Heinzen (LB) ▪ **PRD#20-106: *Coxiella burnetii*; add mice** ▪ Reviewers: Chris Bosio and Clay Jarrett ▪ Summary: Utilize mice for *Coxiella burnetii* ▪ Clay Jarrett summarized the RD. This amendment is to add work with mice to the RD. The Heinzen laboratory already works with the guinea pig model, but that limits the number of tools available for analysis. They would like to work with mice, as there are additional analysis tools available. ▪ Clay Jarrett noted that Chris Bosio had indicated there were no additional concerns. ▪ Animal studies with mice were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved **PRD#20-43 amendment** as written. Research using prokaryotic cells is approved at BSL-2 under section III-D-1-a of the NIH Guidelines.
Item 5:	Registration Documents for Recombinant DNA Experiments (Renew) ▪ Feldmann (LV) ▪ **RD#21-440: Coronavirus** ▪ Reviewers: Clayton Winkler and Sue Priola ▪ Summary: Development and use of reverse genetics systems for coronaviruses. ▪ Clayton Winkler summarized the RD. This is a renewal and combines the previously approved coronavirus work in a single RD. This RD covers reverse genetic systems for bacterial and yeast artificial chromosomes. These can then be use *in vitro* and *in vivo* and are used to study viral entry and pathogenesis. They provided additional information regarding SARS-CoV-2 experiments with variants of concern and mutations in the spike protein. They will be using naturally occurring mutations only for their analysis and reverse genetic systems. ▪ Sue Priola asked about the chimeric viruses between bats and human coronaviruses. That was removed from the registration and the laboratory will not perform that experiment. They will be looking at known point mutations with SARS-CoV-2. (b)(6) confirmed that there will be no human-bat chimeras. ▪ Sue Priola noted that YAC plasmids is not listed under the prokaryote vector plasmid section, but the plasmid map was attached. Sue Priola noted that the final Dual Use question could address why they do not expect an increased virulence with the current mutations. ▪ Animal studies with mice, NHP and bats were proposed. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee approved **RD#21-440** with minor modifications. 1. Update vector list to include YAC vector. 2. Update Dual use question to state that there is no increased virulence expected with current mutations.

	Research using prokaryotic cells is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-3 under section III-D-3-a, III-D-3-b, III-D-1-a and III-E-1 of the NIH Guidelines.
Item 6:	**Full Committee Review of BSL-3 MeOH Inactivation of SchuS4 in Murine Tissues** ▪ Sue Priola informed the committee that there is inactivation data to review for the Bosio lab. Included in this month's submission is testing data for methanol inactivation of SchuS4 in murine tissues. The ability of methanol to inactivate SchuS4 was tested. ▪ Sue Priola summarized the testing results for the inactivation of SchuS4. Sue Priola confirmed with the committee that the titers tested were appropriate and all necessary controls were included. ▪ There were no additional comments or concerns with the inactivation data. Action: The committee unanimously approved the inactivation data of SchuS4 as written.
Item 7:	**Standard Operating Procedure: DRAFT SOP BSL-3 (b)(6) BSL3-C-8 Inactivation of Francisella spp. (Update)** ▪ Sue Priola summarized the SOP for the committee. This update is to include methanol inactivation of SchuS4 in murine tissues. ▪ Clay Jarrett asked about the volume of tissue compared to the volume of fixative and asked to update the language to indicted that the tissue will be completely submerged in fixative. ▪ There were no additional comments or concerns with the updated procedures. Action: The committee unanimously approved: **DRAFT SOP BSL-3 (b)(6) BSL3-C-8 Inactivation of Francisella spp. (Update)** with minor modifications: 1. Include that the tissue will be completely submerged in fixative.
Item 8:	**Standard Operating Procedure: DRAFT SOP Tularemia animal SOP, BSL3-5 (Update)** ▪ Sue Priola summarized the SOP for the committee. This update is to include methanol inactivation of SchuS4 in murine tissues. ▪ There were no additional comments or concerns with the updated procedures. ▪ Clay Jarrett asked about the volume of tissue compared to the volume of fixative and asked to update the language to indicted that the tissue will be completely submerged in fixative. Action: The committee unanimously approved: **DRAFT SOP Tularemia animal SOP, BSL3-5 (Update)** with minor modifications: 1. Include that the tissue will be completely submerged in fixative.
Report:	**Biosafety Officer (BSO) Report/Becky Anderson** ▪ Becky Anderson reviewed the BSO Report. ▪ Becky Anderson reviewed an incident in the BSL-4. An individual was processing samples for inactivation of CCHF. The individual found a hole in their suit in the chemical shower. Following a risk assessment, all work was performed in a BSC and there were no spills in the BSL-4 at the time, therefore there is minimal risk of exposure.
Report:	**Occupational Safety and Health Manager Report/Seth Cooley** • Nothing to report
Report	**IRF Biosafety Manager/Responsible Official Report/Megan Brose**

	• Not present • Becky Anderson informed the committee that Megan Brose is deployed.
Report	**Associate Director Report/Marshall Bloom** • Not present
Around the room	• None

Other issues	▪ None

Next Meeting:

- Date: November 18, 2021
- Place: online via Zoom
- Time: 1:00 PM

Agenda

RML Biosafety Committee Virtual Meeting
December 16, 2021

I. Old Business
   A. Draft minutes of October 21, 2021 meeting

II. New Business
   A. Committee Business
      1. Pathogen Registration Documents (4)
      2. Recombinant DNA Documents (1)
      3. SOPs:
         a. Draft MCL OSP: Annual Review
         b. Draft SOP#4-28-63 Rodent Transmission Caging Operation for Aerosol exposure-add section on cages for analysis of droplets
         c. Draft SOP#4-28-65 Use of X-Cube MicroCT Scanner for in vivo imaging-New SOP
         d. Draft SOP#4-28-39 Chicken Procedures in Level 4 biocontainment-separated procedures for chickens into a single SOP
         e. Draft SOP#4-28-53 Rabbit Procedures in Level 4 biocontainment-separated procedures for rabbits into a single SOP

   B. BSO report (Dr. Becky Anderson)

   E. Occupational Safety & Health Manager report (Seth Cooley)

   F. IRFBSM/Responsible Official Report (Lt. Cmdr. Megan Brose)

   G. Associate Director Report (Dr. Marshall Bloom)

   H. Comments from around the room

Attachments:
1. Draft minutes of September 16, 2021 meeting (1 file)
2. Pathogen Registration Documents (4 files)
3. Recombinant DNA Documents (1 file)
4. SOPs (5 files)
5. Meeting Agenda (1 file)

NEXT MEETING: January 20, 2021 via Zoom

RML Institutional Bio-Safety Committee Minutes

Meeting Date: 12/16/2021
Meeting Time: 1:01 PM **Adjourned:** 1 :45 PM
Due to the COVID-19 pandemic, this meeting was conducted online via Zoom

Members:

	P	A		P	A		P	A
Sue Priola, Chair	☐	☒	Seth Cooley	☒	☐	Alexandra Scranton	☐	☒
Bob Heinzen, Vice Chair	☐	☒	Frank DeLeo (EO)	☐	☒	Brian Vickrey	☐	☒
Becky Anderson (EO)	☒	☐	Heinz Feldmann (EO)	☐	☒	Clayton Winkler	☒	☐
Alan Applebury	☐	☒	Erik Hoover	☒	☐			
Chris Bosio	☐	☒	Clay Jarrett	☒	☐			
Marshall Bloom (EO)	☐	☒	Josh Kellar (EO)	☐	☒			
Megan Brose	☒	☐	Scott Kobayashi	☒	☐			
Larry Brouwer	☐	☒	Jamie Lovaglio	☒	☐			
Carol Calderwood	☐	☒	Andrea Marzi, Acting Chair	☒	☐			
Marcie Caldwell (EO)	☐	☒	Alida Merritt	☒	☐			
Bruce Chesebro (EO)	☐	☒	Greg Saturday	☒	☐			

(P=present; A=absent)
Guests: (b)(6)

Minutes: Meeting minutes from 10/21/2021 meeting

approved ☒ **not-approved** ☐

Old Business: *Summarized discussion not resolved at last meeting*

Item 1:	**Minutes from 10/21/2021** Action: Meeting minutes for 10/21/2021 were unanimously approved with minor modifications. 1. Alida Merritt and Andrea Marzi noted spelling errors to be corrected.

New Business: *Summarized discussion of new items the committee addresses*

Item 1:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amend) ▪ Hackstadt (LB) ▪ **PRD#17-37: *Chlamydia trachomatis*** ▪ Becky Anderson presented the risk assessment. This amendment is to analyze unfixed cells using a flow cytometer. Cells will be transported to the BSC in room (b) (6) that houses the cell sorter. Staining procedures will be conducted at BSL-2 with 3 practices. All work with these samples must be performed in a BSC. Transport of samples between laboratories must be in a durable, leak proof container. PPE for handling samples in (b)(6) includes a front cover disposable gown, gloves, and an N95 respirator. A sign should be posted at the door restricting access when samples are being manipulated. ▪ No new animal studies were submitted, reviewed, or approved.

	▪ Clayton Winkler asked if the additional door to (b)(6) was in place to further isolate the room. Becky Anderson confirmed that this door will be installed. ▪ Work with *C. trachomatis* is approved at BSL-2 with 3 practices. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#17-37** as written.
Item 2:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amend) ▪ Feldmann (LV) ▪ **PRD#17-143: Coronavirus** ▪ Becky Anderson presented the risk assessment. This amendment is to update and inform the committee what SARS-CoV-2 isolates the Feldmann lab has on-site. The Omicron variant was not included in the list but is expected to be obtained soon. ▪ Alex Scranton noted via email that question marks were included in the provider information. Becky Anderson stated that the additional information will be requested from the Feldmann Lab. ▪ No new animal studies were submitted, reviewed, or approved. ▪ Work with Coronavirus is approved at BSL-3. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#17-143** with minor modifications. 1. Update provider information.
Item 3:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Renew) ▪ Feldmann (LV) ▪ **PRD#21-193: Porcine Reproductive and Respiratory Syndrome virus (PRRSV)** ▪ Becky Anderson presented the risk assessment. This is a renewal for work with PRRSV that does not include any new information. The Feldmann lab uses PRRSV to further understand co-infection of PRRSV with Reston Ebola virus. There is no evidence of PRRSV transmission to humans and no treatments available. The associated ASP was attached. ▪ Animal studies with pigs were proposed. ▪ Alex Scranton asked via email on page 3 about the containment equipment that will be used and if it should include the BSL-4. Becky Anderson indicated that PRRSV alone can be worked with at BSL-2/ABSL-2 and the containment language is sufficient. ▪ Work with ATCC strain of PRRSV is approved at BSL-2/ABSL-2 and SPB200809289 can only be worked with at BSL-4/ABSL-4. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#21-193** as written.
Item 4:	Registration of Material (Potentially) Infectious for Humans, Plants, or Animals (Amend) ▪ Feldmann (LV) ▪ **PRD#17-123: Severe Fever with Thrombocytopenia Syndrome virus (SFTSV) and Heartland virus** ▪ Becky Anderson presented the risk assessment. The purpose of this amendment is to adapt SFTSV and Heartland virus to wild type mice. The current mouse model is

	in IFN KO mice. They want to adapt it to further study the innate immune response to viral infection. The natural route of transmission is through ticks, and this would not be altered. Dual Use question #1 was answered yes and additional comments were provided. ▪ Alex Scranton commented via email that adaption to wild type mice could allow for transmission to the wild mice population, even though the possibility is remote, it should be addressed in the Dual Use questions. ▪ The committee agreed that this is not of increased concern because the pathogen will continue to be worked with at BSL-3/ABSL-3. The facility procedures remain the same, and the experiment proposed does not increase the risk or likelihood of pathogen release. ▪ Animal studies with mice were proposed. ▪ Work with SFTSV and Heartland virus is approved at BSL-3/ABSL-3. ▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **PRD#17-123** as written.
Item 5:	Registration Documents for Recombinant DNA Experiments (New) ▪ Bloom (LV) ▪ **RD#21-459: Generation of Flavivirus Virus-Like Particles (VLPs)** ▪ Reviewers: Clayton Winkler and Andrea Marzi ▪ Summary: Construction of Flavivirus VLPs. • Clayton Winkler summarized the RD. This is a new RD, and they propose to make VLPs for multiple flaviviruses, including Langat, Powassan, and Deer Tick virus. These VLPs are constructed using some or all the viral structural genes and are devoid of nucleic acids. These VLPs will be used to identify host receptor proteins and other interacting proteins. VLPs are tagged with a fluorescent protein or FIAsH tag. Host cells to be used are mammalian and tick cells. This will allow for a greater understanding of the role of viral structural proteins. Mutations in the structural proteins will be made. Additional information on these mutants should be provided, including any enhanced pathogenicity. Plasmid maps were included. NIH guidelines III-D-1-a could be removed from the research products and III-E-1 added to both the prokaryotic and eukaryotic sections. Under the prokaryotic section, update percent of the source genome that will be cloned to less than 2/3 of the genome. Address the protein mutations in the dual use questions as it relates to potential increase in virulence. One of the .pdf attachments has an error with overlaid text and should be replaced. • Andrea Marzi agreed and wanted the PI to describe and address the mutants that will be made. If there was increased virulence seen in the mutants, this information would be reported to Biosafety. Describe if the reporter will be fused to the proteins of interest. Include additional information on the number of constructs being used for VLP propagation. Describe if all 3 proteins are on a single plasmid or separated on 3 plasmids. ▪ Alida Merritt asked if the lab did see increased binding or virulence with the mutants, would the experiment be halted until Biosafety and IBC review. Becky Anderson confirmed that is correct. ▪ No animal studies were submitted, reviewed, or approved.

	▪ The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal. Action: The committee unanimously approved **RD#21-459 with modifications:** 1. Remove NIH guideline III-D-1-a. 2. Add III-E-1 to both the prokaryotic and eukaryotic sections. 3. Update prokaryotic section to state >2/3 of genome instead of 19%. 4. Include additional information on the number of constructs being used for VLP propagation. Describe if all 3 proteins are on a single plasmid or separated on 3 plasmids. 5. Describe if the reporter will be fused to the proteins of interest. 6. Update .pdf attachment for the one that has overlaid text. 7. Describe the protein mutations that will be made. 8. Address the protein mutation in the dual use questions as it relates to increased virulence. Research using prokaryotic cells is approved at BSL-2 under section III-D-2-a and III-E-1 of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under section III-D-2-a and III-E-1 NIH Guidelines.
Item 6:	**MCL Operations and Safety Procedures (OSP) - Annual Review** ▪ Becky Anderson summarized the changes to the MCL OSP. Updates included: 1) Updated acronym list, 2) Updated responsible persons for daily checklist, 3) Updated the PI registration process for human or animal pathogen, and 4) Clarified inside buddy duties. ▪ Alida Merritt asked via email if unauthorized access would include security footage review. Becky Anderson confirmed that security footage would be reviewed. ▪ Alida Merritt noted via email that expressing blood from wounds after an exposure is not commonly recommended and asked if there was additional information or literature regarding that recommendation. Becky Anderson noted that our Occupational Medical Services reviews our post-exposure plan and that is the recommendation they have given. ▪ There were no additional comments or concerns with the updated procedures. Action: The committee unanimously approved the MCL OSP (Annual Review) as written.
Item 7:	**Standard Operating Procedure: SOP# 4-28-39 Chicken Procedures in Level 4 Biocontainment (Update)** ▪ Becky Anderson summarized the SOP for the committee. This update is to include all procedures for chickens in a single SOP. No changes were made to the procedures, just reorganized, and put in the same SOP ▪ Alida Merritt asked on pg 3, 6.A.1.a.1, if the statement should be followed with "Do not proceed with any work until issues/concerns are resolved." Becky Anderson confirmed that no work would be done until any issue/concerns were addressed. ▪ There were no additional comments or concerns with the updated procedures. Action: The committee unanimously approved: **SOP# 4-28-39 Chicken Procedures in Level 4 Biocontainment (Update)** as written.
Item 8:	**Standard Operating Procedure: SOP# 4-28-53 Rabbit Procedures in Level 4 Biocontainment (Update)**

	▪ Becky Anderson summarized the SOP for the committee. This update is to include all procedures for rabbits in a single SOP. No changes were made to the procedures, just reorganized, and put in the same SOP. ▪ There were no additional comments or concerns with the updated procedures. Action: The committee unanimously approved: **4-28-53 Rabbit Procedures in Level 4 Biocontainment (Update)** as written.
Item 9:	**Standard Operating Procedure: SOP# 4-28-63 Rodent Transmission Caging Operation for Aerosol Exposure (Update)** ▪ Becky Anderson summarized the SOP for the committee. This SOP describes the aerosol transmission caging for rodents. This update is to add a new caging system that will be used for droplet analysis. Infected hamsters will be placed in the cage and the particle sizes being expelled from the hamsters will be measured. The vacuum pump penetration uses an existing port on the cages. These cages will be placed on shelving in the BSL-4. No sharps are present on the caging system. ▪ Alex Scranton commented via email that there is no mention for 2 people to be present in the protocol. Becky Anderson stated that it is covered in the MCL OSP. ▪ There were no additional comments or concerns with the updated procedures. Action: The committee unanimously approved: **4-28-63 Rodent Transmission Caging Operation for Aerosol Exposure (Update)** as written.
Item 10:	**Standard Operating Procedure: SOP# 4-28-65 Use of X-Cube MicroCT Scanner for *in vivo* Imaging (New)** ▪ Becky Anderson summarized the SOP for the committee. This is a new SOP for a new piece of equipment in the BSL-4. It describes how to operate the X-Cube MicroCT Scanner and insert animals into the instrument. Training will be performed soon, and this SOP may be updated following the training. ▪ There were no additional comments or concerns with the updated procedures. Action: The committee unanimously approved: **SOP# 4-28-65 Use of X-Cube MicroCT Scanner for *in vivo* Imaging (New)** as written.
Report:	**Biosafety Officer (BSO) Report/Becky Anderson** ▪ Becky Anderson reviewed the BSO Report. ▪ Becky Anderson described one incident. An individual was cut while cleaning a cryostat machine. The individual thought the blade was removed and reached into the machine and cut themselves. The individual followed the correct exposure procedures. The individual immediately performed first aid, contacted their supervisor, and reported to OMS. Following the incident, the individual was advised to visually confirm the blade has been removed and to limit distractions when using the cryostat.
Report:	**Occupational Safety and Health Manager Report/Seth Cooley** • Nothing to report
Report	**IRF Biosafety Manager/Responsible Official Report/Megan Brose** • RML is planning another COVID booster clinic. BSL-4 s(b)(6); (b)(3):42 shutdown is scheduled for the beginning of the year. No additional select agent updates.
Report	**Associate Director Report/Marshall Bloom** • Not present

Around the room	• Becky Anderson informed the committee that Andrea Marzi will be the Acting Chair for this meeting, as Sue Priola and Bob Heinzen were both unable to attend. • Andrea Marzi asked for an update on the (b)(6) Dual Use Review that was discussed at the last meeting. • Becky Anderson informed the committee that the Dual Use Research Mitigation Plan (DURMP) was completed by (b)(6) The NIH Dual Use Review Committee asked for additional information after the DURMP was submitted. Currently (b)(6) is adding additional information to the DURMP, and it will be resubmitted to the NIH Dual Use Review Committee.

Other issues	▪ None

Next Meeting:

- Date: January 20, 2021
- Place: online via Zoom
- Time: 1:00 PM

RML Biosafety Committee Meeting
December 16, 2021
Biosafety Officer Report

1) Requests approved by BSO since last meeting:

(1) Feldmann (LV) PRD 18-90 Amend

(a) Add intradermal route of inoculation

2) ***New requests approved by committee via electronic review:***

(a) *None*

3) ***New requests***

a) *Pathogen Registration Documents*

i) ***New***

(a) *None*

ii) ***Renew***

(a) *Feldmann (LV) PRD 21-193*

iii) ***Amend***

(a) *Hackstadt (LB) PRD 17-37*

(b) *Feldmann (LV) PRD 17-143*

(c) *Feldmann (LV) PRD 17-123*

b) *Registration Documents for Recombinant Nucleic Acid Experiments*

i) ***New***

(a) *Bloom (LV) RD 21-459*

ii) ***Renew***

(a) *None*

iii) ***Amend***

(a) *None*

c) ***Inactivation Procedure Reviews***

(a) *None*

d) ***Standard Operating Procedures***

(a) ***Draft MCL Operations and Safety Procedures (OSP)***

(a) *Annual review, minor updates*

(b) ***Draft SOP#4-28-39 Chicken Procedures in Level 4 biocontainment***

(a) *Combined procedures into a single SOP*

(c) ***Draft SOP#4-28-53 Rabbit Procedures in Level 4 biocontainment-***

(a) *Combined procedures into a single SOP*

(d) ***Draft SOP#4-28-63 Rodent Transmission Caging Operation for Aerosol exposure***

(a) Add a section on caging for analysis of droplets

(e) ***Draft SOP#4-28-65 Use of X-Cube MicroCT Scanner for in vivo imaging***

(a) *New SOP*

4) ***Animal Study Protocols Review***

Title	*Associated PRD*	*Associated RD*	*Reviewer*
Testing vaccine efficacy of modified virus-like particles in protection against SARS-CoV2 in mice.	*17-143*	*N/A*	(b)(6); (b)(3):42 U.S.C. 262a(h) (Public Heatlh Security and Bioterrorism Preparedness
Intravital microscopy of neutrophil responses to Y. pestis in the skin of Ltb4R1 knockout mice	*21-66*	*20-320*	
Efficacy of an advanced VSV-based Nipah virus vaccine against heterologous Hendra virus challenge in the Syrian Hamster Model	*18-91* *18-82*	*20-404*	*B. Anderson*
Assessment of Lloviu and Tai Forest virus pathogenicity in a murine infection model	*18-90*	*21-407*	(b)(6)
Contribution of gliosis during prion infection of the CNS in mice	*16-190*	*N/A*	*B. Anderson*
Influence of glucose-6-phosphate dehydrogenase deficiency on prion disease pathogenesis in mice	*17-198*	*N/A*	*B. Anderson*
Influence of GABRA1 & GABRA2 knock-out on prion disease pathogenesis in mice	*17-198*	*N/A*	*B. Anderson*
Bioassay of cerebral organoids for confirmation of prion infection in mice	*17-197* *17-198* *17-199*	*N/A*	*B. Anderson*
Evaluate the adaptive immune response to Francisella tularensis in itaconate deficient mice	*18-73* *18-71*	*N/A*	(b)(6); (b)(3):42 U.S.C. 262a(h)

5) ***Biosafety Training Performed – Megan Brose, Rebecca Anderson,*** (b)(6)

Type of Training	*Number of Sessions*	*Number of Employees Trained*
BSL-3 Laboratory Biosafety	*2*	*2*
BSL-4 Laboratory Biosafety-Initial	*2*	*3*
BSL-4 Laboratory Biosafety-Refresher	*N/A*	*N/A*
Laboratory Biosafety Support Staff-Initial	*N/A*	*N/A*
Laboratory Biosafety Support Staff-Refresher	*N/A*	*N/A*
Select Agent Initial Training	*1*	*1*
Select Agent visitor/BSL-3/4 visitor	*7*	*27*
New Employee Training	*3*	*4*
Full length Clone lab-Annual Refresher	*N/A*	*N/A*

6) ***Safety Audits and Inspections***

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

a) *Biological Incident Report:*
   i) *Summarized cut finger on cryostat in BSL-2 lab.*

7) ***Other Issues –***
   i) *None*

Agenda

RML Biosafety Committee Virtual Meeting
January 20, 2022

I. Old Business
   A. Draft minutes of December 16, 2021 meeting

II. New Business
   A. Committee Business
      1. Pathogen Registration Documents (1)
      2. Inactivation Validation Study
         a. *R. Rickettsia* tick inactivation procedures
      3. SOPs:
         a. Draft BSL-3 (b)(6) Biosafety Plan for Ticks

   B. BSO/Responsible Official report (Dr. Becky Anderson)

   E. Occupational Safety & Health Manager report (Seth Cooley)

   F. IRF Biosafety Manager Report (Lt. Cmdr. Megan Brose)

   G. Associate Director Report (Dr. Marshall Bloom)

   H. Comments from around the room

Attachments:
1. Draft minutes of December 16, 2021 meeting (1 file)
2. Pathogen Registration Documents (1 file)
3. Inactivation validation study (1 file)
4. SOPs (1 file)
5. Meeting Agenda (1 file)

NEXT MEETING: February 17, 2022 via Zoom

NIH RML Institutional Biosafety Committee Minutes
January 20, 2022 (1:01 PM – 1:53 PM)
Zoom Virtual Meeting

Members Present:

☑ Sue Priola, Chair	☐ Marcie Caldwell (EO)	☑ Jamie Lovaglio
☐ Bob Heinzen, Vice Chair	☐ Bruce Chesebro (EO)	☑ Andrea Marzi
☑ Becky Anderson	☑ Seth Cooley	☑ Alida Merritt
☐ Alan Applebury	☐ Frank DeLeo (EO)	☑ Greg Saturday
☑ Chris Bosio	☐ Heinz Feldmann (EO)	☐ Alexandra Scranton
☐ Marshall Bloom (EO)	☐ Erik Hoover	☐ Brian Vickrey
☑ Megan Brose	☑ Clay Jarrett	☑ Clayton Winkler
☐ Larry Brouwer	☐ Josh Kellar (EO)	
☐ Carol Calderwood	☑ Scott Kobayashi	

(EO) *ex officio*

Guests: (b)(6)
(b)(6)

Announcements

I. None

Old Business

I. Review of Past IBC Meeting Minutes
    a. December 16, 2021 Minutes
        i. The minutes were unanimously approved as written.

New Business

I. Registration of Material (Potentially) Infectious for Humans, Plants or Animals
    a. PRD 22-137 Norovirus – Elizabeth Fischer (New)
        i. Becky Anderson summarized the PRD. This new registration is to perform CryoEM on norovirus samples from the VRC. Samples are expected to be received pre-frozen on the grids. Human norovirus is known to cause gastrointestinal infections. There is no vaccine or treatment available. The SOP mentioned in the protocol for placing the samples on the grid was not attached.
        ii. No animal studies were submitted, reviewed, or approved.
        iii. Work with Norovirus is approved at BSL-2. Care should be taken to minimize worker exposure to aerosols.
        iv. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
        v. The committee unanimously approved with minor modifications.
            1. Attach SOP for placing the samples on the grid.

II. Registration of Recombinant DNA Experiments
   a. None

III. Full Committee Review of Inactivation Procedures
   a. (b)(6) Infected Tick Inactivation Experiments – (b)(6)
      i. Sue Priola informed the committee that there is inactivation data to review for BSL-3 (b)(6) lab. Included in this month's submission is testing data for paraformaldehyde, methanol, Laemmli sample buffer, and Trizol inactivation of *Rickettsia rickettsia* in infected backless ticks. The testing results were summarized for the inactivation of *R. rickettsia* in the backless tick model. The maximum titer of *R. rickettsia* was used. All necessary controls were included. Samples were plated in duplicate across three independent experiments.
      ii. Sue Priola noted that the monolayer was disrupted in the first Trizol experiment, but the cells were alive in the two subsequent experiments. Sue Priola asked about the final recovered titer for the positive control. (b)(6) commented that the titer in the positive control was not calculated.
      iii. Andrea Marzi commented the maximum titer should be included in the SOP and the titer calculated from the positive control. (b)(6) oted that there is a possibility of *Rickettsia* growth in the tick tissue as well. The committee agreed that maximum titer that was verified needs to be stated.
      iv. Bob Heinzen asked via email if the bead beater step was done in the BSC. (b)(6) confirmed this was correct. This will be specified in the protocol.
      v. Sue Priola asked if backless ticks would be exposed longer to the *R. rickettsia* solution than listed in the inactivation procedure. (b)(6) onfirmed that they would like to try for longer exposure times than was tested. Becky Anderson noted that inactivation this titer could be approved, and if higher titers are seen then additional inactivation validation data would be needed. The committee agreed.
      vi. Becky Anderson noted that this procedure is currently only for backless ticks. Sue Priola agreed that the back should be removed from all ticks during the inactivation.
      vii. Clayton Winkler noted that the Trizol inactivation states 5 minutes and not 10 minutes on first page of the inactivation procedure.
      viii. There were no additional comments or concerns with the inactivation data.
      ix. The committee unanimously approved with minor modifications.
         1. Determine the positive control titer as the maximum titer that will be inactivated.
         2. Change Trizol incubation time to 10 minutes on first page of the protocol.

IV. Standard Operating Procedures
   a. (b)(6) Biosafety Plan for Ticks (New)
      i. Sue Priola introduced the SOP for the committee.
      ii. Bob Heinzen asked via email if glass capillary tubes were being used. (b)(6) noted that they will only use plastic capillary tubes.
      iii. Clayton Winkler asked about the safety margins described in Section 8.3. It was not doubled for Trizol to 20 minutes. It was also noted that 1mL of solution may not cover a 6-well plate as noted in section 8.0. Remove 6-well plate option from the protocol.
      iv. Sue Priola asked if ticks would be observed during the 15 minutes to 5 hour infection time. (b)(6) confirmed that is correct.

v. Andrea Marzi asked about dissolving the tissue in instead of using the whole tick and bead beating as seen in the inactivation procedures. A(b)(6) noted that immunofluorescence assay could not be done on bead beaded tissue because it will destroy the structure. For Trizol and Western Blot, the bead-beating step could be added to the SOP.
vi. Sue Priola asked about the ticks being placed in tubes versus the 24-well plate which was a change to the validated procedures. Becky Anderson noted that the solution should cover the tick and the sample should be transferred to a clean tube or plate following inactivation.
vii. Becky Anderson noted that in the future (b)(6) would like to do animal work but that is not included here.
viii. There were no additional comments or concerns with the SOP.
ix. The committee unanimously approved with minor modifications.
    1. Add maximum titer that will be inactivated.
    2. Specify plastic capillary tubes will be used.
    3. Double the safety margin of Trizol inactivation to 20 minutes.
    4. Remove 6-well plate in Section 8.0.
    5. Include that bead beating will be done in a BSC.
    6. Included bead beating step for Trizol and Western Blot inactivation procedures.
    7. Add language that samples will be transferred to a clean tube or plate after inactivation.

b. Draft SOP 4-28-17 Nonhuman Primate Procedures in Level 4 Biocontainment (Update)
    i. Becky Anderson summarized the SOP for the committee. RMVB would like the ability to pair house NHPs prior to procedures being done. All subsequent work will be done the NHP's housed separately. The intrarectal route of inoculation was also added.
    ii. Megan Brose asked if we should include that this route of inoculation is only approved for non-select agent work. Becky Anderson noted that we have not done that for other routes of inoculation.
    iii. Sue Priola asked on pg 5 B.3.a.1. Clean the cage before removing the animal from the cage. Andrea Marzi noted that the cages are cleaned daily and the language is correct.
    iv. There were no additional comments or concerns with the updated procedures.
    v. The committee unanimously approved as written.

V. Annual Reviews
    a. None

Reports

I. Biosafety Officer Report – Becky Anderson
    a. Becky Anderson presented the BSO report.
II. Occupational Safety and Health Manager Report – Seth Cooley
    a. Nothing to report
III. IRF Biosafety Manager/Responsible Official Report – Megan Brose
    a. Notified by DSAT that the annual BSL-4 inspection will be scheduled for May 2-6, 2022.
    b. Form 3 submitted for samples containing reconstructed 1918 influenza virus that were removed from the BSL-4 using a non-validated inactivation method. A BSL-4 approved Trizol protocol was used, but this was not approved for Orthomyxoviruses. The PI signing for the removal of the samples did not catch the error, and the samples were removed to the BSL-2. Subsequently,

RNA extraction was performed in the BSC. Once the error was discovered, the samples were moved to a select agent registered space. The samples will be moved to the BSL-4 and destroyed. Trizol is known to inactivate reconstructed 1918 influenza virus and those studies were performed at NIH Bethesda. Corrective actions include retraining the individual and PI on SOPs, reiterating the responsibilities as a PI signing for samples, LV will work to validate more Orthomyxovirus inactivations, a table of viruses and viral families will be included in the inactivation SOPs and the dunk tank logs, and the use of an electronic sample removal log will be considered.

IV. Associate Director Report – Marshall Bloom
    a. Not Present

Around the Room

I. None

Other Issues

I. None

Next Meeting

I. February 17, 2022 at 1pm via Zoom

RML Institutional Biosafety Committee Meeting

Biosafety Officer (BSO) Report

January 20, 2022

Business Conducted since the last IBC Meeting

A. BSO approvals
   a. None

B. Electronic business
   a. None

New business for IBC meeting

A. Pathogen Registration Documents
   a. New
      i. Fischer PRD-22-137
   b. Renew
      i. None
   c. Amend
      i. None

B. Registration Documents for Recombinant Nucleic Acid Experiments
   a. New
      i. None
   b. Renew
      i. None
   c. Amend
      i. None

C. Inactivation Procedure Reviews
   a. (b)(6) *R. rickettsii* infected tick inactivation validation

D. Standard Operating Procedures
   a. (b)(6) Biosafety Plan for Ticks
      i. New plan
   b. SOP#4-28-17 Non-human Primate Procedures in Level 4 Biocontainment
      i. Add language for pair or group housed NHPs
      ii. Add intrarectal inoculation procedures

Biosafety Activities since the last IBC Meeting

A. Animal Study Protocols Review- Performed by Megan Brose, Rebecca Anderson, (b)(6)

ASP Title	Associated PRD	Associated RD	Reviewer
Identify contributions of host derived lipids in control of SARS-CoV-2 in mice	20-223	N/A	(b)(6)
Maintenance of Experimental Flea Colonies Using Mice	21-66	20-32 21-321	R. Anderson
Continued Evaluation of an RNA vaccine for CCHFV in mice	18-92	17-452	M. Brose

B. Biosafety Training- Performed by Megan Brose, Rebecca Anderson (b)(6)

Type of Training	Number of Sessions	Number of Employees Trained
New Employee	1	2
Select Agent-Initial	1	3
Select Agent- Refresher	N/A	N/A
Select Agent- Visitor	1	2
BSL-3 Laboratory Biosafety-Initial	N/A	N/A
BSL-4 Laboratory Biosafety-Initial	N/A	N/A
Suit Training	1	1
Checklist Training	5	1
BSL-4 Laboratory Biosafety-Refresher	N/A	N/A
Laboratory Biosafety Support Staff-Initial	N/A	N/A
Laboratory Biosafety Support Staff-Refresher	4	66

C. Safety Audits and Inspections

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

D. Biological Incidents to Report
   a. None

E. Other Issues
   a. None

NIH RML Institutional Biosafety Committee Meeting

Agenda for March 17, 2022
Location: Virtual via Zoom

Old Business

A. Draft minutes of February 17, 2022 meeting

New Business

A. Committee Business
    1) PRD-22-191 (Renewal) PI: Priola
    2) PRD-22-132 (Renewal) PI: Feldmann
    3) PRD-22-138 (Renewal) PI: Feldmann
    4) PRD-22-81 (Renewal) PI: Feldmann
    5) RD-22-431 (Renewal) PI: Feldmann Reviewers: Clayton Winkler, Scott Kobayashi
    6) Flavivirus methanol inactivation validation (New)
    7) Rickettsia tick inactivation validation (Updated)
    8) Draft (b)(6) BSL-3 OSP; (New SOP) SOP#4-28-17 Methanol Inactivation of Yellow Fever Virus
    9) Draft (b)(6) Biosafety Plan for ticks (Updated)
    10) Draft SOP#4-28-15 Entry-Exit Procedures into Maximum Containment labs (Updated)
    11) Draft SOP#4-28-34 Biosafety Cabinet Procedures (Updated)

B. BSO report (Dr. Becky Anderson)
C. Occupational Safety & Health Manager report (Seth Cooley)
D. IRFBSM/Responsible Official Report (LCDR Megan Brose)
E. Associate Director Report (Dr. Marshall Bloom)
F. Comments from around the room

Next Meeting: April 21, 2022 via Zoom

PRD- Pathogen Registration Document
RD- Recombinant DNA Registration Document
SOP-Standard Operating Procedures
BSO-Biosafety Officer
IRFBSM-Integrated Research Facility Biosafety Manager

NIH RML Institutional Biosafety Committee Minutes

February 17, 2022 (1:00 PM – 1:37 PM)
Zoom Virtual Meeting

Members Present:

☑ Sue Priola, Chair	☐ Marcie Caldwell (EO)	☑ Jamie Lovaglio
☑ Bob Heinzen, Vice Chair	☐ Bruce Chesebro (EO)	☑ Andrea Marzi
☑ Becky Anderson	☑ Seth Cooley	☐ Alida Merritt
☐ Alan Applebury	☐ Frank DeLeo (EO)	☑ Greg Saturday
☑ Chris Bosio	☐ Heinz Feldmann (EO)	☐ Alexandra Scranton
☐ Marshall Bloom (EO)	☐ Erik Hoover	☐ Brian Vickrey
☑ Megan Brose	☑ Clay Jarrett	☑ Clayton Winkler
☐ Larry Brouwer	☐ Josh Kellar (EO)	
☐ Carol Calderwood	☑ Scott Kobayashi	

(EO) *ex officio*

Guests: (b)(6)

Announcements

I. None

Old Business

I. Review of Past IBC Meeting Minutes
   a. January 20, 2022 Minutes
      i. The minutes were unanimously approved with minor modifications.
         1. Correct typos on Pg 3 Section 5 and Pg 3 Section b.

New Business

I. Registration of Material (Potentially) Infectious for Humans, Plants or Animals
   a. PRD-18-103 La Crosse virus – (b)(6) (Amend)
      i. Becky Anderson summarized the PRD. The first amendment is to add Trivittatus virus and the second amendment is to add co-infection studies with California Encephalitis virus (CEV), Trivittatus virus (TVTV) and Cache Valley Virus (CVV) in mice. Co-infection of these viruses may enhance the pathogenicity of less virulent Orthobunyavirus strains, but not over the most virulent strain, La Crosse virus.
      ii. Sue Priola asked if there will be co-infection with recombinant materials. (b)(6) confirmed that this will not be done.
      iii. No new animal studies were submitted, reviewed, or approved.
      iv. Work is approved at BSL-2.
      v. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
      vi. The committee approved both amendments as written. Clayton Winkler recused.

b. PRD-18-91 Henipavirus – Heinz Feldmann (Amend)
    i. Becky Anderson summarized the PRD. This amendment is to add Ghana bat virus. There are limited studies on this virus as it has been sequenced but not yet cultured. No observation of spillover has been seen in humans even in places where animals are in close contact with humans, suggesting limited zoonosis. This virus is related to Hendra and Nipah virus. However fusogenicity of F and G glycoproteins is restricted to cell lines of bat origin further suggesting a species restriction with Ghana bat virus.
    ii. No new animal studies were submitted, reviewed, or approved.
    iii. Work with Ghana bat virus is approved at BSL-3/ABSL-3.
    iv. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
    v. The committee unanimously approved as written.
c. PRD-21-233 Borrelia spp. – (b)(6) (Amend)
    i. Becky Anderson summarized the PRD. This amendment is to add *Borrelia hermsii* and *Borrelia turicatae*. They both cause tickborne relapsing fever similar to the other Borrelia species listed on the PRD. The natural route of infection is through a tick bite. Antibiotic treatment is available.
    ii. No new animal studies were submitted, reviewed, or approved.
    iii. Work with *Borrelia hermsii* and *Borrellia turicatae* is approved at BSL-2/ABSL-2.
    iv. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
    v. The committee unanimously approved as written.

II. Registration of Recombinant DNA Experiments
a. RD-21-134 Borrelia spp. – (b)(6) (Amend)
    i. Chris Bosio and Scott Kobayashi were reviewers.
    ii. Chris Bosio summarized the RD. This amendment is to add *Borrelia hermsii*, *Borrelia turicatae* and shuttle plasmids to the study. The plasmid currently has ampicillin resistance and should be replaced with kanamycin resistance instead. Vector map was included.
    iii. Sue Priola asked for additional confirmation that the ampicillin resistance is replaced on the shuttle plasmid.
    iv. Scott Kobayashi had no additional comments.
    v. Animal studies with mice were proposed.
    vi. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
    vii. Research using prokaryotic cells is approved at BSL-2/ABSL-2 under section III-D-1-a of the NIH Guidelines.
    viii. The committee unanimously approved with minor modification.
        1. Confirm that ampicillin resistance will be replaced with kanamycin resistance.
b. RD-21-127 Lentiviral vectors – Catharine Bosio (Amend)
    i. Clayton Winkler and Andrea Marzi were reviewers
    ii. Clayton Winkler summarized the RD. This amendment is to add pWRI-IRES-Puro-Ak-ACE2 lentiviral particles to derive mouse cell lines for expression of ACE2.
    iii. Andrea Marzi asked if the transduced cells needed to be added to another registration. Becky Anderson confirmed that they did not need to be added to another registration.
    iv. No new animal studies were submitted, reviewed, or approved.

v. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
vi. Research using eukaryotic cells is approved at BSL-2 under section III-D-3-a of the NIH Guidelines.
vii. The committee unanimously approved as written. Chris Bosio recused.

c. RD-21-136 Bordetella pertussis – Catharine Bosio (Amend)
i. Sue Priola and Clay Jarrett were reviewers
ii. Sue Priola summarized the RD. This amendment is to add mouse experiments to their *Bordetella pertussis* registration to track T cell response.
iii. Clay Jarrett had no additional comments.
iv. Animal studies with mice were proposed.
v. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
vi. Research using prokaryotic cells is approved at BSL-2/ABSL-2 under section III-D-1-a of the NIH Guidelines.
vii. The committee unanimously approved as written. Chris Bosio recused.

III. Full Committee Review of Inactivation Procedures
a. None

IV. Standard Operating Procedures
a. Draft SOP 4-28-63 Rodent Transmission Caging Operation for Aerosol Exposure-update cage testing methods
i. Becky Anderson summarized the updates to the protocol. Initially two types of testing were required for testing leaks in the caging system, (1) positive pressure and (2) particulate test. After multiple rounds of testing the caging systems, Seth Cooley and (b)(6) are confident that the particulate test is the more sensitive test, and it would be sufficient to only use that test.
ii. Seth Cooley confirmed that this is correct.
iii. Clayton Winkler asked about the change in the flow rate. Seth Cooley noted that this is due to the changes in the length of the connector tubes between the cages.
iv. There were no additional comments from the committee.
v. The committee unanimously approved as written.

V. Annual Reviews
a. None

Reports

I. Biosafety Officer Report – Becky Anderson
a. Becky Anderson presented the BSO report.
b. An incident report was submitted to Office of Science Policy. This report is for the incident that was reported at the January IBC meeting. The risk of exposure was determined to be negligible. The incident has been investigated to determine the root cause and appropriate corrective actions are being taken.

II. Occupational Safety and Health Manager Report – Seth Cooley
a. Nothing to report.

III. IRF Biosafety Manager/Responsible Official Report – Megan Brose

a. BSL-3 (b)(6) annual shutdowns are completed.
b. BSL-4 (b)(6); (b)(3):42 U.S.C. annual shutdowns will be occurring soon.

IV. Associate Director Report – Marshall Bloom
a. Not present.

Around the Room

I.

Other Issues

I.

Next Meeting

I. March 17, 2022 at 1 pm via Zoom

NIH RML Institutional Biosafety Committee Meeting

Biosafety Officer (BSO) Report

February 17, 2022

Business Conducted since the last IBC Meeting

A. BSO approvals
   a. Steele-Mortimer PRD 18-44. Add work with NHP tissues, blood, and body fluids
   b. Scott PRD 15-176 NHP tissues, blood, and body fluids. Change PI from Dana Scott to Patrick Hanley

B. Electronic business
   a. None

New business for IBC meeting

A. See agenda.

Biosafety Activities since the last IBC Meeting

A. Animal Study Protocols Review- Performed by Megan Brose, Rebecca Anderson, (b)(6)

ASP Title	Associated PRD	Associated RD	Reviewer
Role of Tryptophan in the Development of Murine T cell Responses	18-73 18-71	N/A	(b)(6)
Evaluation of Antivirals using Mouse-adapted Crimean Congo Hemorrhagic Fever Virus	18-92	N/A	R. Anderson
Treatment of Viral Encephalitis with Small Molecule Compounds in Mice	18-103	N/A	(b)(6)

B. Biosafety Training- Performed by Megan Brose, Rebecca Anderson, (b)(6)

Type of Training	Number of Sessions	Number of Employees Trained
New Employee	2	6
Select Agent-Initial	1	1
Select Agent- Refresher	n/a	n/a
Select Agent- Visitor	1	1
BSL-3 Laboratory Biosafety-Initial	n/a	n/a
BSL-4 Laboratory Biosafety-Initial	n/a	n/a
Suit Training	n/a	n/a
Checklist Training	5	1
BSL-4 Laboratory Biosafety-Refresher	n/a	n/a
Laboratory Biosafety Support Staff-Initial	n/a	n/a
Laboratory Biosafety Support Staff-Refresher	2	13

C. Safety Audits and Inspections

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

D. Biological Incidents to Report
   a. January report to Office of Science Policy (OSP)
      a. Request for more information received 3/4/2022. Responses due 3/18/2022

E. Other Issues
   a. None

NIH RML Institutional Biosafety Committee Meeting

Agenda for March 17, 2022
Location: Virtual via Zoom

Old Business

A. Draft minutes of February 17, 2022 meeting

New Business

A. Committee Business
    1) PRD-22-191 (Renewal) PI: Priola
    2) PRD-22-132 (Renewal) PI: Feldmann
    3) PRD-22-138 (Renewal) PI: Feldmann
    4) PRD-22-81 (Renewal) PI: Feldmann
    5) RD-22-431 (Renewal) PI: Feldmann Reviewers: Clayton Winkler, Scott Kobayashi
    6) Flavivirus methanol inactivation validation (New)
    7) Rickettsia tick inactivation validation (Updated)
    8) Draft (b)(6) BSL-3 OSP; (New SOP) SOP#4-28-17 Methanol Inactivation of Yellow Fever Virus
    9) Draft (b)(6) Biosafety Plan for ticks (Updated)
    10) Draft SOP#4-28-15 Entry-Exit Procedures into Maximum Containment labs (Updated)
    11) Draft SOP#4-28-34 Biosafety Cabinet Procedures (Updated)

B. BSO report (Dr. Becky Anderson)
C. Occupational Safety & Health Manager report (Seth Cooley)
D. IRFBSM/Responsible Official Report (LCDR Megan Brose)
E. Associate Director Report (Dr. Marshall Bloom)
F. Comments from around the room

Next Meeting: April 21, 2022 via Zoom

PRD- Pathogen Registration Document
RD- Recombinant DNA Registration Document
SOP-Standard Operating Procedures
BSO-Biosafety Officer
IRFBSM-Integrated Research Facility Biosafety Manager

NIH RML Institutional Biosafety Committee Minutes

March 17, 2022 (1:00 PM – 3:00 PM)
Zoom Virtual Meeting

Members Present:

☑ Sue Priola, Chair	☐ Marcie Caldwell (EO)	☑ Jamie Lovaglio
☑ Bob Heinzen, Vice Chair	☐ Bruce Chesebro (EO)	☑ Andrea Marzi
☑ Becky Anderson	☑ Seth Cooley	☐ Alida Merritt
☐ Alan Applebury	☐ Frank DeLeo (EO)	☑ Greg Saturday
☑ Chris Bosio	☐ Heinz Feldmann (EO)	☐ Alexandra Scranton
☐ Marshall Bloom (EO)	☑ Erik Hoover	☐ Brian Vickrey
☑ Megan Brose	☑ Clay Jarrett	☑ Clayton Winkler
☐ Larry Brouwer	☐ Josh Kellar (EO)	
☐ Carol Calderwood	☑ Scott Kobayashi	

(EO) *ex officio*

Guests: (b)(6)
(b)(6)

Announcements

I. None

Old Business

I. Review of Past IBC Meeting Minutes
   a. February 17, 2022 Minutes
      i. The minutes were unanimously approved with minor modifications.
         1. Update to indicate Chris Bosio abstained for Katy Bosio's amendments RD-21-127 and RD-21-136.

New Business

I. Registration of Material (Potentially) Infectious for Humans, Plants or Animals
   a. PRD-22-191 Transmissible spongiform encephalopathies – Sue Priola (Renewal)
      i. Becky Anderson summarized the PRD. This is a renewal for work with TSE agents. No new work was added. The Priola lab studies prion infection and pathogenesis. Human TSEs are registered on a different PRD.
      ii. Sue Priola asked about updating the permit in the PRD. Becky Anderson will add the permit to the PRD.
      iii. Animal studies with mice and hamsters were proposed.
      iv. Work with TSE is approved at BSL-2/ABSL-2.
      v. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
      vi. The committee unanimously approved as written.

b. PRD-22-132 Influenza virus Type A – Heinz Feldmann (Renewal)
    i. Becky Anderson summarized the PRD. This is a renewal for work with influenza virus type A. No changes were made to this PRD. This PRD covers Influenza A subtypes H1-H18 with the exception of 1918 (H1N1). HPAI subtypes H5 and H7 and Low path avian influenza H7N9 are covered under separate PRDs. The specific biosafety level recommendations are listed in the Recommendations section. Enhanced BSL-2/ABSL-2 will be used for equine and swine influenza. A brief description of these enhancements needs to be included.
    ii. Animal studies with ferrets, NHPs, and mice were proposed.
    iii. Work with Influenza A is approved as follows:
        1. Circulating human strains (e.g. H1/H3/B): BSL-2/ABSL-2
        2. Low pathogenicity avian influenza (LPAI): H1-4, H6, H8-16: Enhanced BSL-2/ABSL-2 as directed by regulatory authorities
        3. Equine and Swine influenza: Enhanced BSL-2/ABSL-2 as directed by regulatory authorities
        4. Bat influenza strains: H17, H18, N10, N11: BSL-2/ABSL-2.
        5. Non-contemporary, wild-type human influenza (H2N2): BSL-3/ABSL-3 (some experiments performed at BSL-4/ABSL-4)
        6. Human and swine origin H1N1: BSL-3/ABSL-3 (some experiments performed at BSL-4/ABSL-4)
        7. SOPs on file for BSL-3 and BSL-4/ABSL-4 work must be followed.
        8. See associated RDs (20-416 and 21-433) for biosafety levels for handling recombinant viruses.
        9. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 375-9755.
    iv. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
    v. The committee unanimously approved with minor modifications.
        1. Update recommendations section to include additional information on enhanced BSL-2/ABSL-2.
c. PRD-22-138 Arenaviruses – Heinz Feldmann (Renewal)
    i. Becky Anderson summarized the PRD. This is a renewal for work with multiple arenaviruses: IPPY, Pichinde, Tacaribe, LCMV, Mopeia and Mobala. The Feldmann lab studies virus pathogenesis for the purpose of developing vaccines and medical countermeasures. There is no new work described in this renewal.
    ii. Sue Priola asked about the toxin questions listed in the Pathogen and/or Toxin section. One is currently marked “No” and should be “N/A”, as they are not working with any toxins. It was also noted in the eukaryotic section that the term “New Work” was used. This language should be removed as there is no new work described in this renewal. Sue Priola also asked if this was human LCMV. Becky Anderson confirmed this was correct.
    iii. No animal studies were submitted, reviewed, or approved.
    iv. Work with Arenaviruses are approved as follows:
        1. BSL-2: IPPY, Pichinde, Tacaribe, and LCMV (see below for additional precautions)
        2. BSL-3: Mopeia, Mobala

3. For LCMV: BSL-2 with additional practices: all work with infectious material is conducted in a biosafety cabinet, centrifugation of infectious materials must be carried out in sealed safety cups or removable rotors that can be loaded and unloaded in a biosafety cabinet. Women who are pregnant or are thinking of becoming pregnant are encouraged to notify the Laboratory Supervisor and the RML OMS Nurse. This is in order to assure that they are aware of any potential risks to themselves or the fetus and to determine if any additional risk reduction measures should be taken.
4. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 375-9600.

v. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
vi. The committee unanimously approved with minor modifications.
1. Update toxin questions to N/A.
2. Delete "New Work" in the eukaryotic section.

d. PRD-22-81 Hantavirus – Heinz Feldmann (Renewal)
i. Becky Anderson summarized the PRD. This is a renewal for work with hantaviruses. There were no changes to the PRD or new work added. The lab studies the viral life cycle, pathogenesis and evaluates medical countermeasures.
ii. Sue Priola asked about the toxin questions listed in the Pathogen and/or Toxin section. One is currently marked "No" and should be "N/A", as they are not working with any toxins.
iii. Animal studies with hamsters, ferrets, rabbits, deer mice, and NHPs were proposed.
iv. Work with Hantaviruses are approved as follows:
1. Laboratory studies with Hantaviruses are approved at BSL-3.
2. Animal studies with Hantaviruses are approved at ABSL-4.
3. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 375-9600.

v. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
vi. The committee unanimously approved with minor modifications.
1. Update toxin questions to N/A.

II. Registration of Recombinant DNA Experiments
a. RD-22-431 – Heinz Feldmann (Renewal)
i. Reviewers: Clayton Winkler and Scott Kobayashi
ii. Clayton Winkler summarized the RD. This is a renewal for the use of recombinant viral, host cellular and reporter proteins expressed by plasmid expression systems to characterize pathogen protein function and host interactions. Pathogen proteins to be used in these studies primarily include those from filo-, bunya-, arena-, paramyxo-, rhabdo-, orthomyxo-, corona-, and flaviviruses, but also include non-viral pathogens such as Plasmodium. None of the sequence are known to be toxic or pathogenic. Only

2/3 of the viral genome will be used, except Nairovirus due to the genome size. There was no additional work added to this renewal. Research products section references Table 2 but it is not present. NIH Guideline III-E-1 should be added to the research products section. pCR-XL-2-TOPO and pCR-Blunt II-TOPO plasmids maps are attached but not listed in the protocol. The exosome plasmid is not referenced in the text either.

iii. Scott Kobayashi had no additional comments.
iv. Andrea Marzi asked about Lloviu virus. This virus has recently been isolated from a bat, and we no longer only have sequence data. For Mengla virus and Bombali virus, they have sequence data only. The description provided in dual use section needs to be updated to reflect this information. The pathogen and protein table at the end of the document may need to be updated.
v. Animal studies with rabbits, hamsters, and NHPs were proposed.
vi. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
vii. Research using prokaryotic cells is approved at BSL-2/ABSL-2 under sections III-D-2-a and III-E-1 of the NIH Guidelines and research using eukaryotic cells is approved at BSL-2/ABSL-2 under section III-D-2-a and III-E-1 of the NIH Guidelines.
viii. The committee unanimously approved with minor modifications.
    1. Remove reference to Table 2.
    2. Add III-E-1 to research products and prokaryote cell section.
    3. Confirm where pCR-XL-2-TOPO and pCR-Blunt II-TOPO are used in the protocol.
    4. Reference exosome plasmid in text.
    5. Update description provided in the dual use question to remove Lloviu virus and add Mengla and Bombali viruses as sequence only.
    6. Update pathogen and protein table.

III. Full Committee Review of Inactivation Procedures
    a. Flavivirus methanol inactivation validation (New)
        i. Sue Priola summarized the inactivation procedure. This procedure is for Yellow Fever virus inactivation by methanol. Appropriate positive and negative controls were provided. Maximum titer was provided. The inactivation validation states 4°C instead of on ice, this should be updated to keep consistent with following SOP.
        ii. There were no additional comments from the committee.
        iii. The committee unanimously approved with minor modifications.
            1. Change on ice or 4°C to be consistent with the SOP.
    b. Rickettsia tick inactivation validation (Updated)
        i. Sue Priola summarized the updates to the inactivation procedure. The inactivation was revalidated for paraformaldehyde and methanol for a higher titer of Rickettsia. The Rickettsia titer in the samples was determined. Part II of the validation covers if bead beating influences the inactivation of the Rickettsia. Results showed that bead beating does not contribute to inactivation of Rickettsia. Appropriate positive and negative controls were provided. The entire sample was assayed.
        ii. There were no additional comments from the committee.
        iii. The committee unanimously approved as written.

IV. Standard Operating Procedures
    a. Draft (b)(6) BSL-3 OSP; (New SOP) SOP#3-28-17 Methanol Inactivation of Yellow Fever Virus

i. Sue Priola summarized the new protocol. This procedure is for methanol inactivation of Yellow Fever virus.
ii. Andrea Marzi asked about the specific notes in the protocol, as the lab may want more flexibility. (b)(6) commented that this is the specific protocol that the lab would follow.
iii. There were no additional comments from the committee.
iv. The committee unanimously approved as written.

b. Draft (b)(6) Biosafety Plan for Ticks (Updated)
i. Sue Priola summarized the updated protocol. This update includes the inactivation validation data discussed above for Rickettsia. The bead beating steps were removed from the protocol.
ii. There were no additional comments from the committee.
iii. The committee unanimously approved as written.

c. Draft SOP#4-28-15 Entry-Exit Procedures into Maximum Containment Labs (Updated)
i. Becky Anderson summarized the updated protocol. This minor change is to update the entry procedure to enter the BSL-4. The autoclaves will no longer be checked upon entry. It will be included in a chore list and not part of the entry sequence.
ii. (b)(6) addressed how the chore list will be implemented.
iii. There were no additional comments from the committee.
iv. The committee unanimously approved as written.

d. Draft SOP#4-28-34 Biosafety Cabinet Procedures (Updated)
i. Becky Anderson summarized the proposed updates to the protocol. This is to change how long the liquid waste from the biosafety cabinets sits in 5% microchem before disposal from overnight to a minimum of 10 minutes.
ii. (b)(6) noted that the high usage of the BSL-4 has led to an increase in the number of liquid waste beakers with 5% microchem that need to sit overnight. They are proposing that an individual would discard their waste after 10 minutes to reduce this issue.
iii. Becky Anderson described the previous microchem validation data. (b)(6) noted that the testing was not performed with high titer stock. In the validation testing, stock virus was added directly to microchem and may not mimic blood or other organic materials. Megan Brose noted that this method of decontamination is used with multiple material types such as plates and blood tubes. Large volumes that contain high organic bioburden was not tested and could potentially be separated out for a longer contact time.
iv. Andrea Marzi noted that specifically during the PBMC procedure, the blood tubes are placed in the beaker at the beginning of the procedure, and they sit for an hour before the procedure is finished. Serum separator tubes may also need a longer contact time due to the presence of the blood clot.
v. Becky Anderson recommended that liquid waste could be inactivated in 10 minutes, and waste with high organic load such as blood tubes and serum separators would sit overnight. The committee agreed with this recommendation.
vi. There were no additional comments from the committee.
vii. The committee unanimously approved with modifications.
1. Update the liquid waste section to allow for 10-minute minimum contact time with 5% microchem and keep waste with higher organic composition, such as blood tubes or serum separators, overnight in 5% microchem.

V. Annual Reviews
    a. None

Reports

I. Biosafety Officer Report – Becky Anderson
    a. Becky Anderson presented the BSO report.
    b. PRD 15-176 will be changed from PI Dana Scott to PI Patrick Hanley. The committee agreed with this change.
    c. In response to the incident reported to OSP last month, a request for more information was requested by OSP. That additional information is being gathered and will be submitted to OSP.
    d. Andrea Marzi asked for an update on (b) (6) proposal that will be presented to the NIH Dual Use Committee. Becky Anderson informed the committee that there were no updates on this proposal.

II. Occupational Safety and Health Manager Report – Seth Cooley
    a. Nothing to report

III. IRF Biosafety Manager/Responsible Official Report – Megan Brose
    a. BSL-4 (b)(6); annual shutdown is complete. BSL-3 (b)(6) annual shutdown is in progress. Our BSL-4 DSAT inspection is scheduled for May.

IV. Associate Director Report – Marshall Bloom
    a. Not present.

Around the Room

I. None

Other Issues

I. None

Next Meeting

I. April 21, 2022 1pm via Zoom

NIH RML Institutional Biosafety Committee Meeting

Biosafety Officer (BSO) Report

February 17, 2022

Business Conducted since the last IBC Meeting

A. BSO approvals
   a. Steele-Mortimer PRD 18-44. Add work with NHP tissues, blood, and body fluids
   b. Scott PRD 15-176 NHP tissues, blood, and body fluids. Change PI from Dana Scott to Patrick Hanley

B. Electronic business
   a. None

New business for IBC meeting

A. See agenda.

Biosafety Activities since the last IBC Meeting

A. Animal Study Protocols Review- Performed by Megan Brose, Rebecca Anderson, (b)(6)

ASP Title	Associated PRD	Associated RD	Reviewer
Role of Tryptophan in the Development of Murine T cell Responses	18-73 18-71	N/A	(b)(6)
Evaluation of Antivirals using Mouse-adapted Crimean Congo Hemorrhagic Fever Virus	18-92	N/A	R. Anderson
Treatment of Viral Encephalitis with Small Molecule Compounds in Mice	18-103	N/A	(b)(6)

B. Biosafety Training- Performed by Megan Brose, Rebecca Anderson, (b)(6)

Type of Training	Number of Sessions	Number of Employees Trained
New Employee	2	6
Select Agent-Initial	1	1
Select Agent- Refresher	n/a	n/a
Select Agent- Visitor	1	1
BSL-3 Laboratory Biosafety-Initial	n/a	n/a
BSL-4 Laboratory Biosafety-Initial	n/a	n/a
Suit Training	n/a	n/a
Checklist Training	5	1
BSL-4 Laboratory Biosafety-Refresher	n/a	n/a
Laboratory Biosafety Support Staff-Initial	n/a	n/a
Laboratory Biosafety Support Staff-Refresher	2	13

C. Safety Audits and Inspections

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

D. Biological Incidents to Report
   a. January report to Office of Science Policy (OSP)
      a. Request for more information received 3/4/2022. Responses due 3/18/2022

E. Other Issues
   a. None

NIH RML Institutional Biosafety Committee Meeting

Agenda for April 21, 2022
Location: Virtual via Zoom

Old Business

A. Draft minutes of March 17, 2022 meeting

New Business

A. Committee Business
    1) RD-22-431 (Renewal) PI: Steele-Mortimer Reviewers: Scott Kobayashi, Chris Bosio
    2) RD-22-137 (New) PI: Steele-Mortimer Reviewers: Clay Jarrett, Clayton Winkler
    3) Orthomyxovirus RLT and Trizol inactivation validation (New)
    4) Draft SOP#4-28-32 Removal of Specimens for Nucleic Acid Extraction (Updated)

B. BSO report (Dr. Becky Anderson)
C. Occupational Safety & Health Manager report (Seth Cooley)
D. IRFBSM/Responsible Official Report (LCDR Megan Brose)
E. Associate Director Report (Dr. Marshall Bloom)
F. Comments from around the room

Next Meeting: May 19, 2022 via Zoom

PRD- Pathogen Registration Document
RD- Recombinant DNA Registration Document
SOP-Standard Operating Procedures
BSO-Biosafety Officer
IRFBSM-Integrated Research Facility Biosafety Manager

NIH RML Institutional Biosafety Committee Minutes

April 21, 2022 (1:01 PM – 1:38 PM)
Zoom Virtual Meeting

Members Present:

☑ Sue Priola, Chair	☐ Marcie Caldwell (EO)	☑ Jamie Lovaglio
☑ Bob Heinzen, Vice Chair	☐ Bruce Chesebro (EO)	☑ Andrea Marzi
☑ Becky Anderson	☑ Seth Cooley	☑ Alida Merritt
☐ Alan Applebury	☐ Frank DeLeo (EO)	☑ Greg Saturday
☑ Chris Bosio	☐ Heinz Feldmann (EO)	☐ Alexandra Scranton
☐ Marshall Bloom (EO)	☑ Erik Hoover	☐ Brian Vickrey
☑ Megan Brose	☑ Clay Jarrett	☑ Clayton Winkler
☑ Larry Brouwer	☐ Josh Kellar (EO)	
☐ Carol Calderwood	☑ Scott Kobayashi	

(EO) *ex officio*

Guests: (b)(6)

Announcements

I. None

Old Business

I. Review of Past IBC Meeting Minutes
   a. March 17, 2022 Minutes
      i. The minutes were unanimously approved with minor modifications.
         1. Sue Priola noted that in new business 1A, Section II, no amendment was needed to submit the updated permit.

New Business

I. Registration of Material (Potentially) Infectious for Humans, Plants or Animals
   a. None

II. Registration of Recombinant DNA Experiments
   a. RD-22-108 – Olivia Steele-Mortimer (Renewal)
      i. Reviewers: Scott Kobayashi and Chris Bosio
      ii. Scott Kobayashi summarized the RD. This is a renewal for *Salmonella typhimurium* mutants and knockouts of different genes will be created. Plasmid maps were attached. Reporter proteins such as GFP will be used. NIH guidelines listed are appropriate and ASPs were attached.
      iii. Chris Bosio had nothing additional to add.
      iv. Sue Priola noted that vectors pIVV3 and pIVV4 were listed but not attached.
      v. Animal studies with mice, rabbits, and guinea pigs were proposed.

vi. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
vii. Research using prokaryotic cells is approved at BSL-2/ABSL-2 under sections III-D-1-a and III-D-2-a of the NIH Guidelines, and research using eukaryotic cells is approved at BSL-2 under sections III-D-1-a of the NIH Guidelines.
viii. The committee unanimously approved with minor modifications.
    1. Add vector maps for pIVV3 and pIVV4.

b. RD-22-137 – Olivia Steele-Mortimer (New)
    i. Reviewers: Clay Jarrett and Clayton Winkler
    ii. Clay Jarrett summarized the RD. This is a new RD to use a commensal *E. coli* reporter system for inflammatory response in *Salmonella* infected mice. Clay Jarrett asked if the integration of the antibiotic resistance gene is stable. The committee agreed that this should be clarified with the PI. The proposed antibiotics resistance genes used are not front-line antibiotics. The NIH guidelines listed in the research products section and prokaryotic section should be updated to III-D-1-a. The biosafety level should also be updated to BSL-2.
    iii. Clayton Winkler had nothing additional to add.
    iv. Animal studies with mice were proposed.
    v. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
    vi. Research using prokaryotic cells is approved at BSL-2/ABSL-2 under sections III-D-1-a of the NIH Guidelines.
    vii. The committee unanimously approved with minor modifications.
        1. Update NIH guidelines under research products and prokaryote section to III-D-1-a.
        2. Update biosafety level to BSL-2.
        3. Clarify that integration of the antibiotics resistance gene is stable in *E. coli*.

III. Full Committee Review of Inactivation Procedures
    a. Orthomyxovirus RLT and Trizol inactivation validation (New)
        i. Sue Priola summarized the inactivation data. This is inactivation testing for the Orthomyoviruses with RLT and Trizol. Infected lung tissue from mice were used as the tissue sample. Appropriate positive and negative controls were included. A maximum titer or tissue weight was described. Sue Priola noted minor typos, including liver tissue should be corrected to lungs and RLT was mentioned instead of Trizol in the Trizol section.
        ii. The committee had no additional comments.
        iii. The committee unanimously approved with minor modifications.
            1. Correct liver to lung tissue.
            2. Correct RLT typos in Trizol section.

IV. Standard Operating Procedures
    a. Draft SOP#4-28-32 Removal of Specimens for Nucleic Acid Extraction (Updated)
        i. Sue Priola summarized the updates to the SOP. This update is to include the validated inactivation methods: RLT and Trizol for Orthomyxoviruses. The SOP matches the inactivation procedure.
        ii. The committee had no additional comments.

iii. The committee unanimously approved as written.

V. Annual Reviews
   a. None

Reports

I. Biosafety Officer Report – Becky Anderson
   a. Becky Anderson presented the BSO report. Additional information was submitted to the Office of Science Policy following their request for information.

II. Occupational Safety and Health Manager Report – Seth Cooley
   a. Nothing to report

III. IRF Biosafety Manager/Responsible Official Report – Megan Brose
   a. BSL-4 (b)(6); (b)(3):42 annual shutdown was completed. CDC DSAT inspection will be April 27-May 5.

IV. Associate Director Report – Marshall Bloom
   a. Not present.

Around the Room

I. Andrea Marzi asked about having a hybrid option for the IBC meeting. This will be further discussed.

Other Issues

I.

Next Meeting

I. May 19, 2022 1pm via Zoom

NIH RML Institutional Biosafety Committee Meeting

Biosafety Officer (BSO) Report

April 21, 2022

Business Conducted since the last IBC Meeting

A. BSO approvals
   a. Haigh PRD 17-197
      i. Add SOP for cutting samples with cryostat. Required staff to wear and N95 for cutting samples. Staff enrolled in respiratory protection program.
   b. Bosio RD-18-125
      i. Add intraperitoneal, intranasal, intravenous and intradermal routes of inoculation for mice
   c. Feldmann RD 20-442
      i. Add an additional CDC Import Permit
   d. Tirloni PRD 20-227
      i. Add intravenous route of inoculation for mice

B. Electronic business
   a. None

New business for IBC meeting

A. See agenda.

Biosafety Activities since the last IBC Meeting

A. Animal Study Protocols Review- Performed by Megan Brose, Rebecca Anderson, (b)(6)

ASP Title	Associated PRD	Associated RD	Reviewer
Determining the effectiveness of a LASV-GP vaccine delivered over a prolonged period with or without nanoparticles in conferring sterile immunity to animals challenged with Lassa virus in a lethal guinea pig model	18-94	17-X-04 (NIH RD)	R. Anderson
Identification of spotted fever group rickettsia determinants of virulence in Guinea pigs.	19-38	19-110	(b)(6); (b)(3):42 U.S.C.
Effect of transgenic Nicotinamide adenine dinucleotide (NAD+) regeneration and oral Nicotinamide	16-190	N/A	M. Brose
Testing the role of natural antibodies with high polyreactivity against exposure to prions in mice	16-190	N/A	R. Anderson
Contribution of bacterial membrane lipids in virulence of *Francisella tularensis* in mice	18-73 18-71	18-125	(b)(6); (b)(3):42 U.S.C.

B. Biosafety Training- Performed by Megan Brose, Rebecca Anderson (b)(6)

Type of Training	Number of Sessions	Number of Employees Trained
New Employee	2	4
Select Agent-Initial	1	1
Select Agent- Refresher	N/A	N/A
Select Agent- Visitor	2	2
BSL-3 Laboratory Biosafety-Initial	1	2
Practical Training	1	2
BSL-4 Laboratory Biosafety-Initial	1	1
Suit Training	1	1
Checklist Training	1	1
BSL-4 Laboratory Biosafety-Refresher	N/A	N/A
Laboratory Biosafety Support Staff-Initial	1	2
Laboratory Biosafety Support Staff-Refresher	1	12

C. Safety Audits and Inspections

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

D. Biological Incidents to Report
   a. Request for Information submitted to the Office of Science Policy 3/18/2022. Requested additional information on incident reporting process, training on incident reporting/process, and status of stated corrective actions.

E. Other Issues
   a. None

NIH RML Institutional Biosafety Committee Meeting

Agenda for May 19, 2022

Location: Virtual via Zoom/Building A (b) (6)

Old Business

A. Draft minutes of April 21, 2022 meeting

New Business

A. Committee Business
   1) PRD-22-237 (New) PI: Groshong
   2) PRD-22-180 (Amend) PI: de Leo
   3) PRD-22-83 (Renew) PI: Feldmann
   4) PRD-22-123 (Renew) PI: Feldmann
   5) RD-22-410 (Renewal) PI: Feldmann Reviewers: Andrea Marzi, Sue Priola
   6) Orthomyxovirus SDS and Heat inactivation validation (New)
   7) Draft SOP#4-28-31 Removal of Specimens for Protein Analysis-update table for Orthomyxovirus inactivation (Updated)

B. BSO report (Dr. Becky Anderson)
C. Occupational Safety & Health Manager report (Seth Cooley)
D. IRFBSM/Responsible Official Report (LCDR Megan Brose)
E. Associate Director Report (Dr. Marshall Bloom)
F. Comments from around the room

Next Meeting: June 16, 2022 via Zoom

PRD- Pathogen Registration Document
RD- Recombinant DNA Registration Document
SOP-Standard Operating Procedures
BSO-Biosafety Officer
IRFBSM-Integrated Research Facility Biosafety Manager

NIH RML Institutional Biosafety Committee Minutes

May 19, 2022 (1:00 PM – 1:44 PM)
Zoom Virtual Meeting

Members Present:

☑ Sue Priola, Chair	☐ Marcie Caldwell (EO)	☑ Jamie Lovaglio
☑ Bob Heinzen, Vice Chair	☐ Bruce Chesebro (EO)	☑ Andrea Marzi
☑ Becky Anderson	☑ Seth Cooley	☑ Alida Merritt
☐ Alan Applebury	☐ Frank DeLeo (EO)	☑ Greg Saturday
☑ Chris Bosio	☐ Heinz Feldmann (EO)	☐ Alexandra Scranton
☐ Marshall Bloom (EO)	☑ Erik Hoover	☐ Brian Vickrey
☐ Megan Brose	☐ Clay Jarrett	☑ Clayton Winkler
☐ Larry Brouwer	☐ Josh Kellar (EO)	
☐ Carol Calderwood	☑ Scott Kobayashi	

(EO) *ex officio*

Guests: (b)(6)
(b)(6)

Announcements

I. None

Old Business

I. Review of Past IBC Meeting Minutes
   a. April 21, 2022 Minutes
      i. Sue Priola noted that the dates of the DSAT inspection were not included.
      ii. The minutes were unanimously approved with minor modifications.
         1. Update to include dates of the DSAT inspection on page 3.

New Business

I. Registration of Material (Potentially) Infectious for Humans, Plants or Animals
   a. PRD-22-237 *Escherichia coli* – (b)(6) (New)
      i. Becky Anderson summarized the PRD. This is a new proposal from the Groshong lab to identify pathogenic water contaminants in ecological water samples, including *Escherichia coli* (O157), *Helicobacter pylori*, *Legionella pneumophilia*, *Mycobacterium abcessus* and *avium*, *Pseudomonas aeruginosa*, *Shigella sonnei*, *Klebsiella pneumoniae*, and *Leptospira spp*. Language will be added to the recommendation section to minimize the production of aerosols.
      ii. Seth Cooley asked about controls needed for field collection to minimize aerosol generation. These controls could include a face shield if there is a potential for splashes.
      iii. (b)(6) expanded on the procedures for collecting well water from a sink and non-turbid creeks or rivers. The water will not be entered.

iv. Scott Kobayashi noted that decon should be changed to decontaminated in the description.
v. No animal studies were submitted, reviewed, or approved.
vi. Work is approved at BSL-2.
vii. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
viii. The committee unanimously approved with minor modifications.
    1. Update recommendations for protection against aerosols and to include a face shield when there is a splash potential.
    2. Change decon to decontaminated in the description.

b. PRD-22-180 *Klebsiella pneumoniae* – Frank de Leo (Amend)
    i. Becky Anderson summarized the PRD. This is an amendment to add recombinant strains of *Klebsiella pneumoniae* from a collaborator. These strains were developed using transposon-directed mutagenesis or CRISPR-Cas9 mediated targeted gene editing. Apramycin is the selectable marker for both and is not clinically relevant for *Klebsiella*. These strains are not expected to have increased pathogenicity. No additional recombinant work will be performed on these strains.
    ii. Sue Priola asked about the strains listed in the original PRD. Scott Kobayashi noted that these new recombinant strains are from the same parent strains listed in the original PRD. Becky Anderson noted that we could add that there is no anticipated increased pathogenicity with these mutants.
    iii. No additional animal studies were submitted, reviewed, or approved.
    iv. Work with *Klebsiella pneumoniae* is approved at BSL-2/ABSL-2.
    v. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
    vi. The committee unanimously approved with minor modifications.
        1. Add that there is no anticipated increased pathogenicity with these mutants.

c. PRD-18-82 VSV – Andrea Marzi (Amend)
    i. Becky Anderson summarized the PRD. This amendment is to add ferret work to this PRD. This is in response to the HPAI outbreak that is ongoing. SOPs are in place for ferret handling in BSL-4.
    ii. Animal studies with ferrets were proposed.
    iii. Work with VSV is approved at BSL-2/ABSL-2.
    iv. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
    v. The committee unanimously approved as written, Andrea Marzi abstained.

d. PRD-22-83 Human and NHP blood and body fluid – Heinz Feldmann (Renewal)
    i. Becky Anderson summarized the PRD. This is a renewal for work with human and non-human primate blood and body fluids and there is no new work described. The recommendations section will be updated to include language regarding handling of COVID-positive human samples.
    ii. Clayton Winkler asked if virus was being isolated from the COVID-positive samples, would this be done in the BSL-3. Becky Anderson confirmed this would be done at BSL-3, and samples where virus isolation will not be occurring can be handled at BSL-2. These samples may also be irradiated and worked with at BSL-2.

iii. (b)(6) noted that there is an updated BSSE Guideline hyperlink listed in the recommendations section.
iv. No animal work was submitted, reviewed, or approved.
v. Work with human and NHP blood and body fluid is approved at BSL-2 with the following recommendations:
    1. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 375-9600.
    2. Research performed with this material is subject to the NIH OACU BSSE Guidelines (https://oacu.oir.nih.gov/system/files/media/file/2021-06/OACU_BSSE_Guidelines.pdf). Please contact RML DOHS for information on how to obtain the required components of the kit.
vi. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
vii. The committee unanimously approved with minor modifications.
    1. Update BSSE link in recommendations, https://oacu.oir.nih.gov/system/files/media/file/2022-03/OACU_BSSE_Guidelines-2022_03_29_0.pdf
    2. Update recommendations to include language for handling of COVID-positive samples.
    3. Clarify in the synopsis what samples will be irradiated.

e. PRD-22-123 Phlebovirus – Heinz Feldman (Renewal)
i. Becky Anderson summarized the PRD. This is a renewal for work with Phleboviruses and no additional work has been added. The Feldmann lab aims to understand the molecular basis of the Phlebovirus life cycle, pathogenesis and mechanisms of virulence. Some of the Phleboviruses are human pathogens.
ii. Sue Priola asked about any updates to the table for the pathogen biosafety levels. Becky Anderson will confirm if there have been any updates.
iii. Clayton Winkler asked about the mention of a recombinant STSV in the registration. Becky Anderson confirmed that this is covered in a separate RD.
iv. Sue Priola asked about the comment on page 3 regarding tick homogenates, stating that this material is currently storage only and work is not currently being performed. Becky Anderson will confirm if this work is still being performed and where this material is stored.
v. Animal studies with mice and NHP were proposed.
vi. Work with Phleboviruses is approved:
    1. Biosafety levels for various Phleboviruses are listed on the last page of the PRD.
    2. BSL-3 Phleboviruses include: SFTSV, Heartland virus, Malsoor virus and Bhanja virus.
    3. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 375-9600.

vii. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
viii. The committee unanimously approved with minor modifications.
    1. Confirm the BSL recommendations.
    2. Confirm location of tick homogenate material and if this work is currently being performed.

II. Registration of Recombinant DNA Experiments
    a. RD-22-410 – Heinz Feldmann (Renewal)
        i. Reviewers: Andrea Marzi and Sue Priola
        ii. Andrea Marzi summarized the RD. This is a renewal for the use of adenovirus vectors for protein expression. All work has been previously approved. This technology is used to create replication-deficient Adenovirus vectors expressing genes of interest for vaccine candidates. Genes of interest will come from filo-, arena-, paramyxo-, orthomyxo-, bunya-, flavi-, and coronaviruses. Vector maps and ASPs were attached. Recommend adding III-D-1-a to research products. The term "new work" is listed on pg. 4 and needs to be deleted as no new work is proposed. Recommend removing III-D-3-a and adding III-D-1-a to the eukaryotic cells section.
        iii. Sue Priola had no additional comments.
        iv. Animal studies with mice, hamsters, NHPs, and guinea pigs were proposed.
        v. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
        vi. Research using prokaryotic cells is approved at BSL-2 under sections III-D-2-a and III-E-1 of the NIH Guidelines, and research using eukaryotic cells is approved at BSL-2/ABSL-2 under sections III-D-1-a and III-E-1 of the NIH Guidelines.
        vii. The committee unanimously approved with minor modifications.
            1. Add III-D-1-a to research products.
            2. Remove III-D-3-a and add III-E-1 under eukaryotic cells.
            3. Remove "New Work" from page 4.

    b. RD-22-404 – Andrea Marzi (Amend)
        i. Reviewers: Full Committee
        ii. Sue Priola reviewed this amendment to add work with ferrets with the laboratory's VSV vaccine platform.
        iii. Animal studies with ferrets were proposed.
        iv. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
        v. Research using prokaryotic cells is approved at BSL-2 under sections III-D-1-a, III-D-2-a, and III-E-1 of the NIH Guidelines, and research using eukaryotic cells is approved at BSL-2/ABSL-2 under sections III-D-1-a, III-D-2-a, and III-E-1 of the NIH Guidelines.
        vi. The committee unanimously approved as written, Andrea Marzi abstained.

III. Full Committee Review of Inactivation Procedures
    a. Orthomyxovirus SDS and Heat inactivation validation (New)
        i. Sue Priola summarized the inactivation data. This is inactivation testing for the Orthomyxoviruses with SDS and Heat. This testing was performed with influenza H5N1. Appropriate positive and negative controls were included. Samples were tested in triplicate.

ii. Sue Priola asked to state the original SDS concentration (4%) in the beginning of the protocol.
iii. The committee had no additional comments.
iv. The committee unanimously approved with minor modifications.
1. Clarify the undiluted concentration of SDS (4%) in the protocol.

IV. Standard Operating Procedures
a. Draft SOP#4-28-31 Removal of Specimens for Protein Analysis (Updated)
i. Sue Priola summarized the updates to the SOP. This update is to include the validated inactivation methods: SDS and Heat for Orthomyxoviruses. The SOP matches the inactivation procedure.
ii. The committee had no additional comments.
iii. The committee unanimously approved as written.

V. Annual Reviews
a. None

Reports

I. Biosafety Officer Report – Becky Anderson
a. Becky Anderson presented the BSO report. The incident originally reported to OSP in March 2022 was closed out. The annual Full Length Clone Lab report was presented and will be submitted to OSP.
b. CDC DSAT inspection has concluded with no findings.

II. Occupational Safety and Health Manager Report – Seth Cooley
a. Nothing to report

III. IRF Biosafety Manager/Responsible Official Report – Megan Brose
a. Not present.

IV. Associate Director Report – Marshall Bloom
a. Not present.

Around the Room

I. Alida Merritt expressed thanks for RML staff who provided training in April 2022 for the APIC.

Other Issues

I. None

Next Meeting

I. June 16, 2022 1pm via Zoom and Building A (b) (6)

NIH RML Institutional Biosafety Committee Meeting

Biosafety Officer (BSO) Report

May 19, 2022

Business Conducted since the last IBC Meeting

A. BSO approvals
   a. Best PRD 20-154 Amend
      i. Add a CDC Import Permit
   b. Feldmann PRD 17-143 Amend
      i. Add a CDC Import Permit
   c. Feldmann PRD 19-158 Amend
      i. Add a CDC Import Permit
   d. Feldmann PRD 19-159
      i. Add a CDC Import Permit
   e. Feldmann PRD 17-143 Amend
      i. Add a CDC Import Permit
   f. Steele-Mortimer PRD 18-44 Amend
      i. Add IP route of inoculation for mice
   g. Steele-Mortimer RD 15-108 Amend
      i. Add IP route of inoculation for mice

B. Electronic business
   a. None

New business for IBC meeting

A. See agenda.

Biosafety Activities since the last IBC Meeting

A. Animal Study Protocols Review- Performed by Megan Brose, Rebecca Anderson, (b)(6)

ASP Title	Associated PRD	Associated RD	Reviewer
Efficacy of a single-bivalent RNA vaccine for CCHFV in non-human primates	18-92	17-452	Anderson
Protective efficacy of a VSV-based vaccine against highly pathogenic avian influenza virus infection in ferrets and cynomolgus macaques	17-202 18-82	20-404	(b)(6)

B. Biosafety Training- Performed by Megan Brose, Rebecca Anderson, (b)(6)

Type of Training	Number of Sessions	Number of Employees Trained
New Employee	1	2
Select Agent-Initial	1	2
Select Agent- Refresher	N/A	N/A
Select Agent- Visitor	1	3
BSL-3 Laboratory Biosafety-Initial	1	6
Practical Training	2	4
BSL-4 Laboratory Biosafety-Initial	1	2
Suit Training	N/A	N/A
Checklist Training	N/A	N/A
BSL-4 Laboratory Biosafety-Refresher	N/A	N/A
Laboratory Biosafety Support Staff-Initial	1	1
Laboratory Biosafety Support Staff-Refresher	N/A	N/A

C. Safety Audits and Inspections

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

D. Biological Incidents to Report

a. Request for Information submitted to the Office of Science Policy 3/18/2022. Requested additional information on incident reporting process, training on incident reporting/process, and status of stated corrective actions. Final correspondence with OSP 4/26/22, incident closed out.

E. Other Issues

a. Annual full length clone lab report for 2021 complete and ready for submission to OSP.

NIH RML Institutional Biosafety Committee Meeting

Agenda for June 16, 2022
Location: Virtual via Zoom

Old Business

A. Draft minutes of May 19, 2022 meeting

New Business

A. Committee Business
   1) PRD-22-238 (New) PI: Long
   2) PRD-22-239 (New) PI: Long
   3) PRD-22-240 (New) PI: Munster
   4) PRD-19-159 (Amend) PI: Feldmann
   5) PRD-18-90 (Amend) PI: Feldmann
   6) PRD-18-91 (Amend) PI: Feldmann
   7) PRD-18-103 (Amend) PI: Peterson
   8) PRD-18-70 (Amend) PI: Heinzen
   9) PRD-20-43 (Amend) PI: Heinzen
   10) RD-21-407 (Amend) PI: Feldmann — Reviewers: Clayton Winkler, Bob Heinzen
   11) RD-20-106 (Amend) PI: Heinzen — Reviewers: Scott Kobayashi, Chris Bosio
   12) Draft Coxiella animal ABSL-3 SOP-updated to add additional IN inoculation route

B. BSO report (Dr. Becky Anderson)
C. Occupational Safety & Health Manager report (Seth Cooley)
D. IRFBSM/Responsible Official Report (LCDR Megan Brose)
E. Associate Director Report (Dr. Marshall Bloom)
F. Comments from around the room

Next Meeting: August 18, 2022 virtual via Zoom/Building A (b) (6)

PRD- Pathogen Registration Document
RD- Recombinant DNA Registration Document
SOP-Standard Operating Procedures
BSO-Biosafety Officer
IRFBSM-Integrated Research Facility Biosafety Manager

NIH RML Institutional Biosafety Committee Minutes

June 16, 2022 (1:00 PM – 1:50 PM)
Zoom Virtual Meeting

Members Present:

☑ Sue Priola, Chair	☐ Carol Calderwood	☑ Scott Kobayashi
☑ Bob Heinzen, Vice Chair	☐ Marcie Caldwell (EO)	☑ Jamie Lovaglio
☑ Becky Anderson	☐ Bruce Chesebro (EO)	☑ Andrea Marzi
☐ Alan Applebury	☑ Seth Cooley	☐ Alida Merritt
☑ Chris Bosio	☐ Frank DeLeo (EO)	☑ Greg Saturday
☐ Marshall Bloom (EO)	☐ Heinz Feldmann (EO)	☐ Alexandra Scranton
☑ Megan Brose	☑ Erik Hoover	☑ Neeltje van Doremalen
☐ Larry Brouwer	☐ Josh Kellar (EO)	☐ Brian Vickrey
		☑ Clayton Winkler

(EO) *ex officio*

Guests: (b)(6)
(b)(6)

Announcements

I. None

Old Business

I. Review of Past IBC Meeting Minutes
   a. May 19, 2022 Minutes
      i. (b)(6) noted that the date on the meeting minutes needs to be updated.
      ii. Sue Priola noted a typo on pg 2 section D I that needs to be corrected from handing to handling.
      iii. The minutes were unanimously approved with minor modifications.
         1. Update meeting minutes date.
         2. Update typo.

New Business

I. Registration of Material (Potentially) Infectious for Humans, Plants or Animals
   a. PRD-22-238 *Candida albicans* – Carrie Long (New)
      i. Becky Anderson summarized the PRD. This is a new proposal from Carrie Long to evaluate the quality and nature of trained immunity induced by *Coxiella burnetii* infection and vaccination. *C. albicans* is used to assess non-specific immune response as a comparison. *C. albicans* can be pathogenic to immunocompromised individuals.
      ii. No animal studies were submitted, reviewed, or approved.
      iii. Work with *Candida albicans* is approved at BSL-2.
         1. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to

and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 375-9600.

iv. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
v. The committee unanimously approved as written.

b. PRD-22-239 Mycobacterium bovis (BCG) vaccine – Carrie Long (New)
   i. Becky Anderson summarized the PRD. This is a new proposal from Carrie Long to work with Mycobacterium bovis (BCG) vaccine to induce non-specific immune responses and compare them to the immune response following vaccination with *Coxiella burnetii*. This is an attenuated vaccine strain of Mycobacterium bovis.
   ii. Sue Priola noted there is a comment about *Candida albicans* on pg 3 that should be deleted.
   iii. No animal studies were submitted, reviewed, or approved.
   iv. Work with Mycobacterium bovis (BCG) is approved at BSL-2.
      1. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 375-9600.
   v. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
   vi. The committee unanimously approved with minor modifications.
      1. Delete Candida albicans comment on pg 3.

c. PRD-22-240 Monkeypox virus – Vincent Munster (New)
   i. Becky Anderson summarized the PRD. This is a new proposal from the Munster lab to study Monkeypox virus. The lab will develop assays to detect Monkeypox in field samples. This is to register both the Select agent Central African/Congo Basin Clade and non-select agent West African clade. Monkeypox is pathogenic to humans. Vaccine and treatments are available. The BSO recommendations language will be updated to include vaccination requirements and separating samples to ensure there is no unintentional mixing of the select agent and non-select agent monkey pox clades.
   ii. Sue Priola noted that SOP#2/3-28-01 is related to field sample processing.
   iii. No animal work was submitted, reviewed, or approved.
   iv. Work with Monkeypox is approved at BSL-3.
      1. Work with the Central African/Congo Basin Clade is pending CDC DSAT approval.
      2. The approval is for only the materials, personnel, and facility specifically provided in the PRD. Only personnel registered on the PRD may have access to this material.
      3. In addition, please be aware of the following conditions for working with this material:
         a. Monkeypox virus (Central African/Congo Basin Clade) is a Select Agent. All personnel with access to this agent must be authorized by the CDC Division of Select Agents and Toxins.
         b. All individuals listed on this PRD and all those with access to the laboratory must be enrolled in and meet all health and security

requirements of the NIH Biosurety Program and complete the RML BSL-3 and/or BSL-4 Biosafety Training Program.

c. IBC approved validated inactivation procedure(s) must be followed when inactivating and removing samples to a lower containment level. Inactivation certificates are required for all samples that are inactivated.

4. The facilities, practices, and procedures for conducting research at various Biological Safety Levels can be found in the CDC/NIH publication entitled "Biosafety in Microbiological and Biomedical Laboratories" and the NIH Guidelines for Research Involving Recombinant DNA Molecules. These documents can be found at:
   http://www.cdc.gov/OD/ohs/biosfty/bmbl5/bmbl5toc.htm
   http://www4.od.nih.gov/oba/rdna.htm
5. It is the responsibility of the Principal Investigator (PI) to supply the IBC with updated information including modifications to the experiments described, location changes, and new research personnel. Amendments may be submitted online at http://oms.ors.nih.gov. Complete review of Pathogen Registration Documents and Recombinant DNA Registration Documents is performed by the IBC every 5 years.
6. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 375-9755.

v. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.

vi. The committee unanimously approved with minor modifications.

1. Update the BSO recommendations language to include vaccination requirements and separating samples to ensure there is no unintentional mixing of the select agent and non-select agent monkey pox clades.

d. PRD-19-159 Modified Vaccinia Virus Ankara (MVA) – Heinz Feldmann (Amend)

i. Becky Anderson summarized the PRD. This is an amendment to add work with Vaccinia virus, Western Reserve (VACV). This will be used to test virus inactivation protocols and diagnostic assay protocols. The BSO recommendations language will be updated to include vaccination requirements and that care should be taken to minimize exposure to aerosols.

ii. No animal work was submitted, reviewed, or approved.

iii. Work with Vaccinia virus, Western Reserve (VACV) is approved at BSL-2.

iv. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.

v. The committee unanimously approved with minor modifications.

1. Update the BSO recommendations language to include vaccination requirements and that care should be taken to minimize exposure to aerosols.

e. PRD-18-90 Filoviruses – Heinz Feldman (Amend)

i. Becky Anderson summarized the PRD. This is an amendment to add ferrets as an animal model with aerosol, intranasal, and intramuscular inoculation routes. SOPs for working with ferrets at BSL-4 are in place.

ii. Animal studies with ferrets were proposed.

iii. Work with Filoviruses in ferrets is approved at ABSL-4.

iv. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
v. The committee unanimously approved as written.

f. PRD-18-91 Henipavirus – Heinz Feldman (Amend)
   i. Becky Anderson summarized the PRD. This is an amendment to add a number of paramyxoviruses most of which have been identified from bats. The full virus list is included in the amendment. There is limited information regarding these viruses. No treatments are available. SOPs are in place for working with other paramyxoviruses at BSL-3.
   ii. No animal work was submitted, reviewed, or approved.
   iii. Work is approved at BSL-3.
   iv. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
   v. The committee unanimously approved as written.

g. PRD-18-103 Bunyaviruses – Karin Peterson (Amend)
   i. (b)(6) summarized the amendment to the PRD. This is an amendment to study viral resistance using N-hydroxycytidine, of which molnupiravir is a prodrug, in La Crosse virus. Molnupiravir is not used to treat La Crosse virus. This would entail repetitive passaging to see if resistance could be selected for in an RNA virus and what downstream effects are seen in viral fitness and the genome.
   ii. Sue Priola noted that this antiviral drug is not used to treat La Crosse virus. Dual use question #3 was marked no and an additional comment could be included to state that resistance is not expected to increase fitness and this drug is not clinically used to treat infection.
   iii. No animal work was submitted, reviewed, or approved.
   iv. Work with Bunyaviruses is approved at BSL-2.
   v. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
   vi. The committee unanimously approved with minor modifications, Clayton Winkler abstained.
      1. Update Dual Use Question #3 to include additional details as to why it was marked "No".

h. PRD-18-70 *Coxiella burnetti* (exempt) – Bob Heinzen (Amend)
   i. Becky Anderson summarized the PRD. This is an amendment to add mice to the registration with intranasal and intraperitoneal routes of inoculation with their exempt strain of *Coxiella burnetti*. Intranasal inoculation will occur in a BSC.
   ii. Animal studies with mice were proposed.
   iii. Work with *Coxiella burnetti* (exempt) in mice is approved at ABSL-2.
   iv. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
   v. The committee unanimously approved as written, Bob Heinzen abstained.

i. PRD-20-43 *Coxiella burnetti* – Bob Heinzen (Amend)
   i. Becky Anderson summarized the PRD. This is an amendment to add intranasal and intraperitoneal routes of infection of mice to the registration with their select agent

Coxiella burnetti strain. There is an applicable SOP for ABSL-3 work with *Coxiella burnetti*.

ii. Animal studies with mice were proposed.
iii. Work with *Coxiella burnetti* in mice is approved at ABSL-3
iv. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
v. The committee unanimously approved as written, Bob Heinzen abstained.

II. Registration of Recombinant DNA Experiments
a. RD-22-407 – Heinz Feldmann (Amend)
i. Reviewers: Clayton Winkler and Bob Heinzen
ii. Clayton Winkler summarized the RD. This is an amendment to add ferrets as an animal model with filoviruses. They propose aerosol, intranasal and intramuscular routes of inoculation. The ASP was attached. Consider including similar language from mouse intranasal route of inoculation on Dual Use question #7B from their previous amendment.
iii. Bob Heinzen had no additional comments.
iv. Animal studies with ferrets were proposed.
v. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
vi. Research using eukaryotic cells is approved at BSL-4/ABSL-4 under sections III-D-1-a, III-D-1-c and III-E-1 of the NIH Guidelines.
vii. The committee unanimously approved with minor modifications.
1. Update language in Dual Use question #7B to similar language from latest mouse amendment.

b. RD-20-404 – Bob Heinzen (Amend)
i. Reviewers: Scott Kobayashi and Chris Bosio
ii. Scott Kobayashi summarized the RD. This amendment to add mice with intranasal and intraperitoneal routes of infection to the registration. Intranasal inoculation of mice is pending CDC DSAT approval.
iii. Chris Bosio had no additional comments.
iv. Animal studies with mice were proposed.
v. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
vi. Research using prokaryotic cells is approved at BSL-2/ABSL-2 or BSL-3/ABSL-3 depending on Phase I or Phase II of *Coxiella burnetii* under sections III-D-1-a and III-D-1-b of the NIH Guidelines.
vii. The committee unanimously approved as written, Bob Heinzen abstained.

III. Full Committee Review of Inactivation Procedures
a. None

IV. Standard Operating Procedures
a. Standard Operating Procedures for Animal Biosafety Level 3 (ABSL-3): *Coxiella burnetii* (Update)
i. Sue Priola summarized the updates to the SOP. This is to add intranasal inoculation of mice.

ii. Becky Anderson noted that the fever language was also updated in the SOP, and (b)(6) (b)(6) will be added as a Laboratory Supervisor in section 2.2.
iii. There were no additional comments or concerns with the updated procedures.
iv. The committee unanimously approved with minor modifications.
    1. Add (b)(6) to section 2.2 of SOP as Laboratory Supervisor.

V. Annual Reviews
    a. None

Reports

I. Biosafety Officer Report – Becky Anderson
    a. Becky Anderson presented the BSO report.
II. Occupational Safety and Health Manager Report – Seth Cooley
    a. Seth Cooley informed the committee of an incident on campus.
III. IRF Biosafety Manager/Responsible Official Report – Megan Brose
    a. Nothing to report.
IV. Associate Director Report – Marshall Bloom
    a. Not present.

Around the Room

I. Becky Anderson noted there will be no meeting in July, and the IBC will reconvene in August.
II. Sue Priola noted that (b)(6) has resigned from the IBC, and (b) (6) will join the committee.

Other Issues

I. None

Next Meeting

I. August 18, 2022 at 1pm via Zoom.

NIH RML Institutional Biosafety Committee Meeting

Biosafety Officer (BSO) Report

June 16, 2022

Business Conducted since the last IBC Meeting

A. BSO approvals
   a. Feldmann PRD 22-123 Amend
      i. Add CDC and APHIS permits
   b. Feldmann PRD 18-90 Amend 04
      i. Add intranasal route of inoculation for mice
   c. Feldmann RD 21-407 Amend 02
      i. Add intranasal route of inoculation for mice
   d. Feldmann PRD 18-90 Amend 05
      i. Add ocular route on inoculation for NHPs
      ii. Add oral route of inoculation for bats

B. Electronic business
   a. None

New business for IBC meeting

A. See agenda.

Biosafety Activities since the last IBC Meeting

A. Animal Study Protocols Review- Performed by Megan Brose, Rebecca Anderson, (b)(6)

ASP Title	Associated PRD	Associated RD	Reviewer
Experimental Henipavirus Infections in the Artibeus jamaicensis bats	18-91	N/A	M. Brose
Establishment of a mouse model for severe fever with thrombocytopenia syndrome virus and Heartland virus	22-123	N/A	(b)(6)
Establishment of the ferret model for filoviruses.	18-90	21-407	R. Anderson
Pathogenesis of novel filoviruses in nonhuman primates	18-90	21-407	R. Anderson
Investigation of non-specific immune effects induced by Coxiella burnetii	20-43 18-70	20-106	(b)(6); (b)(3):42 U.S.C. 262a(h)
Experimental Filovirus Infections in the Artibeus jamaicensis bats	18-90	N/A	M. Brose

B. Biosafety Training- Performed by Megan Brose, Rebecca Anderson, (b)(6)

Type of Training	Number of Sessions	Number of Employees Trained
New Employee	N/A	N/A
Select Agent-Initial	1	1
Select Agent- Refresher	N/A	N/A
Select Agent- Visitor	2	3
BSL-3 Laboratory Biosafety-Initial	N/A	N/A
Practical Training	3	6
BSL-4 Laboratory Biosafety-Initial	N/A	N/A
Suit Training	1	5
Checklist Training	3	6
BSL-4 Laboratory Biosafety-Refresher	N/A	N/A
Laboratory Biosafety Support Staff-Initial	1	1
Laboratory Biosafety Support Staff-Refresher	N/A	N/A

C. Safety Audits and Inspections

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

D. Biological Incidents to Report
   a. None

E. Other Issues
   a. None

NIH RML Institutional Biosafety Committee Meeting

Agenda for August 18, 2022

Location: Virtual via Zoom/Building A (b) (6)

Old Business

A. Draft minutes of June 16, 2022 meeting

New Business

A. Committee Business
   1) PRD-22-241 (New) PI: Long
   2) PRD-18-91 (Amend 05) PI: Feldmann
   3) PRD-22-240 (Amend 01) PI: Munster
   4) PRD-16-184 (Amend 01) PI: Peterson
   5) RD-21-134 (Amend 03) PI: Groshong Reviewers: Scott Kobayashi, Chris Bosio
   6) Draft Exposure Control Plan-Annual Review
   7) Draft SOP#4-28-16 Rodent Procedures in Biocontainment-update for routes of inoculation

B. BSO report (Dr. Becky Anderson)
C. Occupational Safety & Health Manager report (Seth Cooley)
D. IRFBSM/Responsible Official Report (LCDR Megan Brose)
E. Associate Director Report (Dr. Marshall Bloom)
F. Comments from around the room

Next Meeting: September 15, 2022 virtual via Zoom/Building A (b) (6)

PRD- Pathogen Registration Document
RD- Recombinant DNA Registration Document
SOP-Standard Operating Procedures
BSO-Biosafety Officer
IRFBSM-Integrated Research Facility Biosafety Manager

NIH RML Institutional Biosafety Committee Minutes

August 18, 2022 (1:00 PM – 1:42 PM)
Zoom Virtual Meeting

Members Present:

☑ Sue Priola, Chair	☐ Carol Calderwood	☑ Scott Kobayashi
☑ Bob Heinzen, Vice Chair	☐ Marcie Caldwell (EO)	☑ Jamie Lovaglio
☑ Becky Anderson	☐ Bruce Chesebro (EO)	☐ Andrea Marzi
☐ Alan Applebury	☑ Seth Cooley	☐ Alida Merritt
☑ Chris Bosio	☐ Frank DeLeo (EO)	☐ Greg Saturday
☐ Marshall Bloom (EO)	☐ Heinz Feldmann (EO)	☐ Alexandra Scranton
☑ Megan Brose	☐ Erik Hoover	☐ Neeltje van Doremalen
☐ Larry Brouwer	☐ Josh Kellar (EO)	☐ Brian Vickrey
		☑ Clayton Winkler

(EO) *ex officio*

Guests: (b)(6)

Announcements

I. None

Old Business

I. Review of Past IBC Meeting Minutes
   a. June 16, 2022 Minutes
      i. No comments.
      ii. The minutes were unanimously approved as written.

New Business

I. Registration of Material (Potentially) Infectious for Humans, Plants or Animals
   a. PRD-22-241 *Borrelia burgdorferi, Borrelia hermsii* – Carrie Long (New)
      i. Becky Anderson summarized the PRD. This is a new proposal from Carrie Long to characterize host (murine) immune responses to *Borrelia spp.* infection. *B. burgdorferi* causes Lyme disease which presents with fever, chills, headache, fatigue, muscle and joint pains and swollen lymph nodes. It is often characterized by a rash that has a bull's eye appearance. *Borrelia hermsii* causes tick borne relapsing fever which is characterized by recurring febrile episodes that end with a crisis, chill, and flush phase. Treatment for both Borrelia spp. includes antibiotic treatment with doxycycline and amoxicillin. Primary lab hazards include accidental sharps injuries and generation of aerosols.
      ii. Animal studies with mice were proposed.
      iii. Work with *Borrelia burgdorferi, Borrelia hermsii* is approved at BSL-2/ABSL-2.
         1. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to

and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 375-9600.

iv. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
v. The committee unanimously approved as written.

b. PRD-18-91 Henipaviruses – Heinz Feldmann (Amend)
   i. Becky Anderson summarized the PRD amendment. There are three items in this amendment: 1) Clarify inclusion of Menangle-like viruses (AUS-RML-59, AIS-RML-77, and AUS-RML-78). These viruses were not specifically listed in the table that was approved at June IBC meeting. 2) Add New Castle Disease virus LaSota strain (attenuated vaccine strain used for chickens). 3) Add animal work with pigs. The addition of Menangle-like viruses is a clarification to IBC approval that was granted in June. This amendment is to ensure Menangle-like viruses are covered with this PRD. The addition of the New Castle Disease virus LaSota strain, is a vaccine strain for New Castle Disease virus in poultry. The vaccine is safe and stable with no reports of virulence reversion or recombination with field strains. The final part of the amendment is for the addition of animal work with pigs. There are existing SOPs in place for animal work with pigs in the BSL-4 and RMVB has experience working with pigs in the BSL-4 for other pathogens. Key precautions that are taken when working with pigs include: pens with a swing gate to isolate animals during feeding and cleaning. Personnel only enter the pen when necessary, and suit and foot sanitation is performed when leaving the animal holding room/procedure spaces.
   ii. Sue Priola noted that the specific strains of Menangle-like virus should be added to the attached ASP in section K.
   iii. Animal studies with pigs were proposed.
   iv. Work with Menangle-like virus is approved at BSL-3.
   v. Work with New Castle disease virus LaSota strain is approved for work at BSL-2/ABSL-2.
   vi. Animal work with pigs is approved at the biosafety level dependent on the virus used to inoculate the animals.
   vii. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
   viii. The committee unanimously approved with minor modifications.
      1. Add specific strains of Menangle-like virus to the attached ASP in Section K.

c. PRD-22-240 Monkeypox virus – Vincent Munster (Amend)
   i. Becky Anderson summarized the PRD amendment. This is an amendment to add animal work with mastomys rodents to the Monkeypox virus registration. The primary hazards of working with mastomys includes rodent bites or scratches and accidental sharps injuries. An SOP is in place for handling rodents in the BSL-4. The SOP specifies that most procedures with rodents are performed on anesthetized animals. The SOP#4-28-16 is being updated at this meeting to add two new routes of inoculation as the Munster lab works to develop mastomys as a model for Monkeypox virus.
   ii. No animal work was submitted, reviewed, or approved.
   iii. Work with Monkeypox infected mastomys is approved at ABSL-3, however most of the work will be performed at ABSL-4.

iv. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
v. The committee unanimously approved with as written.

d. PRD-16-184 Flavivirus – Karin Peterson (Amend)
i. Becky Anderson summarized the PRD amendment. This is an amendment to add work with West Nile virus and Dengue virus, serotypes 1-4 to compare and contrast with existing Flaviviruses studied in the Peterson lab. Dengue virus causes an acute febrile disease characterized by the sudden onset of fever for 3-5 days with intense headache, myalgia, arthralgia, retro-orbital pain, anorexia and rash. Symptoms are typically self-limiting, however dengue hemorrhagic fever can manifest on second exposure. West Nile virus is the leading cause of mosquito-borne disease in the US and is now endemic in the US. It is most commonly spread through the bite of an infected mosquito. Most people do not have symptoms, however 1 in 5 develop fever, headache, body aches joint pain, vomiting, diarrhea, or rash. About 1 in 150 individuals develop a serious and sometimes fatal illness affecting the central nervous system. West Nile was previously worked with in the BSL-3, but now that the virus is endemic in the US, the 6th Edition of the BMBL now recommends BSL-2.
ii. No animal work was submitted, reviewed, or approved.
iii. Work with West Nile virus and Dengue virus is approved at BSL-2.
1. All work is to be done within a BSC; everything should be sealed prior to removal from the BSC, this includes sealed/gasketed safety cups for centrifuges, parafilming of microtitre plates etc.
2. Employees should be informed of the following risks of working with Dengue virus: there is an increased severity of disease upon second exposure to dengue virus, as well as working with multiple serotypes increases your risk for disease.
iv. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
v. The committee unanimously approved (Clayton Winkler abstained) as written.

II. Registration of Recombinant DNA Experiments
a. RD-21-134 – Ashley Groshong (Amend)
i. Reviewers: Scott Kobayashi and Chris Bosio
i. Scott Kobayashi summarized the RD. This is an amendment to add the pGKT-ST transposon plasmid for *Borrelia hermsii*. This plasmid was previously used by the Rosa lab for *Borrelia burgdorferi*. The plasmid is a Kanamycin and Gentamycin resistant plasmid that contains the Himar1 C9 transposase driven by a Borrelia burgdorferi constitutive promoter, allowing insertion of the transposon (ITR-Gentamycin-ColE1-IRT) fragment to be randomly inserted in bacterial genes. Scott Kobayashi stated that gentamicin and constitutive are both spelled incorrectly and need to be fixed.
ii. Chris Bosio had no additional comments.
iii. No animal work was submitted, reviewed, or approved.
iv. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
v. Research using prokaryote hosts is approved at BSL-2/ABSL-2 under sections III-D-1-a and III-D-2-a of the NIH Guidelines.
vi. The committee unanimously approved with minor modifications.
1. Correct the misspellings for gentamicin and constitutive.

III. Full Committee Review of Inactivation Procedures
   a. None

IV. Standard Operating Procedures
   a. Draft SOP#4-28-16 Rodent Procedures in biocontainment (Updated)
      i. Becky Anderson summarized the updates to the SOP. This update is to add rectal and transdermal routes of inoculation to develop a model for monkeypox virus infections.
      ii. Jamie Lovaglio recommended to the committee that the language for the routes of inoculation be modified so it is less specific for the current animal study. Jamie Lovaglio suggested the rectal language should match the NHP SOP. The committee agreed that the language be modified to be more generic and reference the ASP for specific details.
      iii. There were no additional comments or concerns with the updated procedures.
      iv. The committee unanimously approved with minor modifications.
         1. Update the routes of inoculation language to be less specific for this ASP.

V. Annual Reviews
   a. Exposure Control Plan (ECP)
      i. Becky Anderson summarized the updates to the ECP. There were very minor changes to the plan (phone numbers and abbreviations were updated).
      ii. Jamie Lovaglio suggested on page 13 that "will be" should be changed to "may be" for needleless systems. The committee agreed.
      iii. Jamie Lovaglio suggested on page 22 to remove "vigorously" scrubbed. The committee agreed.
      iv. Jamie Lovaglio suggested on page 22 to add "and/or chlorhexidine". The committee agreed.
      v. There were no additional comments or concerns with the updated procedures.
      vi. The committee unanimously approved as written.

Reports

I. Biosafety Officer Report – Becky Anderson
   a. Becky Anderson presented the BSO report and a recent incident.
II. Occupational Safety and Health Manager Report – Seth Cooley
   a. Nothing to report.
III. IRF Biosafety Manager/Responsible Official Report – Megan Brose
   a. Nothing to report.
IV. Associate Director Report – Marshall Bloom
   a. Not present.

Around the Room

I. Jamie Lovaglio informed the committee that (b) (6) will be onsite next week. Please contact (b) (6) if you would like to meet with him.

Other Issues

I. None

Next Meeting

I. September 15, 2022 at 1pm via Zoom.

NIH RML Institutional Biosafety Committee Meeting

Biosafety Officer (BSO) Report

August 18, 2022

Business Conducted since the last IBC Meeting

A. BSO approvals
   a. PI Change to Sonja Best due to Kim Hasenkrug's retirement
      i. Hasenkrug PRD 21-187
      ii. Hasenkrug PRD 20-114
      iii. Hasenkrug PRD 21-185
      iv. Hasenkrug RD 14-218
   b. Munster PRD 22-240
      i. Added new permits

B. Electronic business
   a. MCL Inactivation validation testing of Pox viruses with irradiation.
      i. Approved 8/12/2022

New business for IBC meeting

A. See agenda.

Biosafety Activities since the last IBC Meeting

A. Animal Study Protocols Review- Performed by Megan Brose, Rebecca Anderson, (b)(6)

ASP Title	Associated PRD	Associated RD	Reviewer
Pathogenic Potential of Novel Bat Paramyxovirus in Pigs (pilot study)	18-91	N/A	R. Anderson
Cross-Protection of VSV-Nipah Against Hendra Virus Challenge in the African Green Monkey Model	18-91 18-82	20-404	R. Anderson
Characterization of Disease in IFNAR Mice Following Infection with Recombinant VSVs	18-82 18-90	20-404	M. Brose

B. Biosafety Training- Performed by Megan Brose, Rebecca Anderson, (b)(6)

Type of Training	Number of Sessions	Number of Employees Trained
New Employee	3	11
Select Agent-Initial	1	2
Select Agent- Refresher	N/A	N/A
Select Agent- Visitor	3	5
BSL-3 Laboratory Biosafety-Initial	1	3
Practical Training	1	1
BSL-4 Laboratory Biosafety-Initial	1	1
Suit Training	N/A	N/A
Checklist Training	2	2
BSL-4 Laboratory Biosafety-Refresher	N/A	N/A
Laboratory Biosafety Support Staff-Initial		
Laboratory Biosafety Support Staff-Refresher	N/A	N/A

C. Safety Audits and Inspections

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

D. Biological Incidents to Report
    a. Small seam separation in BSL-4 suit-assessed as negligible/no risk
    b. Splash to eye in quarantine room of NHPs-assessed as minimal/negligible risk

E. Other Issues
    a. None

NIH RML Institutional Biosafety Committee Meeting

Agenda for September 15, 2022
Location: Virtual via Zoom/Building A (b)(6)

Old Business

A. Draft minutes of August 18, 2022 meeting

New Business

A. Committee Business
    1) PRD-22-237 (Amend 01) PI: Groshong
    2) PRD-20-229 (Amend 03) PI: Berelli Saito
    3) PRD-22-240 (Amend 02) PI: Munster
    4) Draft SOP#4-28-66 Prairie Dog Procedures in Biocontainment- New
    5) Draft BSL-3 Operations and Safety Procedures (OSP)- Annual Review
    6) Draft ABSL-3 Operations and Safety Procedures (OSP)- Annual Review
    7) Draft Inactivation Validation of Monkeypox virus with Trizol-New
    8) Draft SOP#4-28-32 Removal of Nucleic Acids-Updated

B. BSO report (Dr. Becky Anderson)
C. Occupational Safety & Health Manager report (Seth Cooley)
D. IRFBSM/Responsible Official Report (LCDR Megan Brose)
E. Associate Director Report (Dr. Marshall Bloom)
F. Comments from around the room

Next Meeting: October 20, 2022 virtual via Zoom/Building A (b)(6)

PRD- Pathogen Registration Document
RD- Recombinant DNA Registration Document
SOP-Standard Operating Procedures
BSO-Biosafety Officer
IRFBSM-Integrated Research Facility Biosafety Manager

NIH RML Institutional Biosafety Committee Minutes

September 15, 2022 (1:01 PM – 1:45 PM)

Zoom Virtual Meeting/Building A (b)(6)

Members Present:

☑ Sue Priola, Chair	☐ Marcie Caldwell (EO)	☑ Jamie Lovaglio
☑ Bob Heinzen, Vice Chair	☐ Bruce Chesebro (EO)	☑ Andrea Marzi
☑ Becky Anderson	☑ Seth Cooley	☑ Alida Merritt
☐ Alan Applebury	☑ Kendal Cooper	☐ Greg Saturday
☐ Chris Bosio	☐ Frank DeLeo (EO)	☐ Alexandra Scranton
☐ Marshall Bloom (EO)	☐ Heinz Feldmann (EO)	☐ Brian Vickrey
☑ Megan Brose	☑ Erik Hoover	☑ Clayton Winkler
☐ Larry Brouwer	☐ Josh Kellar (EO)	
☐ Carol Calderwood	☑ Scott Kobayashi	

(EO) *ex officio*

Guests: (b)(6)

(b)(6)

Announcements

I. None

Old Business

I. Review of Past IBC Meeting Minutes
   a. August 18, 2022 Minutes
      i. No comments.
      ii. The minutes were unanimously approved as written.

New Business

I. Registration of Material (Potentially) Infectious for Humans, Plants or Animals
   a. PRD-22-237 Pathogenic Water Contaminants, add *Campylobacter jejuni* – Ashley Groshong (Amend)
      i. Becky Anderson summarized the PRD. The amendment is to add another potential water contaminant to the original registration. The proposed work is to identify pathogenic water contaminants in water samples. The original PRD listed several types of bacteria, however *C. jejuni* was missed, the amendment is to add this pathogen.
      ii. No animal work was submitted, reviewed, or approved.
      iii. Work with *Campylobacter jejuni* is approved at BSL-2/ABSL-2.
         1. Care should be taken to minimize worker exposure to aerosols, such as working in a certified Class II BSC and using gasketed bucket covers when centrifuging infectious material.

iv. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
v. The committee unanimously approved as written.

b. PRD-20-229 Ehrlichial spp. – Tais Berelli Saito (Amend)
   i. Becky Anderson summarized the PRD amendment. The amendment is to clarify procedures listed under the aerosol generating procedures. The original language that was provided by the PI and not requested by the IBC stated that centrifugation would be performed only in sealed/gasketed buckets that will only be opened in a BSC. The PI would like to change this language, so they are not required to use sealed buckets and open them only in a BSC. The natural route of transmission in Ehrlichia spp. is through the bite of an infected tick. There is no evidence of infection through aerosols. The committee agreed there were no issues with changing the language.
   ii. Clayton Winkler noted that there were some misspelled words in the comments section.
   iii. No animal work was submitted, reviewed, or approved.
   iv. Work with Ehrlichial spp. is approved at BSL-2/ABSL-2.
   v. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
   vi. The committee unanimously approved with minor modifications.
      1. Correct the misspelled words in the comments section.

c. PRD-22-240 Monkeypox virus – Vincent Munster (Amend)
   i. Becky Anderson summarized the PRD amendment. This is an amendment to add animal work with prairie dogs, dormice, and deer mice to the Monkeypox virus registration. Animal work with the dormice and deer mice is covered under the existing BSL-4 rodent SOP. Most procedures with rodents are performed on anesthetized animals. The current rodent SOP does not cover animal procedures with prairie dogs. RMVB in collaboration with LV has submitted a new BSL-4 SOP for work with prairie dogs that will be reviewed later this meeting. The new SOP describes using leather gloves to handle the prairie dogs and most procedures are performed on anesthetized animals.
   ii. (b)(6) commented that dormice can be very jumpy, RML may want to consider using Coy boxes. Jamie Lovaglio commented that we use isoflurane soaked nestlets for mastomys and this would potentially be used for the dormice as well so they are anesthetized before the cage is opened.
   iii. The other concern with obtaining prairie dogs is the source and the pathogens they may be carrying when we receive them. RMVB will have the animals screened prior to shipment so we can exclude animals or modify PPE for handling animals prior to them going hot in the BSL-4.
   iv. Animal studies with dormice, deer mice, and prairie dogs were proposed.
   v. Work with Monkeypox infected rodents is approved at ABSL-3, however most of the work will be performed at ABSL-4.
   vi. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
   vii. The committee unanimously approved as written.

II. Registration of Recombinant DNA Experiments
   a. None

i. Reviewers: None

III. Full Committee Review of Inactivation Procedures
   a. Poxvirus Trizol inactivation validation (New)
      i. Sue Priola summarized the inactivation data. This is inactivation testing for the Poxvirus with Trizol. This testing was performed with a non-select agent strain of Monkey pox virus. Appropriate positive and negative controls were included. Samples were tested in triplicate.
      ii. Kendal Cooper asked if the titer was appropriate as it seemed low. (b)(6) stated that they used their stock virus and that is currently their highest titer.
      iii. The committee had no additional comments.
      iv. The committee unanimously approved as written.

IV. Standard Operating Procedures
   a. Draft SOP#4-28-66 Prairie Dog Procedures in biocontainment (New)
      i. Becky Anderson informed the committee that this is a new SOP for the development of monkeypox animal models in prairie dogs.
      ii. Sue Priola asked about the MAD Nasal Intranasal Mucosal Atomization Device, she questioned if the device generated aerosols. Jamie Lovaglio stated that it gets inserted into the nasal opening for intranasal inoculation. Sue Priola stated that it might be beneficial for a short description and/or a picture to be added to the SOP. The committee agreed that additional information should be added.
      iii. There were no additional comments or concerns with the updated procedures.
      iv. The committee unanimously approved with minor modifications.
         1. Add additional information about the MAD Nasal Intranasal Mucosal Atomization Device.

   b. Draft SOP#4-28-32 Removal of Specimens for Nucleic Acid Extraction (Update)
      i. Sue Priola informed the committee that the update is to add inactivation with Trizol for Pox viruses.
      ii. There were no additional comments or concerns with the updated procedures.
      iii. The committee unanimously approved as written.

V. Annual Reviews
   a. BSL-3 Operations and Safety Procedures (OSP)
      i. Becky Anderson summarized the updates to the BSL-3 OSP. There were very minor changes to the plan, these include an additional ARO name, cleaned up language for shipping procedures, updated restricted experiment language, and updated the inventory check frequency.
      ii. There were no additional comments or concerns with the updated procedures.
      iii. The committee unanimously approved as written.

   b. ABSL-3 Operations and Safety Procedures (OSP)
      i. Becky Anderson summarized the updates to the ABSL-3 OSP. There were very minor changes to the plan, these include an additional ARO name, removed reference to TSE and updated the select agent list.

ii. Jamie Lovaglio asked if mastomys and hamster weights could be added to the carcass waste procedures. Becky Anderson agreed that those could be added based on the validated weights already tested by biosafety.
iii. There were no additional comments or concerns with the updated procedures.
iv. The committee unanimously approved as written.

Reports

I. Biosafety Officer Report – Becky Anderson
   a. Becky Anderson presented the BSO report and summarized a recent incident.
II. Occupational Safety and Health Manager Report – Seth Cooley
   a. Nothing to report.
III. IRF Biosafety Manager/Responsible Official Report – Megan Brose
   a. Select Agent annual refresher training is underway this month.
   b. The Suite B BSL-4 annual shutdown will occur in October
IV. Associate Director Report – Marshall Bloom
   a. Not present.

Around the Room

I. (b)(6) was present and informed the committee that the NIH charter for the Dual Use committee has been updated. They are working to better align the charter with the government DURC policy. Membership of the committee has been updated and will now include representation from RML.

Other Issues

I. None

Next Meeting

I. November 17, 2022 at 1pm via Zoom or in person in Building A (b)(6)

NIH RML Institutional Biosafety Committee Meeting

Biosafety Officer (BSO) Report

August 18, 2022

Business Conducted since the last IBC Meeting

A. BSO approvals
   i. None

B. Electronic business
   a. MCL Inactivation validation testing of Pox viruses with AVL.
      i. Approved 9/2/2022

New business for IBC meeting

A. See agenda.

Biosafety Activities since the last IBC Meeting

A. Animal Study Protocols Review- Performed by Megan Brose, Rebecca Anderson (b)(6)

ASP Title	Associated PRD	Associated RD	Reviewer
Modelling Nipah virus neurological disease in Syrian hamsters	18-91	N/A	M. Brose
Establishment of a guinea pig model for Lujo virus	18-94	N/A	R. Anderson
Identification of metabolic correlates of resistance to primary and secondary Francisella and SARS-CoV-2 infection in mice	18-73 18-71 20-223	N/A	M. Brose
Normal Laboratory Animal Blood and Tissue Donors to Support Ongoing Research	N/A	N/A	R. Anderson
California Serogroup virus infection in the muscle: Age-restriction and immune control mechanisms	18-103	N/A	M. Brose
Rodent model development for monkeypox transmission	22-240	N/A	R. Anderson

B. Biosafety Training- Performed by Megan Brose, Rebecca Anderson, (b)(6)

Type of Training	Number of Sessions	Number of Employees Trained
New Employee	N/A	N/A
Select Agent-Initial	1	2
Select Agent- Refresher	N/A	N/A
Select Agent- Visitor	1	3
BSL-3 Laboratory Biosafety-Initial	2	3
Practical Training	2	3
BSL-4 Laboratory Biosafety-Initial	1	1
Suit Training	2	1
Checklist Training	5	1
BSL-4 Laboratory Biosafety-Refresher	1	1
Laboratory Biosafety Support Staff-Initial	1	5
Laboratory Biosafety Support Staff-Refresher	N/A	N/A

C. Safety Audits and Inspections

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

D. Biological Incidents to Report
    a. Tick incident in (b)(6)

E. Other Issues
    a. None

NIH RML Institutional Biosafety Committee Meeting

Agenda for October 20, 2022

Location: Virtual via Zoom/Building A (b)(6)

Old Business

A. Draft minutes of September 15, 2022 meeting

New Business

A. Committee Business
   1) PRD-22-240 (Amend 05) PI: Munster
   2) RD-22-452 (Renewal) PI: Feldmann Reviewers: Sue Priola, Andrea Marzi
   3) Draft inactivation validation of *Y. pestis* with methanol on spleen homogenate smears-New
   4) Draft inactivation validation of Monkeypox virus with PFA and formalin-New
   5) Draft (b)(6) BSL-3 SOP-Updated
   6) Draft SOP#4-28-33 Removal of samples for Fixation-Updated

B. BSO report (Dr. Becky Anderson)
C. Occupational Safety & Health Manager report (Seth Cooley)
D. IRFBSM/Responsible Official Report (LCDR Megan Brose)
E. Associate Director Report (Dr. Marshall Bloom)
F. Comments from around the room

Next Meeting: November 17, 2022 virtual via Zoom/Building A (b)(6)

PRD- Pathogen Registration Document
RD- Recombinant DNA Registration Document
SOP-Standard Operating Procedures
BSO-Biosafety Officer
IRFBSM-Integrated Research Facility Biosafety Manager

NIH RML Institutional Biosafety Committee Minutes

October 20, 2022 (1:00 PM – 1:43 PM)

Hybrid Zoom/Building A (b)(6) Meeting

Members Present:

☑ Sue Priola, Chair	☐ Marcie Caldwell (EO)	☐ Jamie Lovaglio
☑ Bob Heinzen, Vice Chair	☐ Bruce Chesebro (EO)	☑ Andrea Marzi
☐ Becky Anderson	☐ Seth Cooley	☑ Alida Merritt
☐ Alan Applebury	☑ Kendal Cooper	☐ Greg Saturday
☑ Chris Bosio	☐ Frank DeLeo (EO)	☐ Alexandra Scranton
☐ Marshall Bloom (EO)	☐ Heinz Feldmann (EO)	☐ Brian Vickrey
☑ Megan Brose	☐ Erik Hoover	☑ Clayton Winkler
☐ Larry Brouwer	☐ Josh Kellar (EO)	
☐ Carol Calderwood	☑ Scott Kobayashi	

(EO) *ex officio*

Guests: (b)(6)

Announcements

I. None

Old Business

I. Review of Past IBC Meeting Minutes
   a. September 15, 2022 Minutes
      i. The minutes were unanimously approved with minor modifications.
         1. Update next meeting date.

New Business

I. Registration of Material (Potentially) Infectious for Humans, Plants or Animals
   a. PRD-22-240 Monkeypox virus – Vincent Munster (Amend)
      i. (b)(6) summarized the PRD. This amendment is to add non-human primate animal work to the Monkeypox virus registration. Animal work with NHPs are covered under the existing BSL-4 NHP SOPs. Also listed in this amendment, is to add IP route of inoculation for mice.
      ii. Sue Priola noted that the original PRD does not list developing or using animal models for Monkeypox studies. It was suggested to state in this amendment that animal models will be developed and used for Monkeypox studies.
      iii. Animal studies with NHP were proposed.
      iv. Work with Monkeypox is approved at ABSL-3.
      v. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
      vi. The committee unanimously approved with minor modifications.

1. Add statement to amendment description stating that animal models will be used to study Monkeypox virus.

II. Registration of Recombinant DNA Experiments
   a. RD-22-452 (Renewal)
      i. Sue Priola summarized the registration. This is a renewal for work with replication deficient alphavirus replicon systems. There was no new work described in the registration. These replicon systems are used to express viral proteins of interest as vaccine candidates. It was noted that pRRVrep-NP-capenhancer is not listed in the plasmid list.
      ii. Andrea Marzi noted that the NIH Guidelines should be updated in the research products to include III-D-1-a and III-E-1 and eukaryotic sections to include III-E-1. A typo also needs to be corrected in the plasmid list, correct pcDNA5/FRT/TR to pcDNA5/FRT/TO.
      iii. Animal studies with mice and NHP were proposed.
      iv. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
      v. Research using prokaryotic cells is approved at BSL-2 under sections III-D-2-a and III-E-1 of the NIH Guidelines and research using eukaryotic cells is approved at BSL-2/ABSL-2 under sections III-D-1-a, III-D-3-a and III-E-1 of the NIH Guidelines.
      vi. The committee unanimously approved with minor modifications.
         1. List pRRVrep-NP-capenhancer in plasmid list.
         2. Update pcDNA5/FRT/TR to pcDNA5/FRT/TO.
         3. Update NIH guidelines in research products section to include III-E-1 and III-D-1-a and update eukaryotic section to include III-E-1.

III. Full Committee Review of Inactivation Procedures
   a. Draft inactivation of Y. pestis with methanol on spleen homogenate smears (New)
      i. Sue Priola summarized the inactivation data. This is inactivation testing for Y. pestis spleen homogenate smears with methanol. Appropriate positive and negative controls were included. Samples were tested in triplicate. Clarification on how the cultures were scored positive or negative is needed.
      ii. Chris Bosio confirmed that the cultures were visually scored as positive or negative.
      iii. The committee agreed that additional testing should be performed by plating the broth samples following inactivation to confirm that no live bacteria are present.
      iv. The committee had no additional comments.
      v. The committee tabled this inactivation procedure pending additional testing. This will be reviewed electronically.
   b. Draft inactivation of Monkeypox virus with PFA and formalin (New)
      i. Sue Priola summarized the inactivation data. This is inactivation testing for Poxvirus with PFA and formalin. This testing was performed with a non-select agent strain of Monkeypox virus. Appropriate positive and negative controls were included. Samples were tested in triplicate.
      ii. Clayton Winkler asked if freezing the samples at -80 C would inactivate the virus. (b)(6) (b)(6) confirmed that this is a stable virus, and it would not be inactivated by freezing at -80 C.
      iii. The committee had no additional comments.
      iv. The committee unanimously approved as written.

IV. Standard Operating Procedures
    a. Draft (b)(6) BSL-3 SOP (Updated)
        i. Sue Priola informed the committee that the update is to add inactivation data with methanol for spleen homogenate smears.
        ii. The committee agreed that additional testing is needed prior to approving this SOP.
        iii. There were no additional comments with the updated procedures.
        iv. The committee tabled this SOP update pending additional testing. This will be reviewed electronically.
    b. Draft SOP#4-28-33 Removal of samples for Fixation (Updated)
        i. Sue Priola informed the committee that the update is to add inactivation data with PFA and formalin for Pox viruses.
        ii. There were no additional comments or concerns with the updated procedures.
        iii. The committee unanimously approved as written.

V. Annual Reviews
    a. None

Reports

I. Biosafety Officer Report – (b)(6)
    a. (b)(6) presented the BSO report.
II. Occupational Safety and Health Manager Report – Seth Cooley
    a. Not present
III. IRF Biosafety Manager/Responsible Official Report – Megan Brose
    a. Upcoming BSL-4 DSAT inspection March 13-17, 2023.
IV. Associate Director Report – Marshall Bloom
    a. Not present

Around the Room

I. (b)(6) and Megan Brose reported that the CDC DSAT were in contact to confirm that experiments which may increase virulence or transmissibility of a pathogen were included in our Select Agent Work Objectives. Megan Brose confirmed that any work of this nature would be reviewed by the IBC and in our Dual Use Research of Concern (DURC) review process.
II. Alida Merritt expressed gratitude for RML representative assisting with training.

Next Meeting

I. November 17, 2022 virtual via Zoom/Building A (b)(6)

NIH RML Institutional Biosafety Committee Meeting

Biosafety Officer (BSO) Report

October 20, 2022

Business Conducted since the last IBC Meeting

A. BSO approvals
   i. Feldmann PRD 19081 Amend 06
      1. Add permits
   ii. Feldmann RRD 22-410 Amend 01
      1. Add permits

B. Electronic business
   i. None

New business for IBC meeting

A. See agenda.

Biosafety Activities since the last IBC Meeting

A. Animal Study Protocols Review- Performed by Megan Brose, Rebecca Anderson, (b)(6)

ASP Title	Associated PRD	Associated RD	Reviewer
The role of mouse skin proteases in wound healing and the effect of tick protease inhibitors on this process	N/A	N/A	(b)(6)
Analysis of viral factors involved in the pathogenesis of California serogroup orthobunyaviruses	18-103	18-225	(b)(6)
Defining mouse strains susceptible and non-susceptible for monkeypox virus using the CC founder mice	22-240	N/A	B. Anderson
Immunogenicity and protective efficacy of a VSV based vaccine against Crimean-Congo hemorrhagic fever virus in mice	18-92 18-90 18-82	20-404	(b)(6)
Virulence comparison of West and Central African monkeypox strains, including the current outbreak strain, in the Cynomolgus macaque model	22-240	N/A	M. Brose
Evaluation of tick salivary proteins in blood feeding and immunity and as anti-tick vaccine candidates in rodents	21-233	N/A	B. Anderson
ChAdOx1 BiEBOV vaccine efficacy against Sudan virus (SUDV) in the cynomolgus macaque model	18-90	22-410	(b)(6)
Protective efficacy of VSV-Sudan against lethal challenge with Sudan virus in nonhuman primates	18-90 18-82	20-404	(b)(6)

B. Biosafety Training- Performed by Megan Brose, Rebecca Anderson, (b)(6)

Type of Training	Number of Sessions	Number of Employees Trained
New Employee	1	2
Select Agent-Initial	1	2
Select Agent- Refresher	3	188
Select Agent- Visitor	1	3
BSL-3 Laboratory Biosafety-Initial	2	3
Practical Training	2	3
BSL-4 Laboratory Biosafety-Initial	2	2
Suit Training	4	2
Checklist Training	6	3
BSL-4 Laboratory Biosafety-Refresher	1	1
Laboratory Biosafety Support Staff-Initial	N/A	N/A
Laboratory Biosafety Support Staff-Refresher	N/A	N/A

C. Safety Audits and Inspections

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

D. Biological Incidents to Report
   a. None

E. Other Issues
   a. None

NIH RML Institutional Biosafety Committee Meeting

Agenda for November 17, 2022

Location: Virtual via Zoom/Building A (b)(6)

Old Business

A. Draft minutes of October 20, 2022 meeting

New Business

A. Committee Business
   1) PRD-22-200 (Renewal) PI: Munster
   2) PRD-22-143 (Renewal) PI: Feldmann
   3) RD-22-196 (Renewal) PI Peterson — Reviewers: Sue Priola, Scott Kobayashi
   4) Draft Bldg (b)(6) BSL-3 SOP-Updated
   5) Draft SOP#4-28-38 Ferret and Mink Procedures in Biocontainment -Updated
   6) Annual IBC Training

B. BSO report (Dr. Becky Anderson)
C. Occupational Safety & Health Manager report (Seth Cooley)
D. IRFBSM/Responsible Official Report (LCDR Megan Brose)
E. Associate Director Report (Dr. Marshall Bloom)
F. Comments from around the room

Next Meeting: December 15, 2022 virtual via Zoom/Building A (b)(6)

PRD- Pathogen Registration Document
RD- Recombinant DNA Registration Document
SOP-Standard Operating Procedures
BSO-Biosafety Officer
IRFBSM-Integrated Research Facility Biosafety Manager

NIH RML Institutional Biosafety Committee Minutes

November 17, 2022 (1:00 PM – 2:05 PM)

Hybrid Zoom/Building A (b)(6) Meeting

Members Present:

☑ Sue Priola, Chair	☐ Marcie Caldwell (EO)	☑ Jamie Lovaglio
☐ Bob Heinzen, Vice Chair	☐ Bruce Chesebro (EO)	☑ Andrea Marzi
☑ Becky Anderson	☑ Seth Cooley	☐ Alida Merritt
☐ Alan Applebury	☑ Kendal Cooper	☑ Greg Saturday
☐ Chris Bosio	☐ Frank DeLeo (EO)	☐ Alexandra Scranton
☐ Marshall Bloom (EO)	☐ Heinz Feldmann (EO)	☐ Brian Vickrey
☐ Megan Brose	☑ Erik Hoover	☑ Clayton Winkler
☐ Larry Brouwer	☐ Josh Kellar (EO)	
☐ Carol Calderwood	☑ Scott Kobayashi	

(EO) *ex officio*

Guests: (b)(6)

Announcements

I. None

Old Business

I. Review of Past IBC Meeting Minutes
   a. October 20, 2022 Minutes
      i. The minutes were unanimously approved as written.

New Business

I. Registration of Material (Potentially) Infectious for Humans, Plants or Animals
   a. PRD-22-200 *E. coli* and other bacterial species – Vincent Munster (Renewal)
      i. Becky Anderson summarized the PRD. The PRD covers *E. coli K12, S. aureus, S. pygogenes, K. pneumonia, P. aeruginosa,* and *B. fragilis.* The purpose of the study is to use the bacteria to perform optimization/validation experiments to ensure they can obtain host and bacterial DNA alongside the typical viral RNA. The Munster lab plans to screen blood samples they obtained from the Ebola outbreak in Monrovia, Liberia, for the presence of enteric bacteria. The Munster lab will first use several known bacteria (listed above) to ensure their procedures will allow them to identify bacteria of interest. Known bacteria will be spiked into NHP blood, extracted and sequenced. Once the system is established, the Munster lab will then test the Monrovia human blood samples.
      ii. Kendal Cooper noted that some of the bacteria listed are pathogenic to animals in addition to humans. The pathogen section should be updated to include that information.

iii. No animal work was submitted, reviewed, or approved.
iv. Work with the listed bacterial species is approved at BSL-2.
v. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
vi. The committee unanimously approved with minor modifications.
    1. Update pathogen section to indicate bacteria are pathogenic to animals.

b. PRD-22-143 Coronaviruses – Heinz Feldmann (Renewal)
i. Becky Anderson summarized the PRD. The PRD is a renewal and no new work is proposed in this renewal. The PRD renewal consolidates the previous amendments that were added to the PRD in the last 5 years (approximately 20 amendments). This PRD covers many Coronaviruses which include the following: HCoV-229E, HCoV-OC43, HCoV-NL-63, HCoV-HKU1, Avian coronavirus Massachusetts, Murine coronavirus icA59, recombinant Canine coronavirus UCD1, Porcine respiratory coronavirus ISU1, Bovine coronavirus Mebus, Alphacoronavirus Purdue P115, SARS-CoV-2 (mouse adapted and isolates listed in attached table), MERS-CoV, Bat Coronaviruses (WIV1, HKU4, SHC014), HKU5 virus with SARS spike protein ectodomain, MERS-CoV recombinant infectious clone with ORF5 red fluorescent protein replacement, and bat SARS-like coronavirus, with SARS spike receptor binding domain. Becky Anderson summarized the signs and symptoms of the viruses, the natural routes of transmission and laboratory hazards.
ii. Sue Priola noted a spelling typo in the description section. Sue Priola also noted that on page 4 the language about emerging Coronaviruses should be deleted as those viruses would need IBC review and approval.
iii. Becky Anderson informed the committee about research that is considered PPP and ePPP. The committee discussed this topic extensively.
iv. Animal work with mice, hamsters, rabbits, NHPs, bats, pigs, sheep and goats were proposed.
v. Work with the listed Coronaviruses is approved at BSL-2/ABSL-2 and/or BSL-3/ABSL-3 as listed below:
    1. HCoV-229E, HCoV-OC43, HCoV-NL-63, HCoV-HKU1, Avian coronavirus Massachusetts, Murine coronavirus icA59, recombinant Canine coronavirus UCD1, Porcine respiratory coronavirus ISU1, Bovine coronavirus Mebus, Alphacoronavirus Purdue P115 are approved at BSL-2/ABSL-2.
    2. SARS-CoV-2 (mouse adapted and isolates listed in attached table), MERS-CoV, Bat Coronaviruses (WIV1, HKU4, SHC014), HKU5 virus with SARS spike protein ectodomain, MERS-CoV recombinant infectious clone with ORF5 red fluorescent protein replacement, and bat SARS-like coronavirus, with SARS spike receptor binding domain are approved at BSL-3/ABSL-3.
vi. The committee discussed the dual-use potential of these experiments. The committee also discussed that this registration could be considered PPP. The committee determined that this registration should be reviewed by the NIH DURC-IRE.
vii. The committee unanimously approved with minor modifications pending review by the NIH DURC-IRE:
    1. Correct spelling typo in Description section.
    2. Update page 4 to remove language about emerging Coronaviruses.

II. Registration of Recombinant DNA Experiments
a. RD-22-196 – Karin Peterson (Renewal)

i. Sue Priola summarized the registration. This is a renewal for continued work with mixed retrovirus infection including interactions of exogenous retroviruses with endogenous retroviruses of the host. Sue Priola noted that this work can be performed at BSL-1 but is done in a BSL-2 lab. There are no NIH Guidelines relevant for this work.
ii. Scott Kobayashi had no comments or concerns.
iii. Becky Anderson noted that the Pathogen section should be updated to state they use a BSC Class II - their lab does not have a BSC Class I.
iv. Animal studies with mice were proposed.
v. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
vi. Research using eukaryotic cells is approved at BSL-2/ABSL-2.
vii. The committee approved (Clayton Winkler abstained) with minor modifications.
    1. Updated Pathogen section, BSC Class II.

III. Full Committee Review of Inactivation Procedures
    a. None

IV. Standard Operating Procedures
    a. Draft Building (b)(6) BSL-3 OSP (Updated)
        i. Becky Anderson informed the committee that an SOP for work with Monkeypox virus was added to the OSP. The Monkeypox virus SOP describes vaccination, signage, and spill procedures.
        ii. Sue Priola noted that the agent summary section should be updated to include a section on Monkeypox virus.
        iii. There were no additional comments with the updated procedures.
        iv. The committee unanimously approved with minor modifications:
            1. Add an agent summary for monkeypox virus

    b. Draft SOP#4-28-38 Ferret and Mink Procedures in Biocontainment (Updated)
        i. Becky Anderson informed the committee about the minor updates made to the SOP.
        ii. There were no additional comments or concerns with the updated procedures.
        iii. The committee unanimously approved as written.

V. Annual Reviews
    a. None

VI. Annual IBC Training
    a. Becky Anderson presented the annual IBC training.

Reports

I. Biosafety Officer Report – Becky Anderson
    a. Becky Anderson presented the BSO report.
II. Occupational Safety and Health Manager Report – Seth Cooley
    a. Seth Cooley informed the committee that annual safety refresher training will be held in December, more information about dates will be sent out.
    b. A new initiative has been started to get an inventory of eyewashes and safety showers on campus.
III. IRF Biosafety Manager/Responsible Official Report – Megan Brose

a. Not present

IV. Associate Director Report – Marshall Bloom
   a. Not present

Around the Room

I. None

Next Meeting

I. January 19, 2023 virtual via Zoom/Building A(b)(6)

NIH RML Institutional Biosafety Committee Meeting

Biosafety Officer (BSO) Report

November 17, 2022

Business Conducted since the last IBC Meeting

A. BSO approvals
   a. None

B. Electronic business
   a. Validation study for inactivation of Y. pestis infected thin spleen homogenate smears with methanol. IBC at October meeting requested additional testing.

New business for IBC meeting

A. See agenda.

Biosafety Activities since the last IBC Meeting

A. Animal Study Protocols Review- Performed by Megan Brose, Rebecca Anderson, (b)(6)

ASP Title	Associated PRD	Associated RD	Reviewer
None reviewed. One ACUC meeting for November/December.			

B. Biosafety Training- Performed by Megan Brose, Rebecca Anderson (b)(6)

Type of Training	Number of Sessions	Number of Employees Trained
New Employee	2	2
Select Agent-Initial	1	1
Select Agent- Refresher	n/a	n/a
Select Agent- Visitor	1	1
BSL-3 Laboratory Biosafety-Initial	1	1
Practical Training	n/a	n/a
BSL-4 Laboratory Biosafety-Initial	n/a	n/a
Suit Training	n/a	n/a
Checklist Training	4	1
BSL-4 Laboratory Biosafety-Refresher	n/a	n/a
Laboratory Biosafety Support Staff-Initial	n/a	n/a
Laboratory Biosafety Support Staff-Refresher	n/a	n/a

C. Safety Audits and Inspections

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

D. Biological Incidents to Report
    a. None

E. Other Issues
    a. None

NIH RML Institutional Biosafety Committee Meeting

Agenda for December 15, 2022
Location: Virtual via Zoom/Building A (b)(6)

Old Business

A. Draft minutes of November 17, 2022 meeting

New Business

A. Committee Business
   1) PRD-20-227 (Amend 02) PI: Tirloni
   2) RD-15-303 (Amend 02) PI: Hinnebusch — Reviewers: Scott Kobayashi, Bob Heinzen
   3) RD 20-416 (Amend 01) PI: Feldmann — Reviewers: Andrea Marzi, Kendal Cooper
   4) RD 22-452 (Amend 01) PI: Feldmann — Reviewers: Chris Bosio, Clayton Winkler
   5) *Draft Inactivation Validation of Monkeypox virus infected tissues with formalin - New
   6) Draft SOP#4-28-33 Removal of samples via fixation - Updated
   7) Draft ABSL-3 OSP- add SOP# ABSL-3-25-7 Procedures for Rodent Studies in (b)(6) New
   8) Draft MCL Operations and Safety Procedures (OSP) – Annual Review

B. BSO report (Dr. Becky Anderson)
C. Occupational Safety & Health Manager report (Seth Cooley)
D. IRFBSM/Responsible Official Report (LCDR Megan Brose)
E. Associate Director Report (Dr. Marshall Bloom)
F. Comments from around the room

Next Meeting: December 15, 2022 virtual via Zoom/Building A (b)(6)

*Data will be sent to IBC on Monday December 12, 2022.

PRD- Pathogen Registration Document
RD- Recombinant DNA Registration Document
SOP-Standard Operating Procedures
BSO-Biosafety Officer
IRFBSM-Integrated Research Facility Biosafety Manager

NIH RML Institutional Biosafety Committee Minutes

December 15, 2022 (1:00 PM – 2:00 PM)

Hybrid Zoom/Building A(b)(6) Meeting

Members Present:

☑ Sue Priola, Chair	☐ Marcie Caldwell (EO)	☑ Jamie Lovaglio
☑ Bob Heinzen, Vice Chair	☐ Bruce Chesebro (EO)	☑ Andrea Marzi
☑ Becky Anderson	☑ Seth Cooley	☐ Alida Merritt
☐ Alan Applebury	☑ Kendal Cooper	☑ Greg Saturday
☐ Chris Bosio	☐ Frank DeLeo (EO)	☐ Alexandra Scranton
☐ Marshall Bloom (EO)	☐ Heinz Feldmann (EO)	☐ Brian Vickrey
☑ Megan Brose	☐ Erik Hoover	☑ Clayton Winkler
☑ Larry Brouwer	☐ Josh Kellar (EO)	
☐ Carol Calderwood	☑ Scott Kobayashi	

(EO) *ex officio*

Guests: (b)(6)

(b)(6)

Announcements

I. None

Old Business

I. Review of Past IBC Meeting Minutes
   a. November 17, 2022 Minutes
      i. Kendal Cooper noted a typo on the BSO report.
      ii. The minutes were unanimously approved with minor modifications.
         1. Correct typo in BSO report.

New Business

I. Registration of Material (Potentially) Infectious for Humans, Plants or Animals
   a. PRD-20-277 *Borrelia burgdorferi* – Lucas Tirloni (Amend)
      i. Becky Anderson summarized the PRD amendment. This amendment is to add *Borrelia hermsii* to the registration. The lab studies skin injury after a tick bite. This pathogen causes relapsing fever and can be treated with antibiotics. The natural route of transmission is by a tick bite.
      ii. No animal work was submitted, reviewed or approved.
      iii. Work is approved at BSL-2.
      iv. The committee discussed the dual-use potential of these experiments. The committee agreed there were no dual-use concerns with the proposal.
      v. The committee unanimously approved as written.

II. Registration of Recombinant DNA Experiments

a. RD-15-303 – Joe Hinnebusch (Amend)

i. Scott Kobayashi summarized the registration. This is an amendment to add a new plasmid (mini-T7-gat) for use in conjunction with the Tn7-based chromosomal insertion method for complementation. The plasmid contains the glyphosate resistance gene gat, (the active ingredient in Roundup©). Glyphosate and resistance to it has no relevance to plague pathogenesis, diagnosis, or treatment. Introduction of the gat gene would be an intermediate step. Gat resistance would be used for selection of integrants, but the gat gene would subsequently be deleted, and the intermediate Gat-resistant clone would then be destroyed. Plasmid map is attached.
ii. Bob Heinzen had no additional comments.
iii. Sue Priola confirmed that there are no additional antibiotics resistance markers on the plasmid map.
iv. Becky Anderson noted that DSAT was notified of this experiment and DSAT confirmed that this is not a restricted experiment.
v. No animal work was submitted, reviewed or approved.
vi. The committee discussed the dual-use potential of these experiments. The committee agreed there were no dual-use concerns with the proposal.
vii. Research using prokaryotic cells is approved at BSL-3 under sections III-D-2-a and III-D-1-b of the NIH Guidelines.
viii. The committee unanimously approved as written.

b. RD-20-416 – Heinz Feldmann (Amend)

i. Andrea Marzi summarized the registration. This is an amendment to add two recombinant influenza A viruses to the lab repository: IAV NS1 R38A/K41A dsRNA binding mutant and IAV NS1-GFP. Both are handled at BSL-2. These will be obtained from a collaborator. The features of the strains are included in the attachments.
ii. Kendal Cooper had no additional comments.
iii. No animal work was submitted, reviewed or approved.
iv. The committee discussed the dual-use potential of these experiments. The committee agreed there were no dual-use concerns with the proposal.
v. Research using eukaryotic cells is approved at BSL-2 under sections III-D-1-a and III-D-3-a of the NIH Guidelines.
vi. The committee unanimously approved as written.

c. RD-22-452 – Heinz Feldmann (Amend)

i. Clayton Winkler summarized the registration. This is an amendment to add guinea pigs as a new animal model. This registration covers use of replication deficient alphaviruses as a vaccine platform.
ii. Chris Bosio emailed Sue Priola prior to the meeting that he had no comments on this amendment.
iii. Animal studies with guinea pigs were proposed.
iv. The committee discussed the dual-use potential of these experiments. The committee agreed there were no dual-use concerns with the proposal.
v. Research using eukaryotic cells is approved at BSL-2/ABSL-2 under sections III-D-1-a, III-D-3-a and III-E-1 of the NIH Guidelines.
vi. The committee unanimously (Andrea Marzi abstained) approved as written.

III. Full Committee Review of Inactivation Procedures
    a. Draft Inactivation Validation of Monkeypox virus infected tissues with formalin
        i. Sue Priola summarized the inactivation data. This is inactivation testing for Poxvirus tissues with 10% formalin. This testing was performed with a non-select agent strain of Monkeypox virus. Appropriate positive and negative controls were included. Samples were tested in triplicate.
        ii. Sue Priola asked if infected intestinal tissues were used to start. (b)(6) confirmed that this is correct, and the tissues were spiked with additional virus. The infected tissues were spiked with small volumes to assist in virus absorption. The final titer should be updated to PFU/gram in both the inactivation testing and SOP. This validation test used the amount of tissue that would fit in a tissue cassette.
        iii. The committee had no additional comments.
        iv. The committee unanimously approved with minor modifications.
            1. Update PFU/mL to PFU/gram.

IV. Standard Operating Procedures
    a. Draft SOP#4-28-33 Removal of samples via fixation (Updated)
        i. Sue Priola informed the committee that the update is to add inactivation data with 10% formalin for Pox viruses infected tissues.
        ii. There were no additional comments or concerns with the updated procedures.
        iii. The committee unanimously approved with minor modifications.
            1. Update to PFU/mL to PFU/gram in table.
    b. Draft ABSL-3 OSP - Add SOP# ABSL-3-25-7 Procedures for Rodent Studies in (b)(6) (New)
        i. Becky Anderson informed the committee that the new SOP is for the renovated (b)(6) in the ABSL-3. (b)(6) This SOP discusses entry, exit and procedures for (b)(6)
        ii. The committee asked about the interlocking of the doors of the anteroom. Becky Anderson confirmed that the door will be mechanically interlocked and an emergency exit button will be installed.
        iii. Kendal Cooper noted that the trench drain language should indicate that the trench drains will be closed when rodent studies are going on.
        iv. Jamie Lovaglio asked on pg 67 to update language on section #1 to “inside” instead of “within” the 2” perimeter of the necropsy table. Also to update language in section #2 to “work-zone” instead of “ 2” perimeter”.
        v. There were no additional comments or concerns with the updated procedures.
        vi. The committee unanimously approved with minor modifications.
            1. Update language that trench drains will be closed when rodent studies are going on in the space.
            2. Update language on pg 67
                a. Section #1 – update within to inside the 2” perimeter of the necropsy table
                b. Section #2 – update 2” perimeter to work-zone

V. Annual Reviews
    a. Draft MCL Operations and Safety Procedures (OSP)
        i. Becky Anderson summarized the updates to the OSP. A section was added for suit room procedures. The ARO list was updated. The list of restricted experiments was updated. A new section for sonication was added.

ii. Jamie Lovaglio noted that the gown used in moving suits is a disposable gown.
iii. (b)(6) described the new section for probe sonicator operation. All sonication will be conducted in a BSC.
iv. The committee discussed the addition of the sonication operations section. Andrea Marzi asked that a sign be placed on the support room door when sonication is occurring. Sue Priola noted that the title should be updated to Probe Sonicator Operation.
v. Kendal Cooper asked about adding a sound enclosure for the procedure. (b)(6) noted that the sound enclosure the lab has will not fit in the BSC.
vi. Sue Priola asked about potential inadvertent aerosolization of a sample during a sonication procedure. (b)(6) noted that if there was aerosolization of the sample in the BSC, it would be cleaned using the standard spill inside the BSC procedures.
vii. The committee recommended that the lab should do a test run at BSL-2 before performing this experiment at BSL-4.
viii. The committee unanimously approved with minor modifications
    1. Update moving suit procedure to indicate a "disposable" gown is worn.
    2. Update to include "Probe" in sonicator operation title.
    3. Update sonicator operation to indicate a sign will be placed on the door when sonication is in progress.

Reports

I. Biosafety Officer Report – Becky Anderson
    a. Becky Anderson presented the BSO report.
II. Occupational Safety and Health Manager Report – Seth Cooley
    a. Nothing to report.
III. IRF Biosafety Manager/Responsible Official Report – Megan Brose
    a. Nothing to report.
IV. Associate Director Report – Marshall Bloom
    a. Not present

Around the Room

I. Becky Anderson updated the committee that the registration referred to the NIH DURC-IRE in November 2022 will be reviewed in January 2023.

Other Issues

I. None

Next Meeting

I. January 19, 2023 hybrid virtual via Zoom/Building A (b)(6)

NIH RML Institutional Biosafety Committee Meeting

Biosafety Officer (BSO) Report

December 15, 2022

Business Conducted since the last IBC Meeting

A. BSO approvals
   a. Feldmann RD 21-440
      i. Add IM route of inoculation for mice

B. Electronic business
   a. None.

New business for IBC meeting

A. See agenda.

Biosafety Activities since the last IBC Meeting

A. Animal Study Protocols Review- Performed by Megan Brose, Rebecca Anderson, (b)(6)

ASP Title	Associated PRD	Associated RD	Reviewer
Establishing a wild caught colony of Mastomys natalensis in Mali	19-158	N/A	R. Anderson
Evaluation of LASV, MPXV and other zoonotic pathogens circulating in small mammals in Ghana	19-158	N/A	(b)(6); (b)(3):42 U.S.C. 262a(h)
Determining the effectiveness of a ChAdOx1-Lassa vaccine in a heterologous challenge of Strain 13 Guinea pigs with relevant LASV lineages	18-94	17-410	M. Brose
Mouse model development for Betacoronaviruses WIV-1 and SHC014 using K18-hACE2 mice	17-143		R. Anderson
Effect of Lrp1 expression on EBOV infectivity and pathogenesis in mice	18-90	21-407	(b)(6); (b)(3):42 U.S.C. 262a(h)
Adaptive immune responses elicited by intramuscular and mucosal SARS-CoV-2 vaccination of mice	17-143	21-440 22-410	M. Brose
Efficacy of a replicating RNA vaccine against Sudan virus infection in Guinea pigs	18-90 18-82	22-452 20-404	R. Anderson

B. Biosafety Training- Performed by Megan Brose, Rebecca Anderson, (b)(6)

Type of Training	Number of Sessions	Number of Employees Trained
New Employee	N/A	N/A
Annual Refresher Lab Biosafety	1	161
Select Agent-Initial	N/A	N/A
Select Agent- Refresher	N/A	N/A
Select Agent- Visitor	N/A	N/A
BSL-3 Laboratory Biosafety-Initial	N/A	N/A
Practical Training	1	1
BSL-4 Laboratory Biosafety-Initial	N/A	N/A
Suit Training	N/A	N/A
Checklist Training	N/A	N/A
Laboratory Biosafety Support Staff-Initial	1	1
Laboratory Biosafety Support Staff-Refresher	3	59

C. Safety Audits and Inspections

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

D. Biological Incidents to Report
    a. Two rodent bites, both in naïve animals

E. Other Issues
    a. None

NIH RML Institutional Biosafety Committee Meeting

Agenda for January 19, 2022

Location: Virtual via Zoom/Building A (b)(6)

Old Business

A. Draft minutes of December 15, 2022 meeting

New Business

A. Committee Business
    1) PRD-19-213 (Amend 04) PI: Bloom
    2) PRD 23-107 (Renewal) PI: Best
    3) Draft Building (b)(6) BSL-3 Operations and Safety Procedures (OSP) – Updates throughout

B. BSO report (Dr. Becky Anderson)
C. Occupational Safety & Health Manager report (Seth Cooley)
D. IRFBSM report (b)(6)
E. Responsible Official Report (LCDR Megan Brose)
F. Associate Director Report (Dr. Marshall Bloom)
G. Comments from around the room

Next Meeting: February 16, 2022 virtual via Zoom/Building A (b)(6)

PRD- Pathogen Registration Document
RD- Recombinant DNA Registration Document
SOP-Standard Operating Procedures
BSO-Biosafety Officer
IRFBSM-Integrated Research Facility Biosafety Manager

NIH RML Institutional Biosafety Committee Minutes

January 19, 2023 (1:04 PM – 1:21 PM)
Virtual via Zoom/Building A (b)(6)

Members Present:

☒Sue Priola, Chair	☐Marcie Caldwell (EO)	☐Jamie Lovaglio
☐Bob Heinzen, Vice Chair	☐Bruce Chesebro (EO)	☒Andrea Marzi
☒Becky Anderson	☒Seth Cooley	☒Alida Merritt
☐Alan Applebury	☒Kendal Cooper	☒Greg Saturday
☒Chris Bosio	☐Frank DeLeo (EO)	☐Alexandra Scranton
☐Marshall Bloom (EO)	☐Heinz Feldmann (EO)	☐Brian Vickrey
☒Megan Brose	☒Erik Hoover	☒Clayton Winkler
☐Larry Brouwer	☐Josh Kellar (EO)	
☐Carol Calderwood	☒Scott Kobayashi	

(EO) *ex officio*

Guests: (b)(6)

Announcements

I. None

Old Business

I. Review of Past IBC Meeting Minutes
   a. December 15, 2022 Minutes
      i. (b)(6) and Sue Priola noted a few minor typos.
      ii. The minutes were unanimously approved with minor corrections.
         1. Update minor typos.

New Business

I. Registration of Material (Potentially) Infectious for Humans, Plants or Animals
   a. PRD-19-213 *Borrelia spp.*– Marshall Bloom (Amend)
      i. Becky Anderson summarized the PRD. This is an amendment to add relapsing fever Borrelia isolates from a RML collaborator. Plans for these strains include long-term storage, cultivation, and assessment of fitness in the mouse-tick infectious cycle. Strains to add to the registration include: *B. hermsii*, *B. turicatae*, *B. parkeri*, *B. corciduae*, *B. coriaceae*, *B. recurrentis*, *B. anserina*, *B. miyamotoi*, *B. andersonii*, and *B. afzelii*.
      ii. No animal studies were submitted, reviewed, or approved.
      iii. Sue Priola asked about Dual Use question #5 which describes mutant strains. These are not noted in the amendment description.
      iv. Work with the following Borrelia species is approved at BSL-2/ABSL-2: *B. hermsii, B. turicatae, B. parkeri, B. corciduae, B. coriaceae, B. recurrentis, B. anserina, B. miyamotoi, B. andersonii, B. afzelii.*
      v. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
      vi. The committee unanimously approved with minor modifications.
         1. Update description to include the addition of mutant strains.

b. PRD-23-107 Powassan virus – Sonja Best (Renewal)
    i. Becky Anderson summarized the PRD. This is a renewal for work with Powassan virus. The lab aims to understand the events associated with the host immune response that are important for virus clearance and to understand how flaviviruses evade these host responses to infection. There is no additional work added to this renewal.
    ii. Animal studies with mice were proposed.
    iii. Work with Powassan virus is approved at BSL-3/ABSL-3. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 375-9600.
    iv. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
    v. The committee unanimously approved as written.

II. Registration of Recombinant DNA Experiments
    a. None

III. Full Committee Review of Inactivation Procedures
    a. None

IV. Standard Operating Procedures
    a. Draft Building (b)(6) BSL-3 Operations and Safety Procedures (OSP) (Updates)
        i. Becky Anderson summarized the updates to the OSP to the committee. The updates included eliminating requirement to remove outer glove when removing hands from BSC. BSL-3-28-14, the Yellow Fever SOP, was updated to match entry requirements to the Monkeypox SOP. Information for influenza viruses was combined with this document and the separate influenza SOP will be inactivated.
        ii. Sue Priola noted the BMBL reference in the influenza section needs to be updated to 6th edition.
        iii. There were no additional comments or concerns with the updated procedures.
        iv. The committee unanimously approved with minor modifications.
            1. Update BMBL reference in influenza section.

V. Annual Reviews
    a. None

Reports

I. Biosafety Officer Report – Becky Anderson
    a. Becky Anderson presented the BSO report.
    b. The DURC-IRE review committee will meet next week. The intake form was reviewed.
    c. NSABB will meet on 1/27/23.

II. Occupational Safety and Health Manager Report – Seth Cooley
    a. Nothing to report.

III. IRF Biosafety Manager Report – (b)(6)
    a. Nothing to report.

IV. Responsible Official Report – Megan Brose
    a. Nothing to report.

V. Associate Director Report – Marshall Bloom
    a. Not present.

Around the Room

I. March 2023 IBC meeting will be cancelled.

Other Issues

I.

Next Meeting

I. February 16, 2023 virtual via Zoom/Building A (b)(6)

NIH RML Institutional Biosafety Committee Meeting

Biosafety Officer (BSO) Report

January 19, 2023

Business Conducted since the last IBC Meeting

A. BSO approvals
   a. None.

B. Electronic business
   a. None.

New business for IBC meeting

A. See agenda.

Biosafety Activities since the last IBC Meeting

A. Animal Study Protocols Review- Performed by Megan Brose, Rebecca Anderson, (b)(6)

ASP Title	Associated PRD	Associated RD	Reviewer
Elucidating the role of prostaglandins in driving efferocytosis during murine pulmonary infection	18-71	N/A	B. Anderson

C. Biosafety Training- Performed by Megan Brose, Rebecca Anderson (b)(6)

Type of Training	Number of Sessions	Number of Employees Trained
New Employee	1	6
Annual Refresher Lab Biosafety	1	130
Select Agent-Initial	1	2
Select Agent- Refresher	N/A	N/A
Select Agent- Visitor	2	2
BSL-3 Laboratory Biosafety-Initial	2	3
Practical Training	2	3
BSL-4 Laboratory Biosafety-Initial	1	2
Suit Training	3	4
Checklist Training	N/A	N/A
Laboratory Biosafety Support Staff-Initial	N/A	N/A
Laboratory Biosafety Support Staff-Refresher	6	20

D. Safety Audits and Inspections

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

E. Biological Incidents to Report
   a. None

F. Other Issues
   a. None

NIH RML Institutional Biosafety Committee Meeting

Agenda for February 16, 2023

Location: Virtual via Zoom/Building A (b)(6)

Old Business

A. Draft minutes of January 19, 2023 meeting

New Business

A. Committee Business
   1) PRD 18-44 (Amend 04) PI: Steele-Mortimer
   2) PRD 23-108 (Renewal) PI: Best
   3) PRD 23-112 (Renewal) PI: Best
   4) PRD 23-113 (Renewal) PI: Best
   5) PRD 23-51 (Renewal) PI: Priola
   6) PRD 23-206 (Renewal) PI: Feldmann
   7) PRD 23-208 (Renewal) PI: Feldmann
   8) RD 21-134 (Amend 04) PI: Groshong — Reviewer: Chris Bosio, Scott Kobayashi
   9) RD 23-429 (Renewal) PI: Feldmann — Reviewer: Kendal Cooper, Clayton Winkler
   10) Draft Building 25 BSL-3 (b)(6) SOP – Add four new SOPs (previously approved inactivation procedures)

B. BSO report (Dr. Becky Anderson)
C. Occupational Safety & Health Manager report (Seth Cooley)
D. IRFBSM report (Dr. (b)(6))
E. Responsible Official Report (LCDR Megan Brose)
F. Associate Director Report (Dr. Marshall Bloom)
G. Comments from around the room

Next Meeting: April 20, 2023 virtual via Zoom/Building A (b)(6)

PRD- Pathogen Registration Document
RD- Recombinant DNA Registration Document
SOP-Standard Operating Procedures
BSO-Biosafety Officer
IRFBSM-Integrated Research Facility Biosafety Manager

NIH RML Institutional Biosafety Committee Minutes

February 16, 2023 (1:00 PM – 3:00 PM)
Virtual via Zoom/Building A (b)(6)

Members Present:

☒Sue Priola, Chair	☐Marcie Caldwell (EO)	☒Scott Kobayashi
☒Bob Heinzen, Vice Chair	☐Bruce Chesebro (EO)	☒Jamie Lovaglio
☒Becky Anderson	☒Seth Cooley	☒Andrea Marzi
☐Alan Applebury	☒Kendal Cooper	☒Alida Merritt
☒Chris Bosio	☐Frank DeLeo (EO)	☐Greg Saturday
☐Marshall Bloom (EO)	☒Haley DeMers	☐Alexandra Scranton
☒Megan Brose	☐Heinz Feldmann (EO)	☐Brian Vickrey
☒Larry Brouwer	☒Erik Hoover	☐Clayton Winkler
☐Carol Calderwood	☐Josh Kellar (EO)	

(EO) *ex officio*

Guests: (b)(6)

Announcements

I. None

Old Business

I. Review of Past IBC Meeting Minutes
    a. January 19, 2023 Minutes
        i. The minutes were unanimously approved as written.

New Business

I. Registration of Material (Potentially) Infectious for Humans, Plants or Animals
    a. PRD-18-44 *Salmonella typhimurium* – Olivia Steele-Mortimer (Amend)
        i. Becky Anderson summarized the PRD. This is an amendment to add *E. coli* and *Yersinia enterocolitica* for comparison to Salmonella enterica serovar Typhimurium. *E. coli* strains are from the ECOR standard reference strains and *E. coli* NC101 an adherent-invasive (AIEC) mouse isolate. The strains include pathogenic and non-pathogenic strains. *Yersinia enterocolitica* work will include strains: CS080 and 8081. The lab will compare growth curves, oxygen consumption and gene expression in liquid culture.
        ii. No animal studies were submitted, reviewed, or approved.
        iii. Work with *E. coli* and *Yersinia enterocolitica* is approved at BSL-2/ABSL-2. For the pathogenic strains of *E. coli*, care will be used to minimize aerosols. This requirement will be added to the recommendations section.
        iv. The committee discussed the dual-use and ePPP (enhanced potential pandemic pathogen) potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.
        v. The committee unanimously approved with minor modifications.
            1. Update precautions to minimize aerosols.
    b. PRD-23-108 West Nile virus – Sonja Best (Renewal)

i. Becky Anderson summarized the PRD. This is a renewal for work with West Nile virus. This renewal has no new work, and all approved amendments were included. The lab looks to understand the events associated with the host immune responses that are important for virus clearance and to understand how flaviviruses evade host responses to infection. Per the updates in the BMBL 6th edition, new samples can be worked with at BSL-2. Additional precautions for minimizing aerosols and all work will be conducted in a BSC will be added.
ii. Animal studies with mice were proposed.
iii. Work with West Nile virus is approved for work at BSL-2/ABSL-2. Existing strains of West Nile virus in the BSL-3 laboratory cannot be removed to the BSL-2 lab, new stocks will need to be obtained to initiate any new West Nile virus work in BSL-2. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact OMS at 406-375-9600.
iv. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.
v. The committee unanimously approved with minor modifications.
    1. Update precautions to minimize aerosols and all work will be done in a BSC.

c. PRD-23-112 Langat virus– Sonja Best (Renewal)
i. Becky Anderson summarized the PRD. This is a renewal for work with Langat virus. This renewal has no new work, and all approved amendments were included. The lab is interested in understanding how Langat virus evades the host interferon response.
ii. Sue Priola noted a typo under synopsis and the associated RD number. On pg 3, update applicable toxin question to N/A.
iii. Animal studies with mice were proposed.
iv. Work with Langat virus is approved at BSL-2/ABSL-2. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact OMS at 375-9600.
v. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.
vi. The committee unanimously approved with minor modifications.
    1. Update minor typos.
    2. Update answer to toxin question on pg. 3 to N/A.

d. PRD-23-113 Kunjin virus – Sonja Best (Renewal)
i. Becky Anderson summarized the PRD. This is a renewal for work with Kunjin virus. This renewal has no new work, and all approved amendments were included. Kunjin virus is an attenuated subtype of West Nile virus. The lab is interested in comparing Kunjin virus and West Nile virus to understand the mechanism of pathogenesis and how the virus manipulates the host immune response.
ii. Sue Priola noted a typo under synopsis and the associated RD number. On pg 3, update applicable toxin question to N/A.
iii. Sue Priola asked if there was a strain or genotype associated. Becky Anderson will confirm.
iv. No animal studies were submitted, reviewed, or approved.

v. Work with Kunjin virus is approved at BSL-2. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact OMS at 375-9600.
vi. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.
vii. The committee unanimously approved with minor modifications.
    1. Update minor typos.
    2. Update answer to toxin question on pg. 3 to N/A.
    3. Confirm strain or genotype designation.

e. PRD-23-51 Human Transmissible spongiform encephalopathies – Sue Priola (Renewal)
    i. Becky Anderson summarized the PRD. This is a renewal for work with Human TSEs. The lab looks to understand how human TSEs replicate and cause different forms of prion diseases in humans.
    ii. Sue Priola noted a typo on pg 2, and indicated that another isolate of familial CJD, isolate Y226X, will be added.
    iii. Animal studies with mice were proposed.
    iv. Work with human TSEs is approved at BSL-2/ABSL-2 with additional precautions. The lab is a restricted access lab, gown and gloves are required and a face mask should be worn, use of a respirator is optional. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact OMS at 375-9600.
    v. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.
    vi. The committee unanimously approved (Sue Priola abstained) with minor modifications.
        1. Update typo.
        2. Add additional isolate.

f. PRD-23-206 Alphavirus – Heinz Feldmann (Renewal)
    i. Becky Anderson summarized the PRD. This is a renewal for work with Alphaviruses (Ross River virus and Chikungunya virus). This renewal has no new work, and all approved amendments were included. The lab investigates the host and virus interaction of these viruses.
    ii. Animal work with NHPs were proposed.
    iii. Work with Alphaviruses is approved as follows:
        1. Ross River virus - BSL-2
        2. Chikungunya virus vaccine strain 181/25 - BSL-2
        3. Chikungunya virus - BSL-3
        4. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact OMS at 406-375-9600.
    iv. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.
    v. The committee unanimously approved as written.

g. PRD-23-208 Borna disease virus – Heinz Feldmann (Renewal)

i. Becky Anderson summarized the PRD. This is a renewal for work with Borna disease virus. This renewal has no new work, and all approved amendments were included. The lab seeks to understand reservoirs, epidemiology, and molecular biology of bornaviruses to provide a model for novel zoonotic infections and to evaluate medical countermeasures.
ii. Animal work with NHPs were proposed.
iii. Work with Borna disease virus is approved as follows:
    1. Borna Disease Virus: BSL-2
    2. Variegated Squirrel bornavirus: BSL-3
    3. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact OMS at 406-375-9600.
iv. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.
v. The committee unanimously approved as written.

II. Registration of Recombinant DNA Experiments
a. RD-21-134 *Borrelia burgdorferi* – Ashley Groshong (Amend)
    i. Chris Bosio summarized the RD amendment. This amendment is to add two additional plasmids, pHSG398 and pCRScriptCm, to generate mutant constructs of *Borrelia burgdorferi* and *Borrelia hermsii*. These plasmids have chloramphenicol resistance genes and will be used in Kanamycin resistant *Borrelia* strains. Chloramphenicol is not used for disease treatment and the resistance gene will not be selected for in *Borrelia*. Plasmid maps were attached.
    ii. Scott Kobayashi noted that the plasmid map indicated CamR instead of CmR.
    iii. No animal studies were submitted, reviewed, or approved.
    iv. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use concerns or ePPP with the proposal.
    v. Research using prokaryotic cells is approved at BSL-2 under section III-D-1-a and III-D-2-a of the NIH Guidelines.
    vi. The committee unanimously approved with minor modifications.
        1. Update plasmid map for pCRScriptCm.
b. RD-23-429 Rabies virus – Heinz Feldmann (Renewal)
    i. Kendal Cooper summarized the RD. This is a renewal for the rabies virus vaccine platform. All work has been previously approved. The lab studies the use of an attenuated rabies virus as a viral vaccine platform. Open reading frames for foreign genes are amplified from viral RNA and inserted into the RABV virus. This includes genes from filo-, bunya-, paramyxo-, orthomyxo, flavi-, arena-, retro-, and coronavirus proteins. It was noted in the synopsis that VLPs may also be produced from the infected cells. These vaccines are being produced by a collaborator for use at RML.
    ii. Andrea Marzi confirmed that VLPs may be produced based on the genes that are inserted in the vaccine platform.
    iii. Clayton Winkler sent electronic comments. Update NIH guidelines to include III-D-1-a and III-E-1. Haley DeMers agreed with the addition of these NIH guidelines.
    iv. Animal studies with hamsters and NHPs were proposed.
    v. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.

vi. Research using eukaryotic cells is approved at BSL-2 under section III-D-1-a and III-E-1 of the NIH guidelines. Vaccination to rabies is recommended for all personnel working directly with rabies vectors. Contact OMS at 406-375-9600 for more information.
vii. The committee unanimously approved as written.
    1. Clarify VLP sentence in the synopsis.
    2. Add NIH guidelines III-D-1-a and III-E-1.

III. Full Committee Review of Inactivation Procedures
    a. None

IV. Standard Operating Procedures
    a. Draft Building 25 BSL-3 (b)(6) Coronavirus SOP (Updates)
        i. Becky Anderson summarized the updates to the SOP to the committee. This is to add four SOPs to the existing BSL-3 (b)(6) SOP. These SOPs were all previously approved for use in the BSL-4 and the lab's previous BSL-3. This PI is moving buildings and will now begin work in (b)(6) There are no new procedures being added.
        ii. Clayton Winkler indicated a formatting issue on pg. 5. For section 2.3.3 on the first new SOP, this could be edited for clarity. For section 3.10.4 on the second new SOP, clarify that tissue fragments will be disposed of as biohazardous waste. The committee agreed with these recommendations.
        iii. Sue Priola noted a typo on section 1.2 (pg. 74).
        iv. There were no additional comments or concerns with the updated procedures.
        v. The committee unanimously approved with minor modifications.
            1. Update formatting and typos.
            2. Clarify section 2.3.3 and 3.10.4.

V. Annual Reviews
    a. None

Reports

I. Biosafety Officer Report – Becky Anderson
    a. Becky Anderson presented the BSO report.
    b. Becky Anderson presented the Full-Length Clone Laboratory report for 2022.
II. Occupational Safety and Health Manager Report – Seth Cooley
    a. Nothing to report.
III. IRF Biosafety Manager Report – Haley DeMers
    a. Nothing to report.
IV. Responsible Official Report – Megan Brose
    a. Upcoming Select Agent Inspection March 14-16, 2023.
V. Associate Director Report – Marshall Bloom
    a. Not present.

Around the Room

I. March 2023 IBC meeting will be cancelled.

Other Issues

I.

Next Meeting

I. April 20, 2023 virtual via Zoom/Building A (b)(6)

NIH RML Institutional Biosafety Committee Meeting

Biosafety Officer (BSO) Report

February 16, 2023

Business Conducted since the last IBC Meeting

A. BSO approvals
   a. Feldmann PRD 22-83
      i. Addition of new permits

B. Electronic business
   a. Hinnebusch inactivation of *Y. pestis* with Qiagen Genomic DNA Extraction Kit
      i. Updated BSL-3 (b)(6) SOP for *Y. pestis*

New business for IBC meeting

A. See agenda.

Biosafety Activities since the last IBC Meeting

A. Animal Study Protocols Review- Performed by Megan Brose, Rebecca Anderson, Haley DeMers

ASP Title	Associated PRD	Associated RD	Reviewer
Further characterization of a disseminating CMV based vaccine for Lass virus infection in mastomys natalensis.	18-94 19-219	20-442	R. Anderson
Continued testing of human antibodies against Andes virus in the hamster HCPS model	22-81	N/A	H. DeMers
Invasion of meninges by Salmonella in a mouse model.	18-44	22-108	M. Brose
Analyzing the impact of a ketogenic diet on disease progression in prion infected mice	16-191 23-51	12-211	R. Anderson
The influence of mosquito salivary gland proteins on vascular permeability in mice during La Crosse virus infection	18-103	N/A	H. DeMers
Generating Monoclonal Antibodies against Human Pathogenic Bunyaviruses in Mice	22-123	22-452	M. Brose

B. Biosafety Training- Performed by Megan Brose, Rebecca Anderson, Haley DeMers

Type of Training	Number of Sessions	Number of Employees Trained
New Employee	1	12
Annual Refresher Lab Biosafety	N/A	N/A
Select Agent-Initial	1	1
Select Agent- Refresher	N/A	N/A
Select Agent- Visitor	N/A	N/A
BSL-3 Laboratory Biosafety-Initial	1	2
Practical Training	1	2
BSL-4 Laboratory Biosafety-Initial	N/A	N/A
Suit Training	1	2
Checklist Training	5	16
Laboratory Biosafety Support Staff-Initial	1	4
Laboratory Biosafety Support Staff-Refresher	1	4

C. Safety Audits and Inspections

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

D. Biological Incidents to Report
    a. None

E. Other Issues
    a. None

NIH RML Institutional Biosafety Committee Meeting

Agenda for April 20, 2023

Location: Virtual via Zoom/Building A (b)(6)

Old Business

A. Draft minutes of February 16, 2023 meeting

New Business

A. Committee Business
   1) PRD 23-243 (New) PI: Best
   2) PRD 23-244 (New) PI: Best
   3) PRD 23-245 (New) PI: Bosio
   4) PRD 22-138 (Amend 01) PI: Feldmann
   5) PRD 23-145 (Renewal) PI: Feldmann
   6) PRD 23-202 (Renewal) PI: Feldmann
   7) PRD 23-82 (Renewal) PI: Marzi
   8) PRD 23-176 (Renewal) PI: Hanley
   9) PRD 23-191 (Renewal) PI: Priola
   10) RD 21-440 (Amend 02) PI: Feldmann Reviewer: Andrea Marzi, Sue Priola
   11) Draft Bldg (b)(6) BSL-3 (b)(6) SOP – Add two new SOPs (CB.8 Microscopy and CB.9 Tissue homogenization)
   12) Draft ABSL-3 Coxiella Animal SOP-add intranasal inoculation for guinea pigs

B. BSO report (Dr. Becky Anderson)
C. Occupational Safety & Health Manager report (Seth Cooley)
D. IRFBSM report (Dr. Haley DeMers)
E. Responsible Official Report (LCDR Megan Brose)
F. Associate Director Report (Dr. Marshall Bloom)
G. Comments from around the room

Next Meeting: May 18, 2023 virtual via Zoom/Building A (b)(6)

PRD- Pathogen Registration Document
RD- Recombinant DNA Registration Document
SOP-Standard Operating Procedures

BSO-Biosafety Officer
IRFBSM-Integrated Research Facility Biosafety Manager

NIH RML Institutional Biosafety Committee Minutes

April 20, 2023 (1:00 PM – 2:12 PM)

Virtual via Zoom/Building A (b)(6)

Members Present:

☒Sue Priola, Chair	☐Carol Calderwood	☒Scott Kobayashi
☒Bob Heinzen, Vice Chair	☒Marcie Caldwell (EO)	☐Jamie Lovaglio
☒Becky Anderson	☒Seth Cooley	☒Andrea Marzi
☐Alan Applebury	☒Kendal Cooper	☐Alida Merritt
☐Sonja Best (EO)	☐Frank DeLeo (EO)	☐Greg Saturday
☒Chris Bosio	☒Haley DeMers	☐Alexandra Scranton
☐Marshall Bloom (EO)	☐Heinz Feldmann (EO)	☐Brian Vickrey
☒Megan Brose	☐Erik Hoover	☒Clayton Winkler
☐Larry Brouwer	☐Josh Kellar (EO)	

(EO) *ex officio*

Guests: (b)(6)

Announcements

I. None

Old Business

I. Review of Past IBC Meeting Minutes
   a. February 16, 2023 Minutes
      i. Kendal Cooper noted a minor typo on pg 5.
      ii. Sue Priola noted Bruce Chesebro is no longer the Lab Chief of LPVD and should be updated to Sonja Best as the *ex officio* member.
      iii. The minutes were unanimously approved with minor corrections.
         1. Update minor typos.
         2. Update Bruce Chesebro to Sonja Best as *ex officio* in members list.

New Business

I. Registration of Material (Potentially) Infectious for Humans, Plants or Animals
   a. PRD-23-243 Human Blood and Body Fluids (BBF) and Non-Human primate BBF – Sonja Best (New)
      i. Becky Anderson summarized the PRD. This is a new registration to work with human and non-human primate blood and body fluids. This material is used for infection analysis.
      ii. No animal studies were submitted, reviewed, or approved.
      iii. Kendal Cooper noted that SARS-CoV-2 patient samples will be inactivated prior to handling, but no inactivation methods are listed in the registration.
      iv. Work with Human Blood and Body fluids is approved at BSL-2:
         1. Research performed with this material is subject to the NIH OACU BSSE Guidelines (https://oacu.oir.nih.gov/system/files/media/file/2022-12/OACU_BSSE_Guidelines-20221027.pdf). Please contact your IC Safety Specialist for information on how to obtain the required components of the kit.

2. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 406-375-9600.

v. The committee discussed the dual-use and ePPP (enhanced potential pandemic pathogen) potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.

vi. The committee unanimously approved with minor modifications.

1. Update inactivation methods to include irradiation.

b. PRD-23-244 Sendai virus – Sonja Best (New)

i. Becky Anderson summarized the PRD. This is a new registration to work with Sendai virus. The lab uses this virus in tissue culture models to examine pathways of innate immune induction.

ii. No animal studies were submitted, reviewed, or approved.

iii. Work with Sendai virus is approved at BSL-2:

1. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 406-375-9600.

iv. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.

1. The committee unanimously approved as written.

c. PRD-23-245 Yersinia pestis – Katy Bosio (New)

i. Becky Anderson summarized the PRD. This is a new registration to work with Yersinia pestis. The lab seeks to understand the cellular and molecular mechanisms of survival and replication of Yersinia pestis in the mammalian host following infection. The lab will study the interaction of Yersinia pestis with host cells.

ii. Clayton Winkler noted that tularemia is listed in the document.

iii. Haley DeMers noted the link to the NIH Guidelines is broken.

iv. (b)(6) noted that this registration will be reviewed by the NIH DURC-IRE committee.

v. No animal studies were submitted, reviewed, or approved.

vi. Work with the following Yersinia pestis is approved at BSL-3:

1. The approval is for only the materials, personnel, and facility specifically provided in the PRD. Only personnel registered on the PRD may have access to this material.
2. In addition, please be aware of the following conditions for working with this material:
    a. Yersinia pestis is a Select Agent. All personnel with access to this agent must be authorized by the CDC Division of Select Agents and Toxins.
    b. All individuals listed on this PRD and all those with access to the laboratory must be enrolled in and meet all health and security requirements of the NIH Biosurety Program and complete the RML BSL-3 and/or BSL-4 Biosafety Training Program.

c. IBC approved validated inactivation procedure(s) must be followed when inactivating and removing samples to a lower containment level. Inactivation certificates are required for all samples that are inactivated.
d. The facilities, practices, and procedures for conducting research at various Biological Safety Levels can be found in the CDC/NIH publication entitled Biosafety in Microbiological and Biomedical Laboratories and the NIH Guidelines for Research Involving Recombinant DNA Molecules. These documents can be found at: https://www.cdc.gov/labs/pdf/SF__19_308133-A_BMBL6_00-BOOK-WEB-final-3.pdf http://www.od.nih.gov/oba/rdna.htm

3. It is the responsibility of the Principal Investigator (PI) to supply the IBC with updated information including modifications to the experiments described, location changes, and new research personnel. Amendments may be submitted online at http://oms.ors.nih.gov. Complete review of Pathogen Registration Documents and Recombinant DNA Registration Documents is performed by the IBC every 5 years.
4. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan.

vii. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.
viii. The committee unanimously approved (Chris Bosio abstained) with minor modifications pending review by the NIH DURC-IRE committee.
1. Update tularemia in the document.
2. Update NIH Guidelines link.

d. PRD-22-138 Arenaviruses – Heinz Feldmann (Amend 01)
i. Becky Anderson summarized the amendment to the PRD. This is an amendment to add Morogoro virus. Morogoro virus in an old-world arenavirus found in east Africa. It is carried by the peri-domestic rodent *mastomys natalensis*. Morogoro virus does not cause disease in humans. The BMBL has categorized it as BSL-3/ABSL-3. This amendment also includes adding animal work with mastomys rodents, and the ASP is attached.
ii. Clayton Winkler asked if there was additional information on if Morogoro could infect humans. Andrea Marzi explained that serology studies have been conducted, and there is no indication that humans have been infected with this virus.
iii. Animal studies with mastomys were proposed.
iv. Work with Morogoro virus is approved at BSL-3/ABSL-3.
v. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.
vi. The committee unanimously approved as written.

e. PRD-23-145 SARS-CoV – Feldmann (Renewal)
i. Becky Anderson summarized the PRD. This is a renewal registration for work with SARS-CoV. All work has been previously approved. The lab's aim is to understand replication and growth kinetics of SARS-CoV and to analyze efficacy of inhibitors.
ii. Sue Priola noted on pg 3 that there is inactivation language listed in the incorrect section. As well, under eukaryotic cells section update to indicate that no viral vectors will be used.

iii. Becky noted that additional language from the NIH DURC-IRE committee's approval will be included.
iv. Animal studies with mice and non-human primates were proposed.
v. Work with SARS-CoV is approved at BSL-3/ABSL-3:
    1. The approval is for only the materials, personnel, and facility specifically provided in the PRD. Only personnel registered on the PRD may have access to this material.
    2. In addition, please be aware of the following conditions for working with this material:
        a. SARS-CoV is a Select Agent. All personnel with access to this agent must be authorized by the CDC Division of Select Agents and Toxins.
        b. All individuals listed on this PRD and all those with access to the laboratory must be enrolled in and meet all health and security requirements of the NIH Biosurety Program and complete the RML BSL-3 and/or BSL-4 Biosafety Training Program.
        c. IBC approved validated inactivation procedure(s) must be followed when inactivating and removing samples to a lower containment level. Inactivation certificates are required for all samples that are inactivated.
        d. Storage only of SARS-CoV at BSL-3 in (b) (6) is approved.
        e. The facilities, practices, and procedures for conducting research at various Biological Safety Levels can be found in the CDC/NIH publication entitled Biosafety in Microbiological and Biomedical Laboratories and the NIH Guidelines for Research Involving Recombinant DNA Molecules. These documents can be found at: https://www.cdc.gov/labs/pdf/SF__19_308133-A_BMBL6_00-BOOK-WEB-final-3.pdf http://www4.od.nih.gov/oba/rdna.htm
    3. It is the responsibility of the Principal Investigator (PI) to supply the IBC with updated information including modifications to the experiments described, location changes, and new research personnel. Amendments may be submitted online at http://oms.ors.nih.gov. Complete review of Pathogen Registration Documents and Recombinant DNA Registration Documents is performed by the IBC every 5 years.
    4. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 406-375-9600.
vi. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.
vii. The committee unanimously approved with minor modifications.
    1. Update location of inactivation methods language.
    2. Update usage of viral vectors to "No".

f. PRD-23-202 High Pathogenicity Avian Influenza viruses and Reconstructed 1918 Influenza virus – Heinz Feldmann (Renewal)
    i. Becky Anderson summarized the PRD. This is a renewal for work with High path avian influenza H5N1, HPAI subtype H7Nx (ex: H7N3, H7N7), Reconstructed 1918, LPAI H7N9 (non-select agent). The lab aims to understand the pathogenesis of and host immune

responses to influenza viruses and developing countermeasures that would prevent and treat infections.

ii. Kendal Cooper noted a typo on the strains list. The strains should be updated to state H5N1 and H7Nx. The committee noted to ensure this is the same throughout the document.

iii. Kendal Cooper noted that it references recombinant work, but it is not described here. Becky Anderson noted that this research is described in the RD for these pathogens.

iv. Sue Priola noted to move inactivation language to correct section. It was also noted that Dual Use question #7 is applicable for reconstructed 1918 and should be answered "Yes," as this is an extinct pathogen.

v. Animal studies with mice, chickens, ferrets, and non-human primates were proposed.

vi. Work with High Pathogenicity Avian Influenza viruses and Reconstructed 1918 Influenza virus is approved at BSL-4/ABSL-4:

    1. The approval is for only the materials, personnel, and facility specifically provided in the PRD. Only personnel registered on the PRD may have access to this material.
    2. In addition, please be aware of the following conditions for working with this material:
        a. High Pathogenicity Avian Influenza viruses and Reconstructed 1918 Influenza virus are Select Agents. All personnel with access to this agent must be authorized by the CDC Division of Select Agents and Toxins.
        b. All individuals listed on this PRD and all those with access to the laboratory must be enrolled in and meet all health and security requirements of the NIH Biosurety Program and complete the RML BSL-3 and/or BSL-4 Biosafety Training Program.
        c. IBC approved validated inactivation procedure(s) must be followed when inactivating and removing samples to a lower containment level. Inactivation certificates are required for all samples that are inactivated.
        d. Please be aware there is potential for reassortants and therefore work with H5 and H7 should be physically and/or temporally separated.
        e. Reconstructed 1918 Influenza virus will be kept physically separate from other high pathogenicity influenza strains. Vaccination with the seasonal influenza vaccine is recommended for all personnel working directly with Reconstructed 1918 influenza virus. Contact OMS Nurses at 375-9755 for more information.
        f. If any of the viruses are to be sent to lower containment, they have to be kept physically separate from Rift Valley Fever Virus.
        g. Nucleic Acids and proteins from HPAI are not regulated as Select Agents, but are regulated pursuant to 9 CFR Part 122 (i.e. permits are required for import or transport within the US)
        h. The facilities, practices, and procedures for conducting research at various Biological Safety Levels can be found in the CDC/NIH publication entitled Biosafety in Microbiological and Biomedical Laboratories and the NIH Guidelines for Research Involving Recombinant DNA Molecules. These documents can be found at: https://www.cdc.gov/labs/pdf/SF__19_308133-A_BMBL6_00-BOOK-WEB-final-3.pdf http://www4.od.nih.gov/oba/rdna.htm

3. It is the responsibility of the Principal Investigator (PI) to supply the IBC with updated information including modifications to the experiments described, location changes, and new research personnel. Amendments may be submitted online at http://oms.ors.nih.gov. Complete review of Pathogen Registration Documents and Recombinant DNA Registration Documents is performed by the IBC every 5 years.
4. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 406-375-9600.

vii. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.
viii. The committee unanimously approved with minor modifications.
1. Ensure influenza strains are up to date and consistently listed throughout the document.
2. Update Dual Use question #7 to yes, specifically for reconstructed 1918 influenza.
3. Update location of inactivation methods language.

g. PRD-23-82 Vesicular Stomatitis virus (VSV) – Andrea Marzi (Renewal)
i. Becky Anderson summarized the PRD. This is a renewal, and all work has been previously approved. VSV is used to study the function of viral proteins derived from Filo-, Bunya-, Paramyxo-, Arena-, Orthomyxo-, Corona-, and Flaviviruses in virus replication and pathogenesis.
ii. Sue Priola noted that there is a formatting issue on the PRD. Becky Anderson will confirm all the information is listed in the system.
iii. Animal studies with guinea pigs, non-human primates, bats, ferrets, pigs, mice and hamsters were proposed.
iv. Work with VSV, Indiana strain is approved at BSL-2/ABSL-2.
v. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.
vi. The committee unanimously approved (Andrea Marzi abstained) as written.

h. PRD-23-176 Human and Non-human Primate Blood and Body Fluids – Patrick Hanley (Renewal)
i. Becky Anderson summarized the PRD. This is a renewal registration to work with human and non-human primate blood and body fluids associated with the animal facilities. Staff collect NHP samples.
ii. Work with the following Human and Non-human Blood and Body fluids is approved at BSL-2/ABSL-2:
1. Research performed with this material is subject to the NIH OACU BSSE Guidelines (https://oacu.oir.nih.gov/system/files/media/file/2022-12/OACU_BSSE_Guidelines-20221027.pdf). Please contact your IC Safety Specialist for information on how to obtain the required components of the kit.
2. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 406-375-9600.

iii. No animal studies were submitted, reviewed or approved.

iv. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.
v. The committee unanimously approved as written.

i. PRD-23-191 Transmissible spongiform encephalopathies – Sue Priola (Renewal)
   i. Becky Anderson summarized the PRD. This is a renewal registration for work with rodent prion strains. The lab looks to understand how transmissible spongiform encephalopathy agents, also known as prions, replicate and cause disease.
   ii. Sue Priola noted that new permits are available and will be sent to Becky Anderson.
   iii. Animal studies with mice and hamsters were proposed.
   iv. Work with Transmissible spongiform encephalopathies are approved at BSL-2/ABSL-2.
   v. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.
   vi. The committee unanimously approved (Sue Priola abstained) with minor modifications.
      1. Update permits.

II. Registration of Recombinant DNA Experiments
   a. RD-21-440 Coronaviruses – Heinz Feldmann (Amend)
      i. Andrea Marzi summarized the RD amendment. This amendment is to the Coronavirus RD to add animal work with hamsters and expression of additional fluorescent markers: neon green, dTOM, BFG and Venus. The ASP was attached. It was noted that BFG should be updated to BFP. All the dual use questions are answered no.
      ii. Sue Priola had no additional comments.
      iii. Becky Anderson noted that this was previously reviewed by the NIH DURC-IRE committee.
      iv. Animal studies with hamsters were proposed.
      v. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.
      vi. Research using prokaryotic cells is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under sections III-D-3-a, III-D-3-b, III-D-1-a, and III-E-1 of the NIH guidelines.
      vii. The committee unanimously approved with minor modifications.
         1. Update BFG to BFP.
   b. RD-23-138 Lentiviral vectors – Olivia Steele-Mortimer (New)
      i. Scott Kobayashi summarized the RD. This registration is to use a 3rd or 4th generation lentiviral expression system to express fluorescent tagged host mammalian proteins in cell culture. The lab will receive pre-packaged particles from a commercial vendor and have proposed packaging their own particles as well. Section III-D-3-a applies to research product section, and III-D-1-a applies to the eukaryotic section. In the prokaryotic section, update to include additional information on the mammalian genes that will be expressed. In the eukaryotic section, update to indicate that infectious virus will be generated. The registration did not discuss how the lab would be packaging the particles, packaging vectors were not included.
      ii. Clayton Winkler concurred with the above comments. The Dual Use questions are answered as N/A, but "No" would be more appropriate. The committee agreed. Minor typos were noted.
      iii. No animal studies were proposed.
      iv. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.

v. Research using prokaryotic cells is approved at BSL-2 under section III-E-1 of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under sections III-D-3-a, III-D-1-a, and III-E-1 of the NIH guidelines. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 406-375-9600.

vi. The committee unanimously approved (Kendal Cooper abstained) with minor modifications.

1. Update NIH guidelines to include III-D-3-a and III-D-1-a.
2. Update Dual Use questions to No.
3. Include mammalian genes of interest that will be expressed.
4. Update to include that infectious particles will be generated.
5. Include additional information on packaging system that will be performed by the lab, including applicable vector maps.
6. Correct minor typos.

III. Full Committee Review of Inactivation Procedures

a. None

IV. Standard Operating Procedures

a. Draft Building (b)(6) BSL-3 (b)(6) SOP – (CB.8 Microscopy and CB.9 Tissue homogenization) (Updates)

i. Becky Anderson summarized the updates to the SOP for the committee. This update is to add additional microscopy and tissue homogenization.

ii. (b)(6) described the microscopy unit to image Coxiella. It is a light and fluorescent microscope and contains an onstage incubator for live cell imaging in plates and flasks. This microscope will be in the BSL-3. The tissue culture plates could be moved on those stage to view another well or location on the plate/flask. Signage will be posted on the door and on the unit if there are samples in the microscope. When transferring a sample to the microscope, it will be sealed and the outside disinfected prior to the transfer from the BSC to the microscope.

iii. Sue Priola asked how often the samples need the media changed. (b)(6) confirmed that if media needs to be changed, it will be moved to the BSC while sealed. The committee extensively discussed the updates to the SOP.

iv. There were no additional comments or concerns with the updated procedures.

v. The committee unanimously approved (Bob Heinzen abstained) as written.

b. Draft ABSL-3 Coxiella Animal SOP (Updates)

i. Becky Anderson summarized the updates to the SOP to the committee. This update is to add the intranasal route of inoculation for guinea pigs. The lab is already approved for intranasal inoculation for mice, this update is to add guinea pigs as well. This new route of approval will also need approval from CDC DSAT.

ii. There were no additional comments or concerns with the updated procedures.

iii. The committee unanimously approved (Bob Heinzen abstained) as written pending CDC DSAT approval.

V. Annual Reviews

a. None

Reports

I. Biosafety Officer Report – Becky Anderson
   a. Becky Anderson presented the BSO report.
II. Occupational Safety and Health Manager Report – Seth Cooley
   a. Nothing to report.
III. IRF Biosafety Manager Report – Haley DeMers
   a. Nothing to report.
IV. Responsible Official Report – Megan Brose
   a. Amendments were submitted to the Select Agent registration to transfer material from Joe Hinnebusch to Katy Bosio.
V. Associate Director Report – Marshall Bloom
   a. Not present.

Around the Room

I.

Other Issues

I.

Next Meeting

I. May 18, 2023 virtual via Zoom/Building A (b)(6)

NIH RML Institutional Biosafety Committee Meeting

Biosafety Officer (BSO) Report

April 20, 2023

Business Conducted since the last IBC Meeting

A. BSO approvals
   a. Transfer of registrations for PI Hinnebusch retirement
      i. PRD 17-05 Yersinia enterocolitica to PI Steele-Mortimer
      ii. PRD 18-07 Yersinia pseudotuberculosis to PI Bosio
      iii. PRD 18-210 E. coli to PI Bosio
      iv. PRD 21-66 Yersinia pestis (exempt) to PI Bosio
      v. RD 20-320 Yersinia pestis (exempt) to PI Bosio
      vi. RD 21-321 Yersinia pseudotuberculosis to PI Bosio
      vii. PRD 18-86 HBBF to PI de Leo
   b. Rosa retirement
      i. All registrations will be inactivated

B. Electronic business
   a. Bloom PRD 23-242
      i. New PRD for *Anaplasma phagocytophilum*

New business for IBC meeting

A. See agenda.

Biosafety Activities since the last IBC Meeting

A. Animal Study Protocols Review- Performed by Megan Brose, Rebecca Anderson, Haley DeMers

ASP Title	Associated PRD	Associated RD	Reviewer
Dexamethasone treatment in Nipah virus-infected Syrian hamsters	18-91	n/a	Anderson
Adaptation of the Lujo virus to Hartley guinea pigs	18-94	n/a	H. DeMers
Impact of obesity on the outcome of intradermal infection with Francisella tularensis in mice	18-71 18-73	n/a	M. Brose
Investigation of non-specific and specific immune effects induced by Coxiella burnetii in guinea pigs	22-238 20-43 18-70	n/a	Anderson
Interactions of tick-borne microbes in Ixodes scapularis	19-213 19-58	n/a	Anderson
Modelling Nipah virus neurologic disease by using intracranial inoculation in Syrian hamsters.	18-91	n/a	H. DeMers
Laboratory Animal Care and Use Training Program	n/a	n/a	H. DeMers
Sentinel Animal Surveillance Program	n/a	n/a	M. Brose
Laboratory Animal Holding	n/a	n/a	Anderson
Characterizing old world arenavirus infections in Mastomy natalensis.	18-94	n/a	Anderson
Characterizing the pulmonary disease in the ANDV hamster model.	22-81	n/a	H. DeMers
ChAdOx1 MARV vaccine efficacy against Marburg virus (MARV) in the hamster and macaque models	18-90 18-82	22-410 20-40	H. DeMers

B. Biosafety Training- Performed by Megan Brose, Rebecca Anderson, Haley DeMers

Type of Training	Number of Sessions	Number of Employees Trained
New Employee	4	12
Annual Refresher Lab Biosafety	2	7
Select Agent-Initial	n/a	n/a
Select Agent- Refresher	n/a	n/a
Select Agent- Visitor	3	11
BSL-3 Laboratory Biosafety-Initial	2	4
Practical Training	2	3
BSL-4 Laboratory Biosafety-Initial	2	4
Suit Training	1	2
Checklist Training	n/a	n/a
Laboratory Biosafety Support Staff-Initial	n/a	n/a
Laboratory Biosafety Support Staff-Refresher	n/a	n/a
BSL-4 Emergency Egress Training	3	38

C. Safety Audits and Inspections

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

D. Biological Incidents to Report
   a. None

E. Other Issues
   a. None

NIH RML Institutional Biosafety Committee Meeting

Agenda for May 18, 2023

Location: Virtual via Zoom/Building A (b)(6)

Old Business

A. Draft minutes of April 20, 2023 meeting

New Business

A. Committee Business
   1) PRD 18-94 (Amend 01) PI: Feldmann
   2) PRD 23-238 (Amend 01) PI: Long
   3) PRD 23-246 (New) PI: Long
   4) PRD 23-247 (New) PI: Best
   5) PRD 23-248 (New) PI: Best
   6) PRD 23-249 (New) PI: Caughey
   7) PRD 23-197 (Renewal) PI: Haigh
   8) PRD 23-198 (Renewal) PI: Haigh
   9) PRD 23-199 (Renewal) PI: Haigh
   10) RD 23-500 (New) PI: Long — Reviewer: Chris Bosio, Scott Kobayashi
   11) RD 23-225 (Renewal) PI: Peterson — Reviewer: Sue Priola, Bob Heinzen

B. BSO report (Dr. Becky Anderson)
C. Occupational Safety & Health Manager report (Seth Cooley)
D. IRFBSM report (Dr. Haley DeMers)
E. Responsible Official Report (LCDR Megan Brose)
F. Associate Director Report (Dr. Marshall Bloom)
G. Comments from around the room

Next Meeting: May 18, 2023 virtual via Zoom/Building A (b)(6)

PRD- Pathogen Registration Document
RD- Recombinant DNA Registration Document
SOP-Standard Operating Procedures
BSO-Biosafety Officer
IRFBSM-Integrated Research Facility Biosafety Manager

NIH RML Institutional Biosafety Committee Minutes

May 18, 2023 (1:00 PM – 3:00 PM)
Virtual via Zoom/Building A (b)(6)

Members Present:

☒Sue Priola, Chair	☐Carol Calderwood	☒Jamie Lovaglio
☐Bob Heinzen, Vice Chair	☐Marcie Caldwell (EO)	☐Andrea Marzi
☐Becky Anderson	☐Seth Cooley	☐Alida Merritt
☐Alan Applebury	☐Kendal Cooper	☒Greg Saturday
☐Sonja Best (EO)	☐Frank DeLeo (EO)	☐Alexandra Scranton
☒Chris Bosio	☐Heinz Feldmann (EO)	☐Brian Vickrey
☐Marshall Bloom (EO)	☐Erik Hoover	☒Clayton Winkler
☒Megan Brose	☐Josh Kellar (EO)	
☐Larry Brouwer	☒Scott Kobayashi	

(EO) *ex officio*

Guests: H(b)(6)
(b)(6)

Announcements

I. (b)(6) will serve as acting Biosafety Officer for this meeting.

Old Business

I. Review of Past IBC Meeting Minutes
    a. April 20, 2023 Minutes
        i. The minutes were unanimously approved as written.

New Business

I. Registration of Material (Potentially) Infectious for Humans, Plants or Animals
    a. PRD-18-94 Arenaviruses – Heinz Feldmann (Amend 01)
        i. (b)(6) summarized the PRD. This is an amendment to generate a guinea pig adapted Lujo virus. The Feldmann lab is interested in developing an animal model for Lujo to understand how the virus causes disease and help with vaccine and antiviral drug development.
        ii. Animal studies with guinea pigs were proposed.
        iii. Clayton Winkler noted that there is a space missing in between mouse adapted.
        iv. Work with Arenaviruses is approved at BSL-4/ABSL-4 pending NIH DURC-IRE review.
        v. The committee discussed the dual-use and ePPP (enhanced potential pandemic pathogen) potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.
        vi. The committee unanimously approved with minor modifications pending DURC-IRE review.
            1. Correct mouseadapted to mouse adapted in the document.
    b. PRD-23-238 Candida albicans – Carrie Long (Amend 01)
        i. (b)(6) summarized the PRD. The amendment is to add animal work with mice.
        ii. Animal studies with mice were proposed.

iii. Work with Candida albicans is approved at BSL-2/ABSL-2.
iv. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.
v. The committee unanimously approved as written.

c. PRD-23-238 Coxiella burnetii – Carrie Long (New)
   i. (b)(6) summarized the PRD. This is a new PRD for the Long Lab. They seek to gain a better understanding of molecular mechanisms of intracellular survival and virulence by C. burnetii. They use in vitro and in vivo models of C. burnetii-host cell interactions, and apply cell biology, microbiology, genomics, and genetic methodologies to identify and characterize determinants of intracellular pathogenesis. Animal models of Q fever are also employed to investigate strain-specific virulence and vaccine candidates.
   ii. Animal studies with mice and guinea pigs were proposed.
   iii. Clayton Winkler noted that the organism will be manipulated to be antibiotic resistant. However, an additional comment should be included that the antibiotic resistance genes will not include clinically relevant antibiotics.
   iv. Sue Priola asked if the strain table included select agent and non-select agent strains of Coxiella burnetii. The committee agreed that an additional column indicating this information would be helpful.
   v. Sue Priola asked if all the listed strains are worked with at BSL-3/ABSL-3.
   vi. Work with Coxiella burnetii is approved at BSL-3/ABSL-3.
      1. The approval is for only the materials, personnel, and facility specifically provided in the PRD. Only personnel registered on the PRD may have access to this material.
      2. In addition, please be aware of the following conditions for working with this material:
         a. Coxiella burnetii is a Select Agent. All personnel with access to this agent must be authorized by the CDC Division of Select Agents and Toxins.
         b. All individuals listed on this PRD and all those with access to the laboratory must be enrolled in and meet all health and security requirements of the NIH Biosurety Program and complete the RML BSL-3 and/or BSL-4 Biosafety Training Program.
         c. IBC approved validated inactivation procedure(s) must be followed when inactivating and removing samples to a lower containment level. Inactivation certificates are required for all samples that are inactivated.
         d. The facilities, practices, and procedures for conducting research at various Biological Safety Levels can be found in the CDC/NIH publication entitled Biosafety in Microbiological and Biomedical Laboratories and the NIH Guidelines for Research Involving Recombinant DNA Molecules. These documents can be found at: https://www.cdc.gov/labs/pdf/SF__19_308133-A_BMBL6_00-BOOK-WEB-final-3.pdf https://osp.od.nih.gov/policies/biosafety-and-biosecurity-policy/
      3. It is the responsibility of the Principal Investigator (PI) to supply the IBC with updated information including modifications to the experiments described, location changes, and new research personnel. Amendments may be submitted online at http://oms.ors.nih.gov. Complete review of Pathogen Registration

Documents and Recombinant DNA Registration Documents is performed by the IBC every 5 years.

4. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 406-375-9600.

vii. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.

viii. The committee unanimously approved with minor modifications.

1. Indicate that the antibiotic resistance will not affect susceptibility to clinically relevant antibiotics.
2. Update the strain table to identify select-agents and non-select agents.
3. Confirm all strains are handled in BSL-3/ABSL-3.

d. PRD-23-247 Zika virus – Sonja Best (New)

i. (b)(6) summarized the PRD. This is a new registration for work with Zika virus. The lab aims to develop and characterize animal models of Zika virus to elucidate mechanisms of mosquito-borne flavivirus pathogenesis.

ii. Animal studies with mice were proposed.

iii. Work with Zika virus is approved at BSL-2/ABSL-2:

1. Care should be taken to minimize worker exposure to aerosols, such as working in a certified Class II BSC at all times and using gasketed bucket covers when centrifuging infectious material. Gasketed bucket covers or sealed rotors must only be loaded/unloaded in a BSC. It is recommended if possible that work with Zika virus be performed in a small or dedicated lab away from the main lab areas. Women of childbearing years must be advised of the risks of working with this agent, please consult with OMS.
2. Animal studies with rodents will be performed in the Human Pathogen Wing of (b)(6) All manipulations must be performed in a BSC. A sign at the suite door will indicate when Zika procedures are in progress. PPE includes: Lab coat, gloves, surgical mask. Husbandry practices will include spraying used cages with disinfectant, autoclaving, and then dumping the used bedding or if disposable caging is used, cages will be bagged and then incinerated.
3. Hazard awareness training must be provided to all individuals listed on the PRD, animal care staff, and staff working in shared lab/animal spaces. This is the responsibility of the PI.
4. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 406-375-9600.

iv. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.

v. The committee unanimously approved as written.

e. PRD-23-248 Vesicular Stomatitis virus – Sonja Best (New)

i. (b)(6) summarized the PRD. This is a new registration for work with VSV Indiana strain. The lab uses VSV to study protein function from viruses in the Corona and Flavivirus families.

ii. Animal studies with mice were proposed.
iii. Sue Priola noted that the registration indicated that no infectious virus will be produced under the eukaryote section and no foreign gene will be expressed. These should both be answered "yes."
iv. Work with VSV, Indiana strain is approved at BSL-2/ABSL-2:
    1. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 406-375-9600.
v. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.
vi. The committee unanimously approved with minor modifications.
    1. Update Eukaryote section to indicate that an infectious virus will be generated, and a foreign gene will be expressed.

f. PRD-23-249 HBBF (HIV Infected) – Byron Caughey (New)
i. (b)(6) summarized the PRD. This is a new registration for work with human blood and body fluids from HIV infected individuals. The Caughey lab plans to take small volumes of CSF and test them using their RT-QuIC assays. The goal is to see if they can detect small amounts of misfolded proteins in CSF of HIV patients.
ii. No animal studies were submitted, reviewed, or approved.
iii. Sue Priola noted a typo in the synopsis.
iv. Work with human blood and body fluids from HIV-positive patients is approved at BSL-2 with BSL-3 practices (BSL-2/3):
    1. BSL-2/3 calls for enhanced practices in a BSL-2 facility: (1) all procedures performed in a biosafety cabinet (BSC) wearing PPE: double gloves, eye and face protection, disposable gown, (2) decontaminating all potentially infectious waste prior to removal from BSC, (3) use of gasketed safety cups for centrifugation, and (4) minimize the use of sharps.
    2. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 406-375-9600.
v. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.
vi. The committee unanimously approved with minor modifications.
    1. Correct typo in synopsis.

g. PRD-23-197 Human TSE – Cathryn Haigh (Renewal)
i. (b)(6) summarized the PRD. This is a renewal for work with human transmissible spongiform encephalopathies. The purpose of the study is to monitor TSE spread and toxic changes in human neurons and cerebral organoids exposed to different human TSE sources.
ii. Animal studies with mice were proposed.
iii. Work with Human TSE is approved at BSL-2/ABSL-2:
    1. The use of a cryostat for cutting human TSE samples is approved at BSL-2 following the attached SOP. PPE for this work includes: Lab coat, safety glasses, N95 respirator, and gloves (including a layer of cut resistant gloves). Individuals

performing cryostat work must be enrolled in the respiratory protection program. Contact OMS at 406-375-9600.

2. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact OMS at 406-375-9600.

iv. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.

v. The committee unanimously approved as written.

h. PRD-23-198 Rodent TSE – Cathryn Haigh (Renewal)

i. (b)(6) summarized the PRD. This is a renewal for work with rodent TSE. The lab seeks to study the pathogenesis of prion disease in animal cell culture models.

ii. Animal studies with mice were proposed.

iii. Sue Priola asked if CWD needed to be worked with at BSL-2 with BSL-3 practices. It was confirmed that they can be worked with at BSL-2.

iv. Work with Rodent TSE is approved at BSL-2/ABSL-2:

v. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.

vi. The committee unanimously approved with minor modifications.

1. Confirm biosafety level for work with CWD.

i. PRD-23-199 HBBF – Cathryn Haigh (Renewal)

i. (b)(6) summarized the PRD. This is a renewal for work with human blood and body fluids. The lab seeks to monitor disease spread and toxic changes in human neurons and cerebral organoids exposed to different human prion sources.

ii. Animal studies with mice were proposed.

iii. Work with HBBF is approved at BSL-2/ABSL-2:

1. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 406-375-9600.

iv. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.

v. The committee unanimously approved as written.

II. Registration of Recombinant DNA Experiments

a. RD-23-500 Coxiella burnetii – Carrie Long (New)

i. Chris Bosio summarized the RD. This work is to gain a better understanding of molecular mechanisms of intracellular survival and virulence by C. burnetii. The lab uses in vitro and in vivo models of C. burnetii-host cell interactions, and applies cell biology, microbiology, genomics, and genetic methodologies to identify and characterize determinants of intracellular pathogenesis.

ii. Scott Kobayashi had no additional comments to add.

iii. Sue Priola requested that III-D-1-b be added to both the prokaryotic and eukaryotic sections.

iv. Animal studies with guinea pigs and mice were proposed.

v. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.

vi. Research using prokaryotic cells is approved at BSL-2 or BSL-3 under section III-D-1-a, III-D-1-b, III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 or BSL-3 under sections III-D-1-a and III-D-1-b of the NIH guidelines.
vii. The committee unanimously approved with minor modifications.
1. Add III-D-1-b to both the prokaryotic and eukaryotic sections.

b. RD-23-225 CSG – Karin Peterson (Renewal)
i. Sue Priola summarized the RD. The purpose of these experiments is to use a La Crosse virus (LACV) reverse genetics system as a backbone to determine specific virulence and genetic factors of the California Serogroup (CSG) of orthobunyaviruses that mediate differences in pathogenicity and host immune responses. The Lab will use the LACV reverse genetics system as a backbone to determine which gene(s) within the CSG orthobunyaviruses are responsible for the differences in pathogenicity observed between them in mice and in vitro. They will use a combination of gene synthesis and standard molecular cloning practices to replace portions of the LACV sequences with the homologous regions of the other CSG viruses.
ii. Sue Priola request that the NIH guidelines be updated for research products to include III-D-2-a, III-E-1, and III-D-1-a, the prokaryote section be updated to include III-E-1 and the eukaryotic section be updated to include III-D-3-a and III-E-1. The lab has indicated that no foreign genes will be expressed and this should be updated to state that foreign genes will be expressed.
iii. Animal studies with mice were proposed
iv. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.
v. Research using prokaryotic cells is approved at BSL-2 under section III-D-2-a and III-E-1 of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-2 under sections III-D-1-a and III-D-1-b of the NIH guidelines.
vi. The committee unanimously approved (Clayton Winkler abstained) with minor modifications.
1. Update research products to include III-D-2-a, III-E-1, and III-D-1-a.
2. Update prokaryotic section to include III-E-1.
3. Update eukaryotic section to include III-D-3-a and III-E-1.
4. Update to indicate that a foreign gene will be expressed.

III. Full Committee Review of Inactivation Procedures
a. None
IV. Standard Operating Procedures
a. None
V. Annual Reviews
a. None

Reports

I. Biosafety Officer Report – Becky Anderson
a. (b)(6) presented the BSO report.
II. Occupational Safety and Health Manager Report – Seth Cooley
a. Not present.
III. IRF Biosafety Manager Report – (b)(6)
a. Nothing to report.
IV. Responsible Official Report – Megan Brose

a. (b)(6) presented the Responsible Official report. The inspection report from the March 2023 CDC DSAT BSL-4 inspection was received.

V. Associate Director Report – Marshall Bloom
   a. Not present.

Around the Room

I. None

Other Issues

I. None

Next Meeting

I. June 15, 2023 virtual via Zoom/Building A (b)(6)

NIH RML Institutional Biosafety Committee Meeting

Biosafety Officer (BSO) Report

May 18, 2023

Business Conducted since the last IBC Meeting

A. BSO approvals
   a. de Wit PRD 21-235 Amend 03
      i. Clarifying BSC class II instead of typo which stated class III

B. Electronic business
   a. None

New business for IBC meeting

A. See agenda.

Biosafety Activities since the last IBC Meeting

A. Animal Study Protocols Review- Performed by Megan Brose, Rebecca Anderson, (b)(6)

ASP Title	Associated PRD	Associated RD	Reviewer
Evaluation of DNA vaccines in the Guinea pig model of Lassa fever	18-94	N/A	(b)(6); (b)(3):42
Development of a hamster model for pre-clinical therapeutic intervention testing against SARS-CoV-2 Omicron variants	22-143	N/A	M. Brose
Co-infection of SARS-CoV-2 and prion disease in Syrian hamsters (pilot)	20-228 16-190	N/A	R. Anderson
An Antioxidant Enzyme to Suppress Hyperinflammation Induced by Viral Infection in Mice	17-143	N/A	R. Anderson

B. Biosafety Training- Performed by Megan Brose, Rebecca Anderson, (b)(6)

Type of Training	Number of Sessions	Number of Employees Trained
New Employee	1	3
Annual Refresher Lab Biosafety	N/A	N/A
Select Agent-Initial	1	3
Select Agent- Refresher	N/A	N/A
Select Agent- Visitor	1	1
BSL-3 Laboratory Biosafety-Initial	2	3
Practical Training	N/A	N/A
BSL-4 Laboratory Biosafety-Initial	2	3
Suit Training	1	2
Checklist Training	5	15
Laboratory Biosafety Support Staff-Initial	1	1
Laboratory Biosafety Support Staff-Refresher	N/A	N/A

C. Safety Audits and Inspections

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

D. Biological Incidents to Report

a. None

E. Other Issues
   a. None

F. DURC-IRE Reviews
   a. Munster PRD 22-240 Mpox

NIH RML Institutional Biosafety Committee Meeting

Agenda for June 15, 2023

Location: Virtual via Zoom/Building A (b)(6)

Old Business

A. Draft minutes of May 18, 2023 meeting

New Business

A. Committee Business
   1) PRD 23-250 (New) PI: Peterson
   2) PRD 20-228 (Amend 05) PI: Best
   3) PRD 23-140 (Renewal) PI: Best
   4) PRD 23-35 (Renewal) PI: Hackstadt
   5) PRD 23-37 (Renewal) PI: Hackstadt
   6) PRD 23-103 (Renewal) PI: Peterson
   7) PRD 23-184 (Renewal) PI: Peterson
   8) RD 22-452 (Amend 02) PI: Feldmann Reviewers: Andrea Marzi, Kendal Cooper
   9) Bloom Flavivirus inactivation with PFA and glut.
   10) Draft (b)(6) SOP Powassan virus-update to add inactivation procedures
   11) Draft Animal SOP SARS-CoV-2 and prion infection-New
   12) Draft SOP#4-28-16 Rodent Procedures in Biocontainment-Update intracranial/intracerebral section

B. BSO report (Dr. Becky Anderson)
C. Occupational Safety & Health Manager report (Seth Cooley)
D. IRFBSM report (b)(6)
E. Responsible Official Report (LCDR Megan Brose)
F. Associate Director Report (Dr. Marshall Bloom)
G. Comments from around the room

Next Meeting: July 20, 2023 virtual via Zoom/Building A (b)(6)

PRD- Pathogen Registration Document
RD- Recombinant DNA Registration Document
SOP-Standard Operating Procedures

BSO-Biosafety Officer
IRFBSM-Integrated Research Facility Biosafety Manager

NIH RML Institutional Biosafety Committee Minutes

June 15, 2023 (1:00 PM – 2:00 PM)
Zoom Virtual Meeting

Members Present:

☑ Sue Priola, Chair	☐ Marcie Caldwell (EO)	☐ Jamie Lovaglio
☑ Bob Heinzen, Vice Chair	☐ Bruce Chesebro (EO)	☑ Andrea Marzi
☑ Becky Anderson	☑ Seth Cooley	☐ Alida Merritt
☐ Alan Applebury	☑ Kendal Cooper	☐ Greg Saturday
☐ Chris Bosio	☐ Frank DeLeo (EO)	☐ Alexandra Scranton
☐ Marshall Bloom (EO)	☐ Heinz Feldmann (EO)	☐ Brian Vickrey
☑ Megan Brose	☐ Erik Hoover	☑ Clayton Winkler
☐ Larry Brouwer	☐ Josh Kellar (EO)	
☐ Carol Calderwood	☑ Scott Kobayashi	

(EO) *ex officio*

Guests: (b)(6)

(b)(6)

Announcements

I. None

Old Business

I. Review of Past IBC Meeting Minutes
   a. May 18, 2023 Minutes
      i. Sue Priola clarified that CWD could be worked with at BSL-2, pertinent to PRD-23-198.
      ii. Sue Priola clarified that in RD-23-225 no foreign genes would be expressed.
      iii. Minutes were unanimously approved.

New Business

I. Registration of Material (Potentially) Infectious for Humans, Plants or Animals
   a. Peterson PRD 23-250 New, Bungarotoxin
      i. Becky Anderson summarized the PRD. This is a new registration to investigate the movement of La Crosse virus along motor neurons. A-bungarotoxin is a potent antagonist of neuromuscular junctions in motor neurons and will be used to assess the movement of La Crosse virus. There is a known and available antivenom to A-Bungarotoxin.
      ii. Animal studies with mice were proposed – ASP attached.
      iii. Andrea Marzi indicated a minor typo to the virus inoculum titer.
      iv. BMBL Appendix I should be referenced for the safe handling and work with toxins
      v. Work with a-bungarotoxin is approved at BSL-2 and ABSL-2. Injections must be conducted within a BSC.

vi. Toxin and toxin stock solutions containing concentrated amounts of material should be manipulated in a BSC or CFH, with close attention to wearing proper PPE- including gloves, laboratory coat and protective eyewear. Animal work is approved at ABSL-2 injections must be conducted within a BSC.
vii. The committee discussed the dual-use potential of these experiments. The committee agreed that there were no dual-use concerns with the proposal.
viii. Sue Priola requested that a toxic dose for people should be included in the PRD, and if it was unknown, to include that the toxic dose was unknown.
ix. (b)(6) mentioned that there was not a known toxic dose in people.
x. Committee unanimously approved the PRD pending the additions and the correction of the typo. Clayton Winkler abstained from voting.

b. Best PRD 20-228 Amend 05, SARS-CoV-2
   i. Becky Anderson summarized the PRD. This is an amendment to PRD-20-228 that seeks to add co-infection with prion disease to the PRD. Emerging research implicates previous viral infections in the development of neurodegenerative diseases. This study seeks to determine the potential impact of SARS-CoV-2 infection on prion pathogenesis. Prion infection will be established in hamsters. Before clinical symptoms of neurodegenerative disease present, animals will be co-infected with SARS-CoV-2.
   ii. Animal work with Syrian Hamsters is in the attached ASP.
   iii. This amendment will be reviewed by DURC-IRE.
   iv. Work with prions is approved at BSL-2/ABSL-2. Work with SARS-CoV-2 is approved at BSL-3/ABSL-3. Animals will be inoculated with prion strains in ABSL-2 and will be brought to ABSL-3 for SARS-CoV-2 co-infection.
   v. This PRD is approved pending DURC-IRE approval.

c. Best PRD 23-140 Renewal, Dengue virus (1-4 serotypte)
   i. Becky Anderson summarized the PRD. This is a renewal of PRD-17-140 and its amendments. The lab aims to understand how the early host innate immune response is activated by dengue virus, and how the virus might escape early immune responses to cause disease.
   ii. No animal studies were attached.
   iii. Question 7C of the Dual Use Questionnaire was marked “yes.” Committee requested this be changed to “no” because the recombinant work discussed has its own associated RD and does not fall under the scope of this specific PRD.
   iv. Precautions to prevent aerosol generation were discussed. All work is to be performed in a BSC with the use of sealed centrifuge cups or rotors. Everything should be sealed prior to removal from the BSC, this includes sealed/gasketed safety cups for centrifuges, parafilming of microtiter plates, etc. Employees should be informed of the following risks of working with Dengue virus: There is an increased severity of disease upon second exposure to dengue virus, as well as working with multiple serotypes increases your risk for disease.
   v. Work with dengue virus is approved at BSL-2/ABSL-2. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 375-9600.
   vi. Pending the removal of the comment under 7C, the PRD was unanimously approved.

d. Hackstadt PRD 23-35, Renewal, Chlamydia spp.
    i. Becky Anderson summarized the PRD. This PRD is a renewal. The lab desires to study the mechanisms by which Chlamydiae survive within mammalian host cells.
    ii. No animal studies were proposed.
    iii. Work with Chlamydia spp. On this PRD are approved at BSL-2 with BSL-3 practices (BSL-2/3). All manipulations of infectious material must be conducted in a BSC, sealed centrifuge rotors must be used when centrifuging infectious material.
    iv. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 375-9600.
    v. PRD was unanimously approved.

e. Hackstadt PRD 23-37, Renewal, Chlamydia trachomatis
    i. Becky Anderson summarized the PRD. This PRD is a renewal. This study is of the basic cell and molecular biology of *C. trachomatis* virulence factors.
    ii. Animal work with mice was included in the attached ASP.
    iii. Work with *Chlamydia trachomatis* is approved at BSL-2/ABSL-2 with BSL-3/ABSL-3 practices. All manipulations of infectious material must be conducted in a BSC, sealed centrifuge rotors must be used when centrifuging infectious material. For animal work with mice, all infection and control solutions will be prepared and administered by laboratory personnel wearing protective clothing, gloves, and safety goggles or a face shield.
    iv. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 375-9600.
    v. PRD was unanimously approved.

f. Peterson PRD 23-103 Renewal, California Serogroup Viruses
    i. (b)(6) summarized the PRD. This is a renewal of PRD-18-103 and its amendments. The work studies how California Serogroup viruses gain access to the CNS and how they induce damage to neurons.
    ii. Animal work with mice, macaques, and rabbits was included in attached ASPs.
    iii. Due to the increased risk from infection for children under 16, all lab personnel are to be provided general hazard awareness regarding the risk of viral infection to children, and a sign is to be placed on the lab door stating " No one under 16 allowed in laboratory". Hazards regarding children will be communicated to lab staff.
    iv. Clayton Winkler described adding another FACS-machine, a Miltenyi Tyto, and another sentence in the PRD to show that no aerosols are generated when it is used in a BSC. This cell-sorting machine does not generate aerosols and language to this affect will be added to the PRD.
    v. PRD is unanimously approved with the minor addition and pending potential DURC-IRE review, if review is deemed necessary. Clayton Winkler abstained from the vote.

g. Peterson PRD 23-184 Renewal, Flavivirus
    i. (b)(6) summarized the PRD. This is a renewal of 16-184 and its amendments. No new work is proposed. The study seeks to investigate flaviviruses and to develop a mouse model of Zika virus-induced microcephaly and to determine how pregnancy influences Zika virus infection in mice.
    ii. Animal work with mice was proposed.
    iii. Care should be taken to minimize worker exposure to aerosols, such as working in a certified Class II BSC at all times and using gasketed bucket covers when centrifuging infectious material. Gasketed bucket covers or sealed rotors must only be loaded/unloaded in a BSC. It is recommended if possible that work with Zika virus be performed in a small or dedicated lab away from the main lab areas. Women of child bearing years must be advised of the risks of working with this agent, please consult with OMS.
    iv. Work with Zika virus is approved at BSL-2/ABSL-2. Hazard awareness training must be provided to all individuals listed on the PRD, animal care staff, and staff working in shared lab/animal spaces.
    v. PRD was unanimously approved with Clayton Winkler abstaining from the vote.

II. Registration of Recombinant DNA Experiments
    a. Feldmann RD 22-452; Amend 02, Alphavirus
        i. Andrea Marzi and Kendal Cooper summarized the RD. This is an amendment to RD-22-452 that seeks to add the T7-VEE-GFP vector to studying Alphavirues. This vector has been used successfully in the lab before – this RD is to create vaccine for SARS-CoV-2.
        ii. Andrea Marzi asked that the group explain more about "Spike protein stabilization" and that they provide more detail as to the mechanisms and nature of said stabilization.
        iii. Kendal Cooper asked the lab group to include more information on which vector T7-VEE-GFP would be replacing. A request was made to spell out "VEE" in order to provide clear information on where the vector originates.
        iv. RD approved pending the addition of the details requested.

III. Full Committee Review of Inactivation Procedures
    a. Bloom Flavivirus inactivation with PFA and glut in infected cerebral organoids.
        i. Sue Priola summarized the method.
        ii. Organoids were infected with one of two titers of virus and treated (fixed) with 2% PFA or 2.5% Glutaraldehyde for four different timepoints. Each condition was repeated in triplicate and included specific controls. Subsequent supernatant was used to infect fresh cultures and no growth was detected in any of the experimental conditions.
        iii. The method was unanimously approved.

IV. Standard Operating Procedures
    a. Draft (b)(6) SOP Powassan virus-update to add inactivation procedures.
        i. Sue Priola summarized the addition to the SOP.
        ii. The addition to the SOP was unanimously approved.
    b. Draft Animal SOP SARS-CoV-2 and prion infection.
        i. A new SOP was developed for the disinfection of both SARS-CoV-2 and prion-soiled materials.
        ii. The SOP was unanimously approved.

c. Draft SOP#4-28-16 Rodent Procedures in Biocontainment-Update intracranial/intracerebral section
    i. Becky Summarized the update to the SOP to define how intracranial/intracerebral injections are distinct from one another in practice and technique.
    ii. Megan Brose explained the procedure in detail. Staff to perform the technique have received extensive training in BSL-2.
    iii. The update to the SOP was unanimously approved.

Reports

I. Biosafety Officer Report – Becky Anderson
    a. Becky Anderson presented the BSO report.
    b. Becky approved two amendments: one to add IM inoculation route for guinea pigs in RD-21-436 and one to add another mouse-adapted strain of SARS-CoV-2 to PRD 20-228.
    c. Reportable incident to NIH Office of Science Policy. Immediate notification provided 6/7/23. Also reported to CDC DSAT.
    d. DURC-IRE reviews for 4 PRDs and 2 RDs were mentioned. These reviews are for PRDs and RDs that have been IBC-approved.

II. Occupational Safety and Health Manager Report – Seth Cooley
    a. Nothing to report

III. IRF Biosafety Manager/Responsible Official Report – (b)(6) Megan Brose
    a. (b)(6) Nothing to report
    b. Megan: Nothing to report

IV. Associate Director Report – Marshall Bloom
    a. Not present

Around the Room

I. None

Other Issues

I. None

Next Meeting

I. 20 July, 2023

NIH RML Institutional Biosafety Committee Meeting

Biosafety Officer (BSO) Report

June 15, 2023

Business Conducted since the last IBC Meeting

A. BSO approvals
   a. Feldmann RD 21-436 Amend 02
      i. Add intramuscular route of inoculation for guinea pigs
   b. Best PRD 20-228 Amend 04
      i. Add another mouse adapted strain of SARS-CoV-2

B. Electronic business
   a. None

New business for IBC meeting

A. See agenda.

Biosafety Activities since the last IBC Meeting

A. Animal Study Protocols Review- Performed by Megan Brose, Rebecca Anderson, (b)(6)

ASP Title	Associated PRD	Associated RD	Reviewer
Analysis of immunity induced by bovine herpesvirus (BoHV-4) vectors expressing SARS-CoV-2 antigens in mice	N/A	20-458	R. Anderson
Testing efficacy of Salmonella Typhimurium therapeutic strains in treatment of tumors	18-44	15-108	(b)(6)
Identifying Tumor Colonization Factors of Salmonella Typhimurium in mice	18-44	15-108	M. Brose
Pathogenesis of hypervirulent Klebsiella pneumoniae strains in a murine bacteremia model	21-180	N/A	R. Anderson
Chronic Wasting Disease exposure to human cerebral organoid tissue implants in cervidized mice	16-190	23-199	(b)(6)
Assessing the role of HNF4α in the pathogenesis of SARS-CoV-2 in mice	20-228	N/A	M. Brose
Co-infection of SARS-CoV-2 and prion disease in Syrian hamsters (pilot)	20-228	16-190	R. Anderson

B. Biosafety Training- Performed by Megan Brose, Rebecca Anderson, (b)(6)

Type of Training	Number of Sessions	Number of Employees Trained
New Employee	2	12
Annual Refresher Lab Biosafety	N/A	N/A
Select Agent-Initial	1	1
Select Agent- Refresher	N/A	N/A
Select Agent- Visitor	1	1
BSL-3 Laboratory Biosafety-Initial	1	1
Practical Training	N/A	N/A
BSL-4 Laboratory Biosafety-Initial	1	1
Suit Training	2	4
Checklist Training	3	3
Laboratory Biosafety Support Staff-Initial	N/A	N/A
Laboratory Biosafety Support Staff-Refresher	N/A	N/A

C. Safety Audits and Inspections

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

D. Biological Incidents to Report
    a. Reportable Incident to NIH Office of Science Policy. Immediate Notification provided 6/7/23. Same incident also reported to CDC DSAT.

E. Other Issues
    a. None

F. DURC-IRE Reviews
    a. Bosio PRD 23-245
    b. Feldmann PRD 18-94, RD 21-436
    c. Feldmann PRD 22-81, RD 20-412
    d. Best PRD 18-135, RD 14-437

NIH RML Institutional Biosafety Committee Meeting

Agenda for July 20, 2023

Location: Virtual via Zoom/Building A (b)(6)

Old Business

A. Draft minutes of June 15, 2023 meeting

New Business

A. Committee Business
   1) PRD 23-251 (New) PI: Best
   2) RD 20-458 (Amend 02) PI: Feldmann — Reviewers: Sue Priola, Kendal Cooper
   3) RD 19-126 (Amend 03) PI: Steele-Mortimer — Reviewers: Chris Bosio, Andrea Marzi
   4) RD 23-437 (Renewal) PI: Best — Reviewers: Clayton Winkler, Sue Priola
   5) Draft SOP#4-28-43 Aerosol Exposure System Operation- Update to add prairie dogs
   6) Draft SOP#4-28-66 Prairie Dog Procedures in Biocontainment-Update to add aerosol route of inoculation

B. BSO report (Dr. Becky Anderson)
C. Occupational Safety & Health Manager report (Seth Cooley)
D. IRFBSM report ([redacted] (b)(6))
E. Responsible Official Report (LCDR Megan Brose)
F. Associate Director Report (Dr. Marshall Bloom)
G. Comments from around the room

Next Meeting: August 17, 2023 virtual via Zoom/Building A (b) (6)

PRD- Pathogen Registration Document
RD- Recombinant DNA Registration Document
SOP-Standard Operating Procedures
BSO-Biosafety Officer
IRFBSM-Integrated Research Facility Biosafety Manager

NIH RML Institutional Biosafety Committee Minutes

July 20, 2023 (1:00 PM – 2:00 PM)
Virtual via Zoom/Building A (b)(6)

Members Present:

☒Sue Priola, Chair	☐Carol Calderwood	☒Scott Kobayashi
☒Becky Anderson	☐Marcie Caldwell (EO)	☒Jamie Lovaglio
☐Alan Applebury	☒Seth Cooley	☒Andrea Marzi
☐Sonja Best (EO)	☒Kendal Cooper	☐Alida Merritt
☐Chris Bosio	☐Frank DeLeo (EO)	☐Greg Saturday
☐Marshall Bloom (EO)	☐Heinz Feldmann (EO)	☐Alexandra Scranton
☒Megan Brose	☐Erik Hoover	☐Brian Vickrey
☐Larry Brouwer	☐Josh Kellar (EO)	☒Clayton Winkler

(EO) *ex officio*

Guests: (b)(6)
(b)(6)

Announcements

I. None

Old Business

I. Review of Past IBC Meeting Minutes
   a. June 15, 2023 Minutes
      i. Bruce Chesebro's name was still added to the participant list of the June minutes.
      ii. Chlamydia was noted to have been spelled incorrectly in one location.
      iii. The minutes were unanimously approved with the correction of the errors.

New Business

I. Registration of Material (Potentially) Infectious for Humans, Plants or Animals
   a. Best PRD 23-251 New, TSEs
      i. (b)(6) summarized the PRD. This is a transfer of PRD 16-190 (Chesebro) with new proposed work to study the pathogenesis of prion diseases with an overarching goal to define the mechanisms that lead to brain neurodegeneration and death.
      ii. Animal studies with mice, rats, and hamsters were proposed.
      iii. Work with Transmissible Spongiform Encephalopathies is approved at BSL-2 and ABSL-2
      iv. Sue Priola discussed adding the specific strains of the mouse and hamster-adapted scrapie, and CWD strains.
      v. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.
      vi. The committee unanimously approved with minor modifications.
         1. Add specific strains of the TSEs

II. Registration of Recombinant DNA Experiments
   a. Feldmann RD 20-458 Amend 02, Bovine Herpesvirus as a vector.
      i. The RD was summarized by Sue Priola and Kendal Cooper.

ii. Animal work with mice is included in the RD.
iii. The amendment is to add SARS-CoV-2 spike protein to Bovine Herpesvirus (BHV) vector. BHV is replication defective virus in mice.
iv. Question 7b is selected "Yes" on the dual use questionnaire. The IBC agreed that the answer was correct, and that an answer of "Yes" did not increase the risk of the proposal.
v. Kendal Cooper asked the group to clarify the description of the proposed amendment, if the mice are being "infected or vaccinated".
vi. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.
vii. The committee unanimously approved with minor modifications
    1. Clarify amendment language to specify if the mice are being infected or vaccinated.

b. Steele-Mortimer RD 19-126 Amendment 03, *Salmonella enterica* strain VNP20009.
    i. Andrea Marzi summarized the RD. The amendment is to add Salmonella strain VNP20009, which does not cause disease in mice or humans. VNP20009 is a genetically modified strain of *S. enterica* that has previously exhibited antitumor activities *in vivo.* The Steele-Mortimer lab wants to use this Salmonella strain for genome characterization and to modify the strain for tumor localization. The deletion of the genes will attenuate the Salmonella strain's ability to infect organs. The modified Salmonella is anticipated to preferentially grow in tumor cells.
    ii. The Steele-Mortimer lab also wants to add pFPV delivery plasmid. The vector map was attached.
    iii. The RD includes the addition of Activation-Induced cytidine Deaminase (AID) to the plasmid for therapeutic purposes.
    iv. Dual use questions were marked no.
    v. Becky Anderson and Sue Priola asked the group to provide a specific list of the strains of *S. enterica* used or to be used in the RD.
    vi. Becky Anderson asked the IBC if they thought the proposed modifications to Salmonella met the definition of dual use. Kendal Cooper described the proposed modifications to the Salmonella strains and clarified that the strains are not targeted to tumor cells.
    vii. Scott Kobayashi questioned the accuracy of the term "targeting a tumor." Kendal Cooper agreed that the strain was not "targeted" towards a tumor, but rather was selected to preferentially grow in tumors as opposed to systemic organs.
    viii. Scott Kobayashi also mentioned that because the Salmonella was driven towards a pathogenic state (e.g. preferentially growing in tumors), the work did not meet the definition of dual use. The IBC discussed extensively and determined this was not dual use and did not require review by the NIH DURC-IRE.
    ix. Animal studies with mice were proposed.
    x. Work with the listed Salmonella strains is approved at BSL-2/ABSL-2
    xi. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.
    xii. The committee approved (Kendal Cooper abstained) with minor modifications
        1. Clarify that the antibiotics used for selection with the new plasmid are not clinically relevant antibiotics for Salmonella infection.
        2. Add detail to the types of genes that will be manipulated.
        3. List the strains that will be used

4. Update the amendment synopsis and ASP language to better describe the genetic modifications that will be made/why that will benefit growth in tumors vs. spleen etc.

c. Best RD 23-437, New, TBEV.
   i. Clayton Winkler and Sue Priola summarized the PRD.
   ii. The RD is a proposal to study TBEV, which is a select agent. There is a new reverse genetics system to be used in the study. The group hopes to study TBEV infectivity by deleting specific genes. This will alter the immune response of mice and NHPs, which will give insight into the modes of TBEV infection.
   iii. CPER cloning was described as the new reverse genetics system. CPER cloning, which will be used to generate the viral genome in 7 separate parts, is approved for work in BSL-2, but as soon as cDNA fragments are generated, they can only be combined in BSL-4/ABSL-4 to generate the complete genome. Section III-D-2-a and III-E-1 of the NIH Guidelines was recommended for the prokaryotic work.
   iv. Sections III-D-3-c, III-D-1-a, and III-D-1c of the NIH Guidelines are relevant to the eukaryote work done in this proposal.
   v. Answers to questions of the dual use questionnaire were answered "No," but Clayton Winkler advocated that question 7b should be selected as "Yes."
   vi. Sonja Best would be asked if the previous reverse genetics system should be removed from the RD, or if it would be included to allow its use, if necessary.
   vii. Research using prokaryotic cells is approved at BSL-2 under section III-D-2-a of the NIH Guidelines. Research using eukaryotic cells is approved at BSL-4 under sections III-D-3-c, III-D-1-a, and III-D-1-c of the NIH guidelines.
   viii. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.
   ix. The committee unanimously approved with minor modifications.
      1. Add sections III-D-3-c, III-D-1-a, and III-D-1c of the NIH Guidelines to the eukaryote cell section
      2. Change dual use questionnaire question 7b to "Yes"
      3. This has already been approved by the DURC-IRE committee.

III. Full Committee Review of Inactivation Procedures
   a. None

IV. Standard Operating Procedures
   a. Draft SOP 4-28-23 Aerosol Exposure System Operation-update
      i. The update is to add work with animal species: prairie dogs. Addition of prairie dogs to the list of methods of handling animals.
      ii. Jamie Lovaglio stated that prairie dogs need to be added to section 6.1.A.1.
      iii. The committee unanimously approved with minor modifications.
         1. Add prairie dogs to section 6.1.A.1.

   b. Draft SOP 4-28-66 Prairie Dog Procedures in Level 4 Biocontainment
      i. Update to include aerosol inoculation of prairie dogs.
      ii. The committee unanimously approved as written

V. Annual Reviews

a. None.

Reports

I. Biosafety Officer Report – Becky Anderson
   a. Becky Anderson presented the BSO report.
II. Occupational Safety and Health Manager Report – Seth Cooley
   a. Nothing to report
III. IRF Biosafety Manager/Responsible Official Report – Megan Brose
   a. Nothing to report
IV. Associate Director Report – Marshall Bloom
   a. Not present

Around the Room

I. Nothing to report.

Other Issues

I.

Next Meeting

I. 17 August, 2023

Meeting ended at 2:00 PM.

NIH RML Institutional Biosafety Committee Meeting

Biosafety Officer (BSO) Report

July 20, 2023

Business Conducted since the last IBC Meeting

A. BSO approvals
   a. Transfer of documents from Heinzen to Long
      i. PRD 18-153-HBBF
      ii. PRD 18-70 C. burnetii exempt
      iii. RD 20-107
      iv. RD 20-133
   b. Peterson PRD 23-184 Amend
      i. Add intradermal route of inoculation for mice
   c. Steele-Mortimer RD 22-108 Amend
      i. Add intraperitoneal route of inoculation for mice

B. Electronic business
   a. None

New business for IBC meeting

A. See agenda.

Biosafety Activities since the last IBC Meeting

A. Animal Study Protocols Review- Performed by Megan Brose, Rebecca Anderson (b)(6)

ASP Title	Associated PRD	Associated RD	Reviewer
Monkeypox virus strain comparison in black-tailed prairie dogs	22-240	N/A	R. Anderson
Effects of social stress on immune responses to West Nile Virus infection in mice	23-108	N/A	(b)(6)
Ornithodoros tick colony feeding and maintenance on mice	20-227	N/A	M. Brose

B. Biosafety Training- Performed by Megan Brose, Rebecca Anderson, (b)(6)

Type of Training	Number of Sessions	Number of Employees Trained
New Employee	2	7
Annual Refresher Lab Biosafety	N/A	N/A
Select Agent-Initial	1	1
Select Agent- Refresher	N/A	N/A
Select Agent- Visitor	4	11
BSL-3 Laboratory Biosafety-Initial	N/A	N/A
Practical Training	N/A	N/A
BSL-4 Laboratory Biosafety-Initial	N/A	N/A
Suit Training	N/A	N/A
Checklist Training	2	2
Laboratory Biosafety Support Staff-Initial	1	1
Laboratory Biosafety Support Staff-Refresher	N/A	N/A

C. Safety Audits and Inspections

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

D. Biological Incidents to Report
   a. Reportable Incident to NIH Office of Science Policy (OSP) on 6/6/23. Incident closed out by OSP on 7/14/23.
   b. Reportable Incident to NIH OSP. Immediate Notification provided 6/22/23. Same incident also reported to CDC DSAT.

E. Other Issues
   a. None

F. DURC-IRE Reviews
   a. Best PRD 20-228 Amend
   b. Hackstadt PRD 19-38/RD 19-110

NIH RML Institutional Biosafety Committee Meeting

Agenda for August 17, 2023

Location: Virtual via Zoom/Building A (b)(6)

Old Business

A. Draft minutes of July 20, 2023 meeting

New Business

A. Committee Business
   1) PRD 22-123 (Amend 02) PI: Feldmann
   2) PRD 22-143 (Amend 02) PI: Feldmann
   3) PRD 23-252 (New) PI: Martens
   4) PRD 23-253 (New) PI: Long
   5) PRD 23-254 (New) PI: Long
   6) PRD 23-255 (New) PI: Best
   7) RD 20-458 (New) PI: Best Reviewers: Andrea, Marzi; Clayton Winkler
   8) Bosio *F. tularensis* inactivation testing Earth Sense Disinfectant
   9) Draft (b)(6) SOP-update disinfectant concentration/time
   10) Draft ABSL-3 Tularemia animal SOP- update disinfectant concentration/time
   11) Draft SOP#4-28-38 Ferret and Mink Procedures in Level 4 biocontainment
   12) Draft Exposure Control Plan-Annual Review

B. BSO report (Dr. Becky Anderson)
C. Occupational Safety & Health Manager report (Seth Cooley)
D. IRFBSM report (b)(6)
E. Responsible Official Report (LCDR Megan Brose)
F. Associate Director Report (Dr. Marshall Bloom)
G. Comments from around the room

Next Meeting: September 21, 2023 virtual via Zoom/Building A (b)(6)

PRD- Pathogen Registration Document
RD- Recombinant DNA Registration Document
SOP-Standard Operating Procedures
BSO-Biosafety Officer
IRFBSM-Integrated Research Facility Biosafety Manager

NIH RML Institutional Biosafety Committee Minutes

August 17, 2023 (1:00 PM – 2:15 PM)
Virtual via Zoom/Building A (b)(6)

Members Present:

☒Sue Priola, Chair	☐Carol Calderwood	☒Scott Kobayashi
☒Becky Anderson	☐Marcie Caldwell (EO)	☒Jamie Lovaglio
☐Alan Applebury	☒Seth Cooley	☒Andrea Marzi
☐Sonja Best (EO)	☒Kendal Cooper	☒Alida Merritt
☒Chris Bosio	☐Frank DeLeo (EO)	☒Greg Saturday
☐Marshall Bloom (EO)	☐Heinz Feldmann (EO)	☐Alexandra Scranton
☒Megan Brose	☒Erik Hoover	☐Brian Vickrey
☐Larry Brouwer	☐Josh Kellar (EO)	☒Clayton Winkler

(EO) *ex officio*

Guests: (b)(6)
(b)(6)

Announcements

I. None

Old Business

I. Review of Past IBC Meeting Minutes
   a. July 20, 2023 Meeting Minutes
      i. Minutes were unanimously approved with the correction of typos.
         1. Update minor typos.

New Business

I. Registration of Material (Potentially) Infectious for Humans, Plants or Animals
   a. PRD-22-123 Phlebovirus – Heinz Feldmann (Amend 02)
      i. (b)(6) summarized the PRD. This is an amendment to add the intravenous route of inoculation for nonhuman primates. The Feldmann Lab would also like to add the SFTSV (Severe Fever with Thrombocytopenia Syndrome Virus) strains YL-1 and SPL010.
      ii. No new animal studies were proposed.
      iii. Work with SFSTV, including strains YL-1 and SPL010, is approved at BSL-3/ABSL-3.
      iv. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.
      v. The committee unanimously approved the amendment as written.
   b. PRD-23-143 Coronaviruses – Heinz Feldmann (Amend 02)
      i. Becky Anderson summarized the PRD. The Feldmann Lab seeks to evaluate mutations that have arisen in SARS-CoV-2, and how they affect transmission and pathogenesis. The Feldmann Lab will focus on P681R, a mutation found in the Delta variant of concern.
      ii. (b)(6) of the Feldmann Lab described the coinfection and transmission study. While recombinant viruses may be generated, only a limited portion of the viral genome encompassing the mutation will be sequenced. Samples will be destroyed after sequencing is complete and no viruses will be isolated.

iii. Sue Priola asked that the information on the recombinant viruses not found in natural populations are added to the proposal.
iv. Clayton Winkler noted that question 7B of the DURC questionnaire should be answered "Yes" because synthetic biology techniques would be used to generate the viruses.
v. The committee discussed the dual-use and ePPP potential of these experiments at length. Question 4 of the Dual Use Questionnaire was marked "Yes." The rationale stated by the Feldmann Lab hypothesizes that while the P681R mutation may increase transmissibility, this mutation occurs naturally and would not increase transmissibility compared to other variants of SARS-CoV-2. The committee agreed that there were no dual-use or ePPP concerns with the proposal. However, the committee also agreed that this work needs to be evaluated by the NIH DURC-IRE.
vi. No new animal studies were proposed.
vii. Animal work will be performed at ABSL-4.
viii. The committee unanimously approved with minor modifications pending DURC-IRE review:
    1. Indicate that no recombinant viruses will be isolated and the samples will be destroyed following sequencing.,
    2. Explain that the viruses will be created by reverse genetics techniques,
    3. Changing question 7B to "Yes"

c. PRD-23-252 NHP HBBF – Craig Martens (New)
i. Becky Anderson summarized the PRD. The Martens Lab will extract the RNA from samples provided by an off-site Investigator at Bethesda, MD. Samples will be inactivated with Trizol, then sequenced. Samples may be positive for Human Immunodeficiency Virus (HIV) or Simian-Human Immunodeficiency Virus (SHIV).
ii. No animal studies were proposed.
iii. The committee discussed the dual-use and ePPP potential of the experiment. The committee agreed that there were no dual-use or ePPP concerns with the proposal.
iv. (b)(6) brought up the need for language to be added to the PRD for the Bite, Scratch, Splash Exposure Guidelines (BSSE) and ensure the lab has a BSSE kit. Jamie Lovaglio mentioned that staff working with NHP samples would have to undergo NHP training.
v. The committee unanimously approved with minor modifications:
    1. Ensure staff are aware they need to contact Jamie Lovaglio for the required training.
    2. Add BSSE language to recommendation section and to ensure the lab has a kit containing prophylaxis for bites, scratches and splashes.

d. PRD-23-253, PRD-23-254 *Naegleria fowleri* and *Acanthamoeba spp.* – Carrie Long (New)
i. (b)(6) summarized the two PRDs. The aims of these projects are to detect and characterize amoeba present in source water samples provided by the Long Lab's collaborators. With increased yearly temperatures, amoeba host range will likely increase; therefore, the Long Lab seeks to establish current host ranges of amoeba in climate sensitive areas.
ii. Work with *Naegleria fowleri* and *Acanthamoeba spp.* is approved at Biosafety Level 2, with Biosafety Level 3 practices (BSL-2/3). BSL-2/3 includes enhanced practices in a BSL-2 facility: (1) fastidious adherence to proper microbiological techniques, (2) decontaminating all potentially infectious waste prior to moving to MPW waste boxes for incineration, (3) working in a BSC wearing proper PPE- double gloves, full eye protection and mucus membrane protection, tie-back gown, (4) use of gasketed safety

cups for centrifugation procedures, and (5) minimizing the use of sharps, among other considerations to minimize worker exposure to aerosols, such as only working in a certified Class II BSC for any procedures that may generate aerosols.

iii. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 406-375-9600.

iv. The committee discussed the dual-use and ePPP potential of the studies. The committee agreed that there were no dual-use or ePPP concerns.

v. No animal studies were proposed.

vi. Kendal Cooper asked that the Long Lab adds the specific species of bacteria that will be used in co-culture experiments with the amoeba.

1. The committee unanimously approved with minor modifications:Clarify co-culture conditions with bacteria and amoeba.

e. PRD-23-255 Alphaviruses – Sonja Best (New)

i. (b)(6) summarized the PRD. This study will investigate the pathogenesis of alphaviruses during acute infection of mammalian host organisms and identify mechanisms that promote successful infection of the host nervous system.

ii. The following strains are approved for work at BSL-2: Chikungunya virus 181/25 (vaccine strain), Mayaro virus, O'nyong-nyong Virus, Ross River Virus, & Sindbis virus.

iii. The following strains are approved for work at BSL-3: Madariaga Virus, Western equine encephalitis virus, Venezuelan equine encephalitis virus (select agent exempt), Chikungunya virus.

iv. The work is subject to section III-D-1-A of the NIH Guidelines.

1. Becky Anderson instructed the Best Lab to move work covered under the NIH Guidelines to the associated RD-23-501.

v. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 406-375-9600.

vi. No animal studies were proposed.

vii. The committee discussed the dual-use and ePPP potential of the study. The committee agreed that there were no dual-use or ePPP concerns. Becky Anderson indicated that the PRD would be reviewed by the DURC-IRE.

viii. The committee unanimously approved with minor modifications pending approval by the DURC-IRE.

1. Remove language for recombinant experiments and add to associated RD-23-501.

II. Registration of Recombinant DNA Experiments

a. RD-23-501 Alphavirus – Sonja Best (New)

i. Andrea Marzi and Clayton Winkler summarized the RD. This study will investigate the pathogenesis of alphaviruses during acute infection of mammalian host organisms and identify mechanisms that promote successful infection of the host nervous system.

ii. Reverse genetics systems for positive-strand RNA will be used to generate recombinant material. Virus or virus infected cells will be used as a template for reverse-transcriptase (RT)-PCR to generate: 1) cDNA encoding individual genes or 2) overlapping segments of cDNA that span the entire genome. Alternatively, commercially available

oligonucleotide synthesis will be used to source cDNA encoding individual viral genes or larger genome segments.

iii. Research using prokaryotic cells is approved at BSL-2 under sections III-D-2-a, III-E-1, and III-D-2-b of the NIH Guidelines.
iv. Research using eukaryotic cells is approved at BSL-4 sections III-D-1-a and III-D-3-b of the NIH Guidelines.
v. The committee discussed the dual-use and ePPP potential of the studies. The committee agreed that there were no dual-use or ePPP concerns, but acknowledged that the DURC-IRE will be reviewing the RD.
vi. No animal studies were proposed.
vii. Andrea Marzi highlighted several minor typos for correction.
viii. Andrea Marzi indicated that "future plans" to include animal work should be removed if there was no attached ASP.
ix. List of items to be addressed before review:
    1. Specify whether or not the recombinant viruses are CPER generated or chimeric viruses.
    2. Change name of Laboratory from "LVPD" to "LNII."
    3. Specify if recombinant viruses will be fluorescently tagged, like the engineered proteins.
    4. Add sections III-D-3-a and III-D-3-b of the NIH Guidelines to Eukaryotic Work section.
    5. Add BSL-3 to Biosafety Level for Eukaryotic Work
    6. Add III-D-1-a to Prokaryotic Work section.
    7. Change question 7B on the DURC questionnaire to "Yes" because synthetic techniques will be used to generate virus.
    8. Specify the specific vector plasmids and remove general vector plasmids (remove "e.g.").
x. The committee tabled the RD and will review when the updates have been provided.

III. Full Committee Review of Inactivation Procedures
    a. Katy Bosio – *Francisella tularensis,* 5% Earthsense for 5 minutes
        i. The Bosio group wanted to test a lower percentage of Earthsense (5%) and a higher contact time (5 min) than in the original validation study (10% and 2 min, respectively) for inactivation of F. tularensis since 10% Earthsense was leaving a stick residue on surfaces.
        ii. Kendal Cooper suggested that the Bosio group use a higher volume of stock SchuS4 bacteria for an inactivation method.
        iii. Andrea Marzi asked if the time listed in the SOP would be "10 minutes" as, the IBC typically asks for a doubling of validated disinfectant contact time
        iv. The committee unanimously tabled the review of inactivation procedures and requested re-testing with the following parameters:
            1. Test a shorter contact time or double the tested time
            2. Increase the titer tested
            3. Wash out the 5% earthsense prior to plating test samples

IV. Standard Operating Procedures
    a. Draft (b)(6) SOP *F. tularensis* (Updates)

i. Becky Anderson summarized the updates to the SOP to the committee. The updates include the change from 10% Earthsense to 5% Earthsense and the change from "10 minutes" to "five minutes" throughout the SOP.
ii. There were no additional comments or concerns with the updated procedures.
iii. The committee unanimously tabled review of the SOP until the inactivation procedures have been retested.

b. Draft Standard Operating Procedures for Animal Biosafety Level 3 (ABSL-3): *Francisells tularensis* (Updates)
   i. Becky Anderson summarized the updates to the SOP to the committee. The updates include the change from 10% Earthsense to 5% Earthsense throughout the SOP.
   ii. There were no additional comments or concerns with the updated procedures.
   iii. The committee unanimously tabled review of the SOP until the inactivation procedures have been retested.

c. Draft SOP 4-28-38 Ferret and Mink Procedures in Level 4 Biocontainment (updates)
   i. Jamie Lovaglio summarized the updates to the SOP to the committee. The updates include:
      1. Procedures for transferring animals to clean cages.
      2. Adding escaped-animal capture procedures, including the use of leather gloves and/or a net.
      3. Adding less-strenuous options for anesthesia
         a. Adding the option to move the unanesthetized animals to locations with oxygen drops so they may be anesthetized.
         b. Adding instructions on how to recapture animals that have been moved to locations with oxygen drops.
      4. Adding options for inhalation anesthesia
      5. Adding options for injectable anesthetics – using a restraint device
      6. Adding options for aerosol anesthesia
      7. Adding subcutaneous, intraperitoneal, and intramuscular injection of anesthesia
      8. A minor typo was noted in the updated section 6.A.4.e.2.The committee unanimously approved as written.

d. Annual review: RML Biological Exposure Control Plan:
   i. Becky Anderson summarized the updates to the ECP. Minor updates were made to staff titles, contacts, and responsibilities.
      1. The committee unanimously approved as written.

Reports

I. Biosafety Officer Report – Becky Anderson
   a. Becky Anderson presented the BSO report.
II. Occupational Safety and Health Manager Report – Seth Cooley
   a. Nothing to report.
III. IRF Biosafety Manager Report – (b)(6)
   a. Nothing to report.
IV. Responsible Official Report – Megan Brose
   a. Nothing to report.
V. Associate Director Report – Marshall Bloom
   a. Not present.

Around the Room

I. Next month the meeting will be held in (b)(6)

II. New Public Health Officer, Todd Wollman, is replacing Carol Calderwood on the IBC.

Other Issues

I. None

Next Meeting

I. September 21, 2023 virtual via Zoom/(b)(6)

NIH RML Institutional Biosafety Committee Meeting

Biosafety Officer (BSO) Report

August 17, 2023

Business Conducted since the last IBC Meeting

A. BSO approvals
   a. None

B. Electronic business
   a. None

New business for IBC meeting

A. See agenda.

Biosafety Activities since the last IBC Meeting

A. Animal Study Protocols Review- Performed by Megan Brose, Rebecca Anderson, (b)(6)

ASP Title	Associated PRD	Associated RD	Reviewer
Protection of hamsters against SARS-CoV-2 Omicron by ancestral and omicron-specific vaccines	22-143	22-410	R. Anderson
Comparative pathogenesis of SFTSV in non-human primates	22-123	N/A	(b)(6)
Pilot infection of rhesus macaques with Heartland virus	22-123	N/A	M. Brose
Establishment of the LD50 of Klebsiella pneumoniae in mice via intratracheal infection.	19-218	N/A	R. Anderson
Lactoferrin as a treatment for prion disease in mice	20-166 16-190	N/A	R. Anderson

B. Biosafety Training- Performed by Megan Brose, Rebecca Anderson (b)(6)

Type of Training	Number of Sessions	Number of Employees Trained
New Employee	2	6
Annual Refresher Lab Biosafety	N/A	N/A
Select Agent-Initial	1	1
Select Agent- Refresher	N/A	N/A
Select Agent- Visitor	1	2
BSL-3 Laboratory Biosafety-Initial	1	2
Practical Training	1	1
BSL-4 Laboratory Biosafety-Initial	1	2
Suit Training	4	4
Checklist Training	1	1
Refresher Training	1	2
Laboratory Biosafety Support Staff-Initial	N/A	N/A
Laboratory Biosafety Support Staff-Refresher	N/A	N/A

C. Safety Audits and Inspections

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

D. Biological Incidents to Report
    a. Reportable Incident to NIH OSP. Immediate Notification provided 6/22/23. Same incident also reported to CDC DSAT. Incident closed out by OSP on 7/28/23.

E. Other Issues
    a. NIH OSP- NIH Seeks Input on Proposed Revisions to the NIH Guidelines. Public comment accepted until October 10, 2023.

F. DURC-IRE Reviews
    a. Peterson PRD 23-103, RD 18-225
    b. Bloom PRD 19-75, PRD 20-224
    c. Bosio PRD 20-223

NIH RML Institutional Biosafety Committee Meeting

Agenda for September 21, 2023

Location: Virtual via Zoom/Building A (b)(6)

Old Business

A. Draft minutes of August 17, 2023 meeting

New Business

A. Committee Business
   1) PRD 23-245 (Amend 01) PI: Bosio
   2) PRD 23-256 (New) PI: Fischer
   3) PRD 23-257 (New) PI: Best
   4) PRD 23-258 (New) PI: Long
   5) RD 23-501 (New) PI: Best — Reviewers: Andrea Marzi; Clayton Winkler
   6) RD 23-218 (Renew) PI: Best — Reviewers: Sue Priola, Chris Bosio
   7) RD 20-457 (Amend 02) PI: Best — Reviewers: Kendal Cooper, Sue Priola
   8) RD 22-108 (Amend 03) PI: Steele-Mortimer — Reviewers: Scott Kobayashi, Chris Bosio
   9) Draft (b)(6) SOP-Update to add new SOP- BSL-3-Cb-10 Cellaca PLX Analysis of *C. burnetii* infected samples
   10) Draft ABSL-3 Tularemia animal SOP- update to add *Y. pestis* throughout
   11) Draft BSL-3 OSP- Annual Review
   12) Draft ABSL-3 OSP- Annual Review

B. BSO report (Dr. Becky Anderson)
C. Occupational Safety & Health Manager report (Seth Cooley)
D. IRFBSM report (Dr. (b)(6)
E. Responsible Official Report (LCDR Megan Brose)
F. Associate Director Report (Dr. Marshall Bloom)
G. Comments from around the room

Next Meeting: October 19, 2023 virtual via Zoom/Building A (b)(6)

PRD- Pathogen Registration Document
RD- Recombinant DNA Registration Document
SOP-Standard Operating Procedures
BSO-Biosafety Officer
IRFBSM-Integrated Research Facility Biosafety Manager

NIH RML Institutional Biosafety Committee Minutes

September 21, 2023 (1:00 PM – 1:55 PM)

Virtual via Zoom/(b)(6)

Members Present:

☐Sue Priola, Chair	☐Marcie Caldwell (EO)	☒Jamie Lovaglio
☒Becky Anderson	☒Seth Cooley	☒Andrea Marzi
☐Alan Applebury	☒Kendal Cooper	☒Alida Merritt
☐Sonja Best (EO)	☐Frank DeLeo (EO)	☒Greg Saturday
☒Chris Bosio	☐Heinz Feldmann (EO)	☐Alexandra Scranton
☐Marshall Bloom (EO)	☐Erik Hoover	☐Brian Vickrey
☐Megan Brose	☐Josh Kellar (EO)	☒Clayton Winkler
☐Larry Brouwer	☒Scott Kobayashi	☐Todd Wollman

(EO) *ex officio*

Guests: (b)(6)

(b)(6)

Announcements

I. None

Old Business

I. Review of Past IBC Meeting Minutes
   a. August 17, 2023 Meeting Minutes
      i. Minutes were unanimously approved with minor modifications.
         1. Update minor typos.

New Business

I. Registration of Material (Potentially) Infectious for Humans, Plants or Animals
   a. PRD-23-245 *Yersinia pestis* – Katy Bosio (Amend 01)
      i. (b)(6) ummarized the PRD. This is an amendment to add animals to the registration.
      ii. Animal work with mice was discussed. The associated ASP was attached.
      iii. Work with *Y. pestis* in mice is approved in ABSL-3.
      iv. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.
      v. *Y. pestis* is a Select Agent. All personnel with access to this agent must be authorized by the CDC Division of Select Agents and Toxins.
      vi. The committee approved the amendment as written. Chris Bosio abstained from the vote.
   b. PRD-23-256 Vaccinia Virus – Beth Fischer (New)
      i. (b)(6) summarized the PRD. (b)(6) would like to use Cryo electron tomography to study the core structure of vaccinia virus, strain WR. There is a palisade structure comprised of trimers of the A10 protein. The (b)(6) Lab has a mutant with a deletion of the A4 protein that interacts with A10. There is a defect in morphogenesis with immature and aberrant particles forming. (b)(6) would like to see if the absence

of A4 leads to a major alteration or disruption of the palisade. The (b)(6) lab will provide the purified wild type and mutant virus.

ii. (b)(6) mentioned the synopsis section describes work in a CFH and recommended that the Fischer Lab remove the language and work only in an approved BSC.

iii. Remove the prokaryote host section, it is not relevant to the PRD.

iv. Delete "We could provide the purified. . . " at the end of the "Describe your experiment, identifying the objectives of the work" section.

v. No animal studies were proposed.

vi. The committee discussed the dual-use and ePPP potential of the experiment. The committee agreed that there were no dual-use or ePPP concerns with the proposal.

vii. Vaccinia virus is approved for work at BSL-2. Care should be taken to minimize worker exposure to aerosols, such as working in a certified Class II BSC and using gasketed bucket covers when centrifuging infectious material. Vaccination must be offered for personnel working directly with this agent.

viii. The committee unanimously approved the PRD with minor modifications:

1. Language referencing work in a Chemical Fume Hood will be removed and replaced with "Biosafety Cabinet."
2. The work proposed will be moved from "prokaryotic work". Delete "We could provide the purified. . . " at the end of the "Describe your experiment, identifying the objectives of the work" section.

c. PRD-23-257 Coronaviruses – Sonja Best (New)

i. (b)(6) summarized the PRD. The purpose is to study and characterize coronaviruses in vitro.

ii. Coronavirus HCoV-229E and HCoV-OC43 are approved for work at BSL-2. MERS-CoV is approved for work at BSL-3. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 406-375-9600.

iii. The committee discussed the dual-use and ePPP potential of the studies. The committee agreed that there were no dual-use or ePPP concerns.

iv. No animal studies were proposed.

v. Andrea Marzi pointed out that only cell culture work was described but that work involving animal tissues was mentioned in the cell sorting/tissue grinding section. (b)(6) (b)(6) mentioned that this was an artifact that would be removed.

vi. The committee unanimously approved the PRD with minor modifications:

1. Remove language describing work with animal tissues in the cell sorting/tissue grinding section.

d. PRD-23-258 *Legionella pneumophilia* – Carrie Long (New)

i. (b)(6) summarized the PRD. Legionella pneumophilia has been detected in metagenomic analysis of environmental water samples following amoeba enrichment via culturing. The Long Lab hypothesizes that *L. pneumophilia* is living inside free-living amoeba and desire to interrogate the nature of this interaction.

ii. Work with Legionella pneumophila is approved at BSL-2. All work with infectious material is conducted in a biosafety cabinet, centrifugation of infectious materials must be carried out in sealed safety cups or removable rotors that can be loaded and unloaded in a biosafety cabinet.

iii. Co-culture studies with *Naegleria fowleri* and *Acanthamoeba spp*. are approved at Biosafety Level 2, with Biosafety Level 3 practices (BSL-2/3). BSL-2/3 includes enhanced practices in a BSL-2 facility: (1) fastidious adherence to proper microbiological techniques, (2) decontaminating all potentially infectious waste prior to removal from BSC, (3) working in a BSC wearing proper PPE- double gloves, full eye protection and mucus membrane protection, tie-back gown, (4) use of gasketed safety cups for centrifugation procedures, and (5) minimizing the use of sharps, among other considerations to minimize worker exposure to aerosols, such as only working in a certified Class II BSC for any procedures that may generate aerosols.
iv. No animal studies were proposed.
v. The committee discussed the dual-use and ePPP potential of the study. The committee agreed that there were no dual-use or ePPP concerns.
vi. The committee unanimously approved the PRD pending that the unanswered DURC questions are answered "no."
    1. If any questions are answered "yes," the PRD will return to the IBC for re-review.

II. Registration of Recombinant DNA Experiments
    a. RD-23-501 Alphavirus – Sonja Best (New)
        i. Clayton Winkler summarized the RD. This study will investigate the pathogenesis of alphaviruses during acute infection of mammalian host organisms and identify mechanisms that promote successful infection of the host nervous system.
        ii. This is a re-review of the same RD tabled in the prior month's IBC Meeting. The main items discussed at the previous meeting were addressed by the Best Lab; however, the NIH Guidelines were not selected properly, and minor typos remained.
        iii. Reverse genetics systems for positive-strand RNA will be used to generate recombinant material. Virus or virus infected cells will be used as a template for reverse-transcriptase (RT)-PCR to generate: 1) cDNA encoding individual genes or 2) overlapping segments of cDNA that span the entire genome. Alternatively, commercially available oligonucleotide synthesis will be used to source cDNA encoding individual viral genes or larger genome segments.
        iv. Andrea Marzi recommended that the synopsis be reworded to remove implications suggesting future animal work, as there is no attached ASP under the current RD. Andrea Marzi also noted that a few of the vector maps attached do not exactly match the document, this should be updated.
        v. Clayton Winkler recommended updating the NIH Guidelines for the Research Product section to III-D-2-a, III-E-1, III-D-1-a, III-D-3-a, III-D-3-b.
        vi. Research using prokaryotic cells is approved at BSL-2 under sections III-D-2-a, III-E-1 of the NIH Guidelines.
        vii. Research using eukaryotic cells is approved at BSL-2 for Chikungunya virus 181/25 (vaccine strain), Mayaro virus, O'nyong-nyong Virus, Ross River Virus, & Sindbis virus and is approved at BSL-3 for Madaraiga virus, Wester Equine Encephalitis Virus, Venezuelan Equine Encephalitis Virus, and Chikungunya Virus under sections III-D-1-a. III-D-1-b, III-D-3-a, III-D-3-b, and III-E-1 of the NIH Guidelines.
        viii. The committee discussed the dual-use and ePPP potential of the studies. The committee agreed that there were no dual-use or ePPP concerns, but acknowledged that the DURC-IRE will review the RD.
        ix. No animal studies were proposed.

x. The committee voted unanimously to approve the RD pending DURC-IRE review and the following minor modifications:
    1. Change name of Lab Section from "LVPD" to "LNII."
    2. Add sections III-D-3-a and III-D-3-b of the NIH Guidelines to Eukaryotic Work section.
    3. Update the Research Product NIH Guidelines to include: III-D-2-a, III-E-1, III-D-1-a, III-D-3-a, III-D-3-b.
    4. Modify language in the synopsis to remove implications of animal studies.
    5. Update vector maps and document to match.

b. RD-23-218 – Sonja Best (Renewal)
    i. Chris Bosio summarized the RD.
    ii. This is a renewal working with Friend Virus. No new work is proposed.
    iii. Andrea Marzi summarized Sue Priola's comments *in absentia*. Sue asked for clarification on the synopsis section – while the RD is describing Friend Virus, the synopsis mentions recombinant *L. monocytogenes*, which will be the host for infection with FV.
    iv. Scott Kobayashi asked that the Best Lab confirms that no wild type Listeria is used and only recombinant *L. monocytogenes* is used.
    v. The committee discussed the dual-use and ePPP potential of the study. The committee agreed that there were no dual-use or ePPP concerns.
    vi. The renewal was approved unanimously with minor modifications:
        1. Change the title from Friend virus to *L. monocytogenes*.
        2. Update the synopsis section so the proposed work is clear.
        3. Clarify if only recombinant *L. monocytogenes* is used.

c. RD-20-457 – Best (Amend 02)
    i. Kendal Cooper summarized the RD.
    ii. The RD describes using a hybrid alpha pseudovirus to develop a VLP that encapsulates an RNA genome for rapid report expression. The system is a rapid detection of infection. The Best Lab also wants to add a source of recombinant RNA for vectors in addition to the commercial system.
    iii. Kendal Cooper stated they need to add commercial source of the hybrid-alpha pseudovirus system. Andrea Marzi asked for clarification on what the VLPs would be used for.
    iv. The committee discussed the dual-use and ePPP potential of the study. The committee agreed that there were no dual-use or ePPP concerns.
    v. The amendment was approved pending the following:
        1. Clarification of what the VLPs will be used for.
        2. Addition of the Commercial source of the system.

d. RD-22-108 – Olivia Steele-Mortimer (Amend 03)
    i. Scott Kobayashi and Chris Bosio summarized the RD.
    ii. Scott Kobayashi summarized the RD. This is an amendment to add TlpD chemotaxis protein-containing plasmid to RD-22-108. TlpD comes from *Heliobacter pylori*. The Steele-Mortimer lab wishes to add express this protein during GI colonization of mice to determine if it can functionally complement McpA-deficient Salmonella.
    iii. Work with *H. pylori* is approved at BSL-2 under section III-D-1-a and III-D-2-a.
    iv. The committee discussed the dual-use and ePPP potential of the study. The committee agreed that there were no dual-use or ePPP concerns.
    v. The committee approved the amendment. Kendal Cooper abstained from the vote.

III. Full Committee Review of Inactivation Procedures
    a. None.

IV. Standard Operating Procedures
    a. Draft (b)(6) New SOP-BSL3-Cb-10 Cellaca PLX analysis of *C. burnetii* infected samples (New).
        i. The Cellaca PKLX can perform cell viability, counting, and fluorescence with no fluidics. Users place samples in a 96-well plate that can be sealed. Samples will be transferred from a BSC to the bench in a durable leak proof container.
        ii. Scott Kobayashi pointed out minor typos.
        iii. The committee unanimously approved the updates to the SOP with minor modifications:
            1. Correct minortypos.
    b. Draft ABSL-3 *F. tularensis* animal SOP (Updates)
        i. Becky Anderson summarized the updates to the SOP to the committee. The update was to include *Y. pestis* to the animal SOP throughout.
        ii. There were no additional comments or concerns with the updated procedures.
        iii. The committee approved the updates to the SOP.
    c. Draft BSL-3 OSP (Annual Review)
        i. Becky Anderson summarized the updates to the OSP to the committee. The updates included minor updates including name and title changes, and updates to the language pertaining to the new electronic inactivation certificate system.
        ii. There were no additional comments or concerns with the updated procedures.
        iii. The committee unanimously approved the changes to the BSL-3 OSP for its annual review.
    d. Draft ABSL-3 OSP (Annual Review)
        i. Becky Anderson summarized the updates to the ABSL-3 OSP to the committee. The updates include:
            1. Updated names
            2. Inclusion of the new electronic inactivation certificate system
            3. Updated the load weight and procedures for carcass loads in the autoclave.
            4. Updated language for electrical failures.
            5. Updated waste handling procedures in the ABSL-3 facility.
        ii. (b)(6) uggested including language for flexibility of storing thawing carcasses before autoclaving to state select agent registered rooms instead of only one room number.
        iii. The committee unanimously approved the changes to the ABSL-3 OSP for its annual review with minor modifications:
            1. Update the language for storing carcasses to be thawed for autoclaving.

Reports

I. Biosafety Officer Report – Becky Anderson
    a. Becky Anderson presented the BSO report.
II. Occupational Safety and Health Manager Report – Seth Cooley
    a. Nothing to report.
III. IRF Biosafety Manager Report – (b)(6)
    a. RML Campus Coordination meeting has been transitioned to the RML High Containment Operations Team
IV. Responsible Official Report – Megan Brose

a. BSL-3/4 inspection is tentatively March 11, 2024.

V. Associate Director Report – Marshall Bloom
   a. Not present.

Around the Room

I. Next month the meeting will be held in its usual location, (b)(6)

Other Issues

I. Alida Merritt discussed procedures involving staff access to tools and techniques.

Next Meeting

I. October 19, 2023 virtual via Zoom/Building A (b)(6)

NIH RML Institutional Biosafety Committee Meeting

Biosafety Officer (BSO) Report

September 21, 2023

Business Conducted since the last IBC Meeting

A. BSO approvals
   a. Steele-Mortimer PRD 17-05
      i. Approved amendment to change to storage only

B. Electronic business
   a. Review AVL inactivation validation data of Pox viruses
   b. Approved SOP#4-28-32 Removal of Nucleic Acid Extraction

New business for IBC meeting

A. See agenda.

Biosafety Activities since the last IBC Meeting

A. Animal Study Protocols Review- Performed by Megan Brose, Rebecca Anderson, (b)(6)

ASP Title	Associated PRD	Associated RD	Reviewer
Supportive Critical Care in Nonhuman Primates	N/A	N/A	R. Anderson
Determination of intranasal and intradermal LD50 of Yersinia pestis infection in mice	23-245	N/A	M. Brose
Rearing and maintenance of tick colonies in the mouse and rabbit	N/A	N/A	(b)(6)
Cross-Protective Potential of Hantavirus Monoclonal Antibodies in the Syrian Hamster Model for Andes Virus Disease	22-81	N/A	R. Anderson
Testing vaccine efficacy of modified virus-like particles in protection against SARS-CoV2 in mice	17-143	20-457	R. Anderson

B. Biosafety Training- Performed by Megan Brose, Rebecca Anderson, (b)(6)

Type of Training	Number of Sessions	Number of Employees Trained
New Employee	2	7
Annual Refresher Lab Biosafety	N/A	N/A
Select Agent-Initial	N/A	N/A
Select Agent- Refresher	N/A	N/A
Select Agent- Visitor	1	1
BSL-3 Laboratory Biosafety-Initial	N/A	N/A
Practical Training	N/A	N/A
BSL-4 Laboratory Biosafety-Initial	N/A	N/A
Suit Training	3	4
Checklist Training	6	14
BSL-4 Laboratory Biosafety-Refresher	1	52
Laboratory Biosafety Support Staff-Initial	1	1
Laboratory Biosafety Support Staff-Refresher	1	43

C. Safety Audits and Inspections

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

D. Biological Incidents to Report
    a. None

E. Other Issues
    a. None

F. DURC-IRE Reviews
    a. Best PRD 19-212/RD 19-454 for Yellow Fever virus
    b. Best PRD 23-107/RD20-456 for Powassan virus
    c. Feldmann PRD 22-143 Amend 02 for SARS-CoV-2 study

NIH RML Institutional Biosafety Committee Meeting

Agenda for October 19, 2023

Location: Virtual via Zoom/Building A (b)(6)

Old Business

A. Draft minutes of September 21, 2023 meeting

New Business

A. Committee Business
   1) PRD 23-259 (New) PI: Peterson
   2) PRD 23-260 (New) PI: Bloom
   3) RD 19-454 (Amend 01) PI: Best — Reviewers: Clayton Winkler, Kendal Cooper
   4) RD 19-221 (Amend 01) PI: Peterson — Reviewers: Sue Priola, Andrea Marzi
   5) RD 23-502 (New) PI: Bloom — Reviewers: Chris Bosio, Scott Kobayashi
   6) RD 23-503 (New) PI: Bloom — Reviewers: Andrea Marzi, Clayton Winkler
   7) Draft ABSL-3 OSP- Update to add procedures for chemical waste that cannot be autoclaved
   8) Draft ABSL-3 SARS-CoV-2 Animal SOP_LV- update PPE to PAPR or N95
   9) Annual IBC Training

B. BSO report (Dr. Becky Anderson)
C. Occupational Safety & Health Manager report (Seth Cooley)
D. IRFBSM report ((b)(6)
E. Responsible Official Report (Cmdr. Megan Brose)
F. Associate Director Report (Dr. Marshall Bloom)
G. Comments from around the room

Next Meeting: November 16, 2023 virtual via Zoom/Building A (b)(6)

PRD- Pathogen Registration Document
RD- Recombinant DNA Registration Document
SOP-Standard Operating Procedures
BSO-Biosafety Officer
IRFBSM-Integrated Research Facility Biosafety Manager

NIH RML Institutional Biosafety Committee Minutes

October 19, 2023 (1:00 PM – 2:30 PM)

Virtual via Zoom/Building A (b)(6)

Members Present:

☒Sue Priola, Chair	☐Larry Brouwer	☐Scott Kobayashi
☒Andrea Marzi, Vice-chair	☐Marcie Caldwell (EO)	☐Jamie Lovaglio
☒Becky Anderson	☒Chad Clancy	☒Alida Merritt
☐Alan Applebury	☐Seth Cooley	☐Alexandra Scranton
☒Paul Beare	☒Kendal Cooper	☐Brian Vickrey
☐Sonja Best (EO)	☐Frank DeLeo (EO)	☒Clayton Winkler
☒Chris Bosio	☐Heinz Feldmann (EO)	☒Todd Wohlman
☐Marshall Bloom (EO)	☐Erik Hoover	
☒Megan Brose	☐Josh Kellar (EO)	

(EO) *ex officio*

Guests: (b)(6)

Announcements

I. Sue Priola informed the committee about some changes in membership. Andrea Marzi is now the vice chair. Chad Clancy has replaced Greg Saturday, and Paul Beare is filling the vacancy from Bob Heinzen's retirement.

Old Business

I. Review of Past IBC Meeting Minutes
   a. September 21, 2023 Meeting Minutes
      i. Sue Priola addressed several minor typos.
      ii. Minutes were unanimously approved with minor modifications.
         1. Update minor typos.

New Business

I. Registration of Material (Potentially) Infectious for Humans, Plants or Animals
   a. PRD-23-259 HBBF. human sera, CSF, iPSCs – Karin Peterson (New)
      i. (b) (6) summarized the PRD. To gain better tools and understanding of human encephalitis cases, the Peterson lab will utilize human serum, cerebral spinal fluid (CSF) and autopsy tissue from patients with viral encephalitis as well as non-encephalitic controls to analyze for viral RNA, immune responses and virus-specific neutralizing antibodies. They will also utilize multiple human cell lines to study virus infections, including primary human muscle cell lines, primary human fibroblasts and human neural stem cell lines. Finally, they will utilize induced pluripotent stem cells (iPSCs) generated from patients with different autoimmune and autoinflammatory diseases and purchased control iPSCs to generate human cerebral organoids, specific neuronal lineage cells or to directly infect with virus.
      ii. No work with animals was discussed.

iii. Sue Priola noted that the work should be listed as ongoing in the Synopsis section instead of 10 years. She also stated that the sentence, "Any new viruses will be registered with the IBC . . . " should be deleted from the Synopsis section.
iv. Sue Priola commented that the IRB number should be listed on the first page. She also noted a couple of minor typos with the cell line names.
v. Work with iPSCs, primary cell lines, human sera and CSF is approved for work in BSL-2. Work with viral encephalitis and related viruses is covered in associated PRDs.
    1. Care should be taken to minimize worker exposure to aerosols, such as working in a certified Class II BSC at all times and using gasketed bucket covers when centrifuging infectious material. Gasketed bucket covers or sealed rotors must only be loaded/unloaded in a BSC.
vi. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.
vii. The committee approved the PRD, Clayton Winkler abstained, with minor modifications:
    1. Describe the work as ongoing in the Synopsis section.
    2. Delete the sentence , "Any new viruses will be registered with the IBC . . . ".
    3. Add IRB number for iPSCs and for the patient samples.
    4. Correcting minor typos

b. PRD-23-260 Jingmenviruses – Marshall Bloom (New)
i. (b)(6) summarized the PRD. Initial experiments will be to study the expression of the Jingment tick virus (JMTV) and Alongshan virus (ALSV) genomic segments in cell lines using fluorescent and electron microscopy and subsequently to co-transfect all the segments in multiple cell types in an attempt to recover infectious virus. To determine viral growth kinetics, infection will be monitored using cytopathic effects, qRT-PCR for viral RNA, immunofluorescent assay, electron and confocal microscopy, and viral titration.
ii. No animal studies were proposed.
iii. Clayton Winkler pointed out that the responses under the Eukaryotic section were not completely accurate and that question 7b of the DURC Questionnaire should be answered "yes." He recommended that the Eukaryote Cell section, question, "Will studies include attempts to obtain expression of a foreign gene" response should be updated to yes and should include the fluorescent proteins to be used.
iv. Clayton Winkler also informed the committee that the abbreviation ALS should be corrected to ALSV.
v. Sue Priola commented that the start date needs to be updated.
vi. Sue Priola and Paul Beare noted that the biosafety level needs to be corrected in the Eukaryote Cell section, the PI needs to indicate the agent is pathogenic to animals (in addition to humans) and tick cells lines should be added to the Eukaryote Cell section.
vii. The committee discussed the dual-use and ePPP potential of the experiment. The committee agreed that there were no dual-use or ePPP concerns with the proposal.
viii. Work with Jingmen tick virus and Alongshan virus is approved at BSL-2 with BSL-3 practices (BSL-2/3). BSL-2/3 calls for enhanced practices in a BSL-2 facility: (1) all procedures performed in a biosafety cabinet (BSC) wearing PPE: double gloves, eye and face protection, disposable gown, (2) decontaminating all potentially infectious waste prior to removal from BSC, (3) use of gasketed safety cups for centrifugation, and (4) minimize the use of sharps.
    1. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to

and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 406-375-9600.

ix. The committee unanimously approved the PRD with minor modifications:
    1. Update the biosafety level and add tick cell lines to the Eukaryote Cell Section.
    2. Question 7b of DURC Questionnaire should be answered "yes."
    3. Fluorescent proteins should be added to the Eukaryotic Section and the response changed from no to yes.
    4. Add "animals" to list of organisms the agent affects.
    5. Correct the start date.
    6. Correct ALS to ALSV

II. Registration of Recombinant DNA Experiments

a. RD-19-454 Flavivirus – Sonja Best (Amendment 01)
    i. Clayton Winkler summarized the RD. This amendment adds infectious clones of YFV Asibi and 17D vaccine strains. The Best lab will make a series of chimeras between the two strains to determine the specific proteins that evade the host immune response. Clayton Winkler noted that question 7b in the DURC Questionnaire should be yes. The source of the Asibi and 17D clones should be included and the genomic map should include the complete Asibi strain.
    ii. Sue Priola stated that the strains should clearly indicate vaccine and virulent in the synopsis section.
    iii. Research using prokaryotic cells is approved at BSL-2 under section III-D-2-a of the NIH Guidelines.
    iv. Research using cell lines is approved at BSL-3 under sections III-D-1-b and III-D-3-b of the NIH Guidelines
    v. The committee discussed the dual-use and ePPP potential of the studies. The committee agreed that there were no dual-use or ePPP concerns, but acknowledged that the DURC-IRE will review the RD.
    vi. No animal studies were proposed.
    vii. The committee unanimously approved the RD with minor modifications. Approval is pending DURC-IRE review.
        1. Change the answer to yes on question 7b of the DURC Questionnaire
        2. Add source of Asibi and 17D strain YFV to the RD.
        3. Correct minor typos.
        4. Add complete Asibi strain to the genomic map in Figure 1.
        5. Update the plasmid maps to include plasmid backbone data
        6. Define the strains Asibi and 17D explicitly in the synopsis.

b. RD-19-221 – Karin Peterson (Amendment 01)
    i. Sue Priola summarized the RD.
    ii. The Peterson Lab seeks to add another Lentiviral Vector system from Takara Biosciences. This will be used primarily to knock out genes expressed in cells, which will then be infected with LaCrosse virus to determine proteins involved in the immune response.
    iii. Scott Kobayashi asked that the Best Lab confirm that no wild type Listeria is used and only recombinant *L. monocytogenes* is used.
    iv. The committee discussed the dual-use and ePPP potential of the study. The committee agreed that there were no dual-use or ePPP concerns.

v. The amendment was approved, Clayton Winkler abstained, with minor modifications:
    1. Reference PRD-23-259 to obtain the IRB number for the cells from the University of Minnesota.

c. RD-23-502 – Marshall Bloom (New)
    i. Chris Bosio summarized the RD.
    ii. This new RD describes an evaluation of Lyme disease vaccine candidates engineered by biotech collaborators.
    iii. Becky Anderson mentioned that, while the recombinant nucleic acid work is being performed by the biotech collaborator, the nucleic acids are not commercially available and thus need to be registered. Becky Anderson stated that section III-D-4 should be added to the Research Product and Eukaryote cell sections.
    iv. The committee discussed that the sentence, "Although referred to as a VLP. . ." should be moved to synopsis section.
    v. The committee also noted that the PI should change the answer to N/A for the question, "If you are working with viral rDNA, what percent genome. . ."
    vi. The committee discussed the dual-use and ePPP potential of the study. The committee agreed that there were no dual-use or ePPP concerns.
    vii. The RD was unanimously approved with minor modifications:
        1. Update the NIH guidelines to include III-D-4 in the Research Product and Eukaryote cell sections.
        2. Remove III-E-1 from the Prokaryotic and Eukaryotic sections.
        3. Move the following sentence to the synopsis section, "Although referred to as a VLP. . .".
        4. Change the answer to N/A for the question, "If you are working with viral rDNA, what percent genome. . ."

d. RD-23-503 – Marshall Bloom (New)
    i. Andrea Marzi summarized the RD.
    ii. Associated RD to PRD-23-260 (see section 1.b above). Reverse genetics system will be used to generate these viruses. Plasmids will be synthesized and cloned outside of RML at GenScript Biotech. These plasmids will be transfected into cell lines. Andrea Marzi noted that III-D-2-a and III-E-1 need to be added to the Research Product section. III-D-1-a, III-D-3-a, and III-E-1 of the NIH Guidelines need to be added to the Eukaryote Cell Section. Andrea Marzi also stated the question 7b of the DURC Questionnaire needs to be updated.
    iii. Clayton Winkler stated several of the items noted in the PRD review need to be added to the RD. This includes, the addition of tick cells lines, the same ALS typo needs to be corrected to ALSV, the estimated start dates needs to be after the IBC meeting, the biosafety level needs to be updated in the Eukaryote cell section.
    iv. The committee discussed if a Prokaryote Host section is required for the registration. Becky Anderson will follow-up with the PI. The committee also discussed having the PI specify in the Synopsis section that they are using wild type sequences and will not be modifying the virus.
    v. The committee discussed the dual-use and ePPP potential of the study. The committee agreed that there were no dual-use or ePPP concerns. The committee unanimously approved the amendment.
        1. Add III-D-2-a and III-E-1 of the NIH Guidelines to Prokaryote Host section.
        2. Add III-D-1-a, III-D-3-a, and III-E-1 of the NIH Guidelines to Eukaryote Cell Section

3. Update the Biosafety level in the Eukaryote Cell Section to BSL-2/3
4. Determine if a Prokaryote Host section is required for the registration
5. Add tick cell lines to the cell list
6. Specify that only WT viruses will be generated, rather than recombinant viruses.
7. Correct DURC Questionnaire question 7b
8. Correct minor typos

III. Full Committee Review of Inactivation Procedures
   a. None.

IV. Standard Operating Procedures
   a. Draft ABSL-3 OSP
   b. Becky Anderson summarized the update, which adds procedures for chemical waste that cannot be autoclaved.
      i. Sue Priola noted a couple of typos. On page 3, line 54, change "drug us" to "drug use" in the reason for updates section. On page 27, 5.a. add "where" to clarify where the waste is generated.
      ii. There were no additional comments or concerns with the updated procedures.
      iii. The committee unanimously approved the SOP with minor modifications:
         1. On page 3, line 54, change "drug us" to "drug use" in the reason for updates section.
         2. On page 27, 5.a. add "where" to clarify where the waste is generated.
         3.
   c. Draft ABSL-3 SARS-CoV-2 Animal SOP_LV (Updates)
      i. Becky Anderson summarized the updates to the SOP to the committee. PAPRs and N95 respirators are approved PPE.
      ii. Jamie Lovaglio noted a typo on page 3, section 5.1.2 does not match 5.2.1. It should either state eye protection or safety glasses.
      iii. There were no additional comments or concerns with the updated procedures.
      iv. The committee unanimously approved the SOP with minor modifications:
         1. Correct eye protection/safety glasses to be consistent.

V. Annual IBC Training
   a. Becky Anderson presented the annual IBC training to members.

Reports

I. Biosafety Officer Report – Becky Anderson
   a. Becky Anderson presented the BSO report.
II. Occupational Safety and Health Manager Report – Seth Cooley
   a. Nothing to report.
III. IRF Biosafety Manager Report – (b)(6)
   a. Nothing to report
IV. Responsible Official Report – Megan Brose
   a. BSL-3/4 inspection is tentatively March 11, 2024.
V. Associate Director Report – Marshall Bloom
   a. Not present.

Around the Room

I. Next month the meeting will be held in its usual location, (b)(6)

Other Issues

I. None

Next Meeting

I. November 16, 2023 virtual via Zoom/Building A (b)(6)

NIH RML Institutional Biosafety Committee Meeting

Biosafety Officer (BSO) Report

October 19, 2023

Business Conducted since the last IBC Meeting

A. BSO approvals
   a. None

B. Electronic business
   a. None

New business for IBC meeting

A. See agenda.

Biosafety Activities since the last IBC Meeting

A. Animal Study Protocols Review- Performed by Megan Brose, Rebecca Anderson, (b)(6)

ASP Title	Associated PRD	Associated RD	Reviewer
Effects of tick salivary serpins on the biology of helper and cytotoxic T cells	N/A	N/A	(b)(6)
Pilot study evaluating the efficacy of a Lyme disease vaccine in mice	19-213	23-502	R. Anderson
Investigation of *Coxiella burnetii* Vaccine Dissemination in Mice	N/A	N/A	M. Brose
Determination of T cell response following vaccination with conjugate vaccine directed against *Burkholderia pseudomallei* in mice	N/A	23-504	R. Anderson
Modeling Ebola virus Recrudescence in the Male Reproductive Tract in Collaborative Cross Mice	18-90	N/A	(b)(6); (b)(3):42 U.S.C. 262a(h)
Multi-platform vaccine comparison against Ebola virus in the CD-1 mouse model.	18-90 23-82	22-410 20-404 22-452 22-431	R. Anderson

B. Biosafety Training- Performed by Megan Brose, Rebecca Anderson (b)(6)

Type of Training	Number of Sessions	Number of Employees Trained
New Employee	1	1
Annual Refresher Lab Biosafety	N/A	N/A
Select Agent-Initial	1	9
Select Agent- Refresher	2	52
Select Agent- Visitor	1	1
BSL-3 Laboratory Biosafety-Initial	N/A	N/A
Practical Training	N/A	N/A
BSL-4 Laboratory Biosafety-Initial	N/A	N/A
Suit Training	N/A	N/A
Checklist Training	1	1
BSL-4 Laboratory Biosafety-Refresher & SA Refresher	1	13
Laboratory Biosafety Support Staff-Initial	1	6
Laboratory Biosafety Support Staff-Refresher	1	5
Laboratory Biosafety Support Staff-Refresher & SA Refresher	1	30

C. Safety Audits and Inspections

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

D. Biological Incidents to Report
    a. None

E. Other Issues
    a. None

F. DURC-IRE Reviews
    a. Best PRD 23-255 Alphaviruses
    b. Best RD 23-501 Alphaviruses

NIH RML Institutional Biosafety Committee Meeting

Agenda for November 16, 2023

Location: Virtual via Zoom/Building A (b)(6)

Old Business

A. Draft minutes of October 19, 2023 meeting

New Business

A. Committee Business
   1) RD 23-504 (New) PI: Bosio — Reviewers: Kendal Cooper, Paul Beare
   2) RD 22-431 (Amend 01) PI: Feldmann — Reviewers: Sue Priola, Scott Kobayashi
   3) Draft BSL-3 (b)(6) Alphavirus SOP- New
   4) Draft SOP#4-28- 55 Sheep and Goat Procedures in Biocontainment- Update

B. BSO report (Dr. Becky Anderson)
C. Occupational Safety & Health Manager report (Seth Cooley)
D. IRFBSM report (Cmdr. Megan Brose)
E. Responsible Official Report (Cmdr. Megan Brose)
F. Associate Director Report (Dr. Marshall Bloom)
G. Comments from around the room

Next Meeting: December 21, 2023 virtual via Zoom/Building A (b)(6)

PRD- Pathogen Registration Document
RD- Recombinant DNA Registration Document
SOP-Standard Operating Procedures
BSO-Biosafety Officer
IRFBSM-Integrated Research Facility Biosafety Manager

NIH RML Institutional Biosafety Committee Minutes

November 16, 2023 (1:00 PM – 1:40 PM)

Virtual via Zoom/Building A (b)(6)

Members Present:

☒Sue Priola, Chair	☐Larry Brouwer	☐Josh Kellar (EO)
☒Andrea Marzi, Vice-chair	☐Marcie Caldwell (EO)	☒Scott Kobayashi
☒Becky Anderson	☒Chad Clancy	☒Jamie Lovaglio
☒Paul Beare	☐Seth Cooley	☒Alida Merritt
☐Sonja Best (EO)	☒Kendal Cooper	☐Alexandra Scranton
☒Chris Bosio	☐Frank DeLeo (EO)	☐Brian Vickrey
☐Marshall Bloom (EO)	☐Heinz Feldmann (EO)	☐Clayton Winkler
☒Megan Brose	☐Erik Hoover	☒Todd Wohlman

(EO) *ex officio*

Guests: (b)(6)

Announcements

I. None.

Old Business

I. Review of Past IBC Meeting Minutes
   a. October 19, 2023 Meeting Minutes
      i. Sue Priola addressed several minor typos.
      ii. Minutes were unanimously approved with minor modifications.
         1. Update minor typos.

New Business

I. Registration of Material (Potentially) Infectious for Humans, Plants or Animals
   a. None.

II. Registration of Recombinant DNA Experiments
   a. RD-23-504– Bosio (New)
      i. Kendal Cooper summarized the RD. A new conjugate vaccine against melioidosis has been created comprised of a specific *B. pseudomallei* antigen (Hcp1) that has shown promise for protecting mice. The conjugate vaccine will be generated off-site by a research collaborator but will be tested in mice at RML.
      ii. ASP is attached.
      iii. Paul Beare indicated that research with described viral components and used in animals is approved at BSL-2/ABSL-2 under section III-D-2-a and III-D-4-a of the NIH Guidelines. Section III-E-1 is not appropriate and should be deleted.
      iv. Kendal Cooper discussed that there was no prokaryotic work to be done, so the Prokaryote Host section could be removed.
      v. Sue Priola discussed removing unnecessary detail in the Recombinant DNA section and having the investigator keep the description brief for clarity's sake.
         1. Current Recombinant DNA was copy-pasted from PDF, which led to many transcription errors, reducing clarity.

2. Sue Priola suggested having the investigator condense the Recombinant DNA section.

vi. The committee discussed the dual-use and ePPP potential of the studies. The committee agreed that there were no dual-use or ePPP concerns.

vii. The committee approved the RD with minor modifications, Chris Bosio abstained:

1. Update NIH Guidelines section covering described work, add III-D-2-a, III-D-4-a, and delete III-E-1.
2. Remove Prokaryote Host section.
3. Remove unnecessary detail in the Recombinant DNA section.

b. RD-23-431 – Feldmann (Amendment 01)

i. Sue Priola summarized the RD. This RD is for generating clones of viral proteins. The current amendment is to characterize the immunogenicity and function of these proteins in a virus-like particle (VLP) that will be used as a vaccine in mice. The VLPs expressing pathogen proteins will not be created or modified on-site but will be supplied by a collaborator.

ii. Andrea Marzi indicated that the Amend Registration section should be condensed.

iii. Paul Beare asked if the VLPs supplied by the collaborator would be approved by the collaborator's IBC.

1. Sue Priola and Becky Anderson indicated thatthe material would be registered by the collaborator with their IBC and does not need to be listed on the Feldmann registration.

iv. The committee discussed the dual-use and ePPP potential of the studies. The committee agreed that there were no dual-use or ePPP concerns.

v. Alida Merritt asked what the onboarding process to writing/compiling RDs at RML was.

1. Sue Priola indicated that instructions for writing RDs would be disseminated to Staff.

vi. The Amendment to the RD was unanimously approved with the following modification:

1. Summarize the work to be done with mice and remove extraneous information.

III. Full Committee Review of Inactivation Procedures

a. None.

IV. Standard Operating Procedures

a. Draft SOP BSL-3 (b)(6) Alphaviruses (New)

i. Becky Anderson summarized the new SOP, which outlines the procedure for work with Alphaviruses in Building (b)(6) (b)(6)

ii. The SOP explicitly states that only non-Select Agent Alphaviruses will be worked with in BSL-3 (b)(6) No inactivation procedures were attached.

iii. Sue Priola asked for several updates:

1. Pagination
2. Clarification on decontamination procedures
3. Add general "pipettes" when discussing manipulation instead of branded pipettes.
4. Correction of minor typos.

iv. The committee unanimously approved the SOP with minor modifications.

b. Draft SOP 4-28-55 Sheep and Goat Procedures in Biocontainment (Updates)

i. Jamie Lovaglio summarized the updates to the SOP to the committee.

ii. The policy was updated to add weight limits (up to 70 lbs.) for sheep and goats in the MCL.

iii. The policy was updated to reflect the specific types of animals shipped to RML for studies. RML has no control if animals with horns will be delivered, but the previous procedure said that animals with horns would *not* be used in studies. Updating the word choice allows for animals with horns to be used in studies, so long as safety procedures to deal with horns are in place.
iv. Procedures involving inoculation and anesthetization were updated to reflect best practices.
v. The committee unanimously approved the updates to the SOP.

Reports

I. Biosafety Officer Report – Becky Anderson
   a. Becky Anderson presented the BSO report.
II. Occupational Safety and Health Manager Report – Seth Cooley
   a. Not present.
III. IRF Biosafety Manager Report – Megan Brose
   a. Nothing to report
IV. Responsible Official Report – Megan Brose
   a. Update to Select Agent registration has started – All ABSL-3 suites to be added to SA registration.
V. Associate Director Report – Marshall Bloom
   a. Not present.

Around the Room

I. None

Other Issues

I. None

Next Meeting

I. December 21, 2023 virtual via Zoom/Building A (b)(6)

NIH RML Institutional Biosafety Committee Meeting

Biosafety Officer (BSO) Report

November 16, 2023

Business Conducted since the last IBC Meeting

A. BSO approvals
   a. Feldmann RD 21-440
      i. Amendment to add aerosol route of inoculation for hamsters.

B. Electronic business
   a. None

New business for IBC meeting

A. See agenda.

Biosafety Activities since the last IBC Meeting

A. Animal Study Protocols Review- Performed by Megan Brose, Rebecca Anderson, (b)(6)

ASP Title	Associated PRD	Associated RD	Reviewer
None – November ACUC meeting will be combined with December.	N/A	N/A	N/A

B. Biosafety Training- Performed by Megan Brose, Rebecca Anderson, (b)(6)

Type of Training	Number of Sessions	Number of Employees Trained
New Employee	N/A	N/A
Annual Refresher Lab Biosafety	N/A	N/A
Select Agent-Initial	N/A	N/A
Select Agent- Refresher	N/A	N/A
Select Agent- Visitor	N/A	N/A
BSL-3 Laboratory Biosafety-Initial	N/A	N/A
Practical Training	N/A	N/A
BSL-4 Laboratory Biosafety-Initial	N/A	N/A
Suit Training	N/A	N/A
Checklist Training	1	1
BSL-4 Laboratory Biosafety-Refresher & SA Refresher	N/A	N/A
Laboratory Biosafety Support Staff-Initial	N/A	N/A
Laboratory Biosafety Support Staff-Refresher	5	18
Laboratory Biosafety Support Staff-Refresher & SA Refresher	N/A	N/A

C. Safety Audits and Inspections

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

D. Biological Incidents to Report
   a. None

E. Other Issues
   a. None

F. DURC-IRE Reviews
    a. Best PRD 23-257 MERS-CoV
        b. Best RD 19-454 Amend 01
        c. Best RD 20-457 Amend 02

NIH RML Institutional Biosafety Committee Meeting

Agenda for December 21, 2023

Location: Virtual via Zoom/Building A (b)(6)

Old Business

A. Draft minutes of November 16, 2023 meeting

New Business

A. Committee Business
   1) PRD 23-209 (Renew) PI: Haigh
   2) PRD 23-261 (New) PI: Haigh
   3) RD 22-452 (Amend 03) PI: Feldmann Reviewers: Andrea Marzi, Clayton Winkler
   4) Draft BSL-3 (b)(6) Alphavirus SOP- Add inactivation procedures previously approved for (b)(6) BSL-3 (transfer of Best lab procedures to (b)(6)
   5) Draft SOP#4-28- 44 Swine Procedures in Biocontainment- Update
   6) Draft MCL Operations and Safety Procedures (OSP)- Annual Review

B. BSO report (Dr. Becky Anderson)
C. Occupational Safety & Health Manager report (Seth Cooley)
D. IRFBSM report (Cmdr. Megan Brose)
E. Responsible Official Report (Cmdr. Megan Brose)
F. Associate Director Report (Dr. Marshall Bloom)
G. Comments from around the room

Next Meeting: January 18, 2024 virtual via Zoom/Building A (b)(6)

PRD- Pathogen Registration Document
RD- Recombinant DNA Registration Document
SOP-Standard Operating Procedures
BSO-Biosafety Officer
IRFBSM-Integrated Research Facility Biosafety Manager

NIH RML Institutional Biosafety Committee Minutes

December 21, 2023 (1:00 PM – 1:30 PM)

Virtual via Zoom/Building A (b)(6)

Members Present:

☐Sue Priola, Chair	☒Larry Brouwer	☐Josh Kellar (EO)
☒Andrea Marzi, Vice-chair	☐Marcie Caldwell (EO)	☒Scott Kobayashi
☒Becky Anderson	☐Chad Clancy	☒Jamie Lovaglio
☒Paul Beare	☐Seth Cooley	☒Alida Merritt
☐Sonja Best (EO)	☒Kendal Cooper	☐Alexandra Scranton
☒Chris Bosio	☐Frank DeLeo (EO)	☐Brian Vickrey
☐Marshall Bloom (EO)	☐Heinz Feldmann (EO)	☒Clayton Winkler
☒Megan Brose	☒Erik Hoover	☐Todd Wohlman

(EO) *ex officio*

Guests (b)(6)
(b)(6)

Announcements

I. None.

Old Business

I. Review of Past IBC Meeting Minutes
   a. November 16, 2023 Meeting Minutes
      i. Minutes were unanimously approved.

New Business

I. Registration of Material (Potentially) Infectious for Humans, Plants or Animals
   a. PRD 23-209 – Haigh (Renewal)
      i. (b)(6) summarized the PRD. This is a 5-year renewal, there is no new work being added. The purpose of this study is to use the select agent toxin, tetrodotoxin, for blocking synaptic activity.
      ii. No work with animals was discussed.
      iii. Work with tetrodotoxin is approved at BSL-2. Work with concentrated or solid lyophilized toxin must be performed in a chemical fume hood or ducted biosafety cabinet equipped with exhaust HEPA filters and a charcoal filter for activities with a high potential for aerosol, such as powder samples or large quantities of toxin. Personnel must wear appropriate PPE (gloves, labcoat, eye protection) and all toxin containing waste should be inactivated and sent to the medical pathological waste stream. Surfaces should be lined with disposable liners. Avoid contact with skin or eyes and avoid aerosolization of this agent. Fresh 0.5% NaOCl treatment for 30 minutes is effective and preferred for inactivation of tetrodotoxin containing solutions as autoclaving is ineffective, please See BMBL 6th edition, Appendix I regarding work with biological toxins. Work with this agent is exempt from Select Agent registrations provided aggregate amounts in the laboratory do NOT exceed 500mg at any one time.

iv. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 406-375-9600.
v. Paul Beare discussed the laboratory rooms listed on PRD and requested that the rooms approved for work with Tetrodotoxin are updated for consistency.
vi. The committee discussed the dual-use and ePPP potential of the studies. The committee agreed that there were no dual-use or ePPP concerns.
vii. The committee unanimously approved the PRD with the following change:
    1. Update the rooms registered for work with Tetrodotoxin.

b. PRD 23-261 – Haigh, *Borrelia spp.* (New)
    i. (b)(6) summarized the PRD. Human-derived neural cells and cerebral organoids will be infected with various Lyme and relapsing fever Borrelia species including *B. burgdorferi, B. garinii, B. afzelii, B. miyamotoi,* and *B. hermsii*. The pathogenic neurotropic isolates will be compared with non-pathogenic controls to investigate how infection changes neuronal function, causes neuroinflammation and the interaction of the borrelia with the 3D tissue environment.
    ii. No work with animals was discussed.
    iii. All individuals listed on the PRD must receive initial and annual refresher training on controlling exposure to Bloodborne Pathogens, must have access to and be familiar with the RML Exposure Control Plan, and must be offered the Hepatitis B vaccine. For more information, please contact the OMS Nurse at 406-375-9600.
    iv. The committee discussed the dual-use and ePPP potential of the studies. The committee agreed that there were no dual-use or ePPP concerns.
    v. The committee unanimously approved the PRD.

II. Registration of Recombinant DNA Experiments
a. RD-22-452 – Feldmann (Amendment)
    i. Andrea Marzi summarized the RD. The amendment is to add the use of control antigen from a variety of unrelated viruses in this alphavirus (Venezuela Equine Encephalitis virus) derived vaccine system.
    ii. ASP is attached.
    iii. The committee discussed the dual-use and ePPP potential of the studies. The committee agreed that there were no dual-use or ePPP concerns.
    iv. Andrea Marzi and Clayton Winkler asked the Feldmann Lab to specify which control antigens will be used, instead of broadly listing species.
    v. The amendment was unanimously approved with the following change:
        1. Specify which viral proteins are to be used in the vaccine system.

III. Full Committee Review of Inactivation Procedures
a. None.

IV. Standard Operating Procedures
a. Draft SOP BSL-3 (b)(6) Alphaviruses (New)
    i. Becky Anderson summarized the new SOP, which outlines the addition of inactivation procedures for work with Alphaviruses in Building (b)( ) (b)(6)
    ii. The SOP explicitly states that only non-Select Agent Alphaviruses will be worked with in BSL-3 (b)(6)

iii. This is a transfer of inactivation procedures from the (b)(6) BSL-3 that have already been reviewed by the IBC and approved for this PI.
iv. Clayton Winkler requested that the SOP be updated to use a check mark, rather than an "X," to indicate approved means of inactivation.
v. The committee unanimously approved the SOP with the following change:
1. Indicate approved inactivation procedures with a check mark, rather than an "X."

b. Draft SOP 4-28-44 Swine Procedures in Biocontainment (Updates)
i. Becky Anderson summarized the updates to the SOP to the committee.
ii. The policy was updated to add weight limits (up to 70 lbs.) for swine in the MCL.
iii. Procedures involving inoculation and anesthetization were updated to reflect best practices.
iv. The committee unanimously approved the updates to the SOP.

c. Annual review of the MCL OSP (annual review)
i. Becky Anderson summarized the updates to the SOP to the committee.
ii. Updated ARO list.
iii. Removed references to Dover BSL-4 Suit.
iv. Updated references of DSAT to the new name, DRSC.
v. The committee unanimously approved the updates to the MCL OSP.

Reports

I. Biosafety Officer Report – Becky Anderson
a. Becky Anderson presented the BSO report.

II. Occupational Safety and Health Manager Report – Seth Cooley
a. Not present.

III. IRF Biosafety Manager Report – Megan Brose
a. Nothing to report

IV. Responsible Official Report – Megan Brose
a. DRSC inspection will be week of 12 March, 2024

V. Associate Director Report – Marshall Bloom
a. Not present.

Around the Room

I. None

Other Issues

I. None

Next Meeting

I. January 18, 2024 virtual via Zoom/Building A (b)(6)

NIH RML Institutional Biosafety Committee Meeting

Biosafety Officer (BSO) Report

November 16, 2023

Business Conducted since the last IBC Meeting

A. BSO approvals
   a. None

B. Electronic business
   a. None

New business for IBC meeting

A. See agenda.

Biosafety Activities since the last IBC Meeting

A. Animal Study Protocols Review- Performed by Megan Brose, Rebecca Anderson, (b)(6)

ASP Title	Associated PRD	Associated RD	Reviewer
Determine if ID01 expression is provoked following vaccination with improved Francisella vaccine in mice	18-73 18-71	18-125	M. Brose
Defining the effect of Plasmodium infection on Ebola virus vaccine efficacy in mice	23-90	N/A	M. Brose
Impact of obesity on the resolution of Bordetella pertussis infection in mice	17-195	N/A	(b)(6)
Impact of obesity on the outcome of Yersinia pestis challenge by intranasal and intradermal infection in mice	23-245	N/A	(b)(6); (b)(3):42 U.S.C. 262a(b)
Infection of Ixodes scapularis ticks with tick-borne flaviviruses by blood-feeding on mice	19-58	N/A	R. Anderson
Dose response to Ebola virus infection in nonhuman primates with implantable telemetry devices	18-90	N/A	R. Anderson

B. Biosafety Training- Performed by Megan Brose, Rebecca Anderson, (b)(6)

Type of Training	Number of Sessions	Number of Employees Trained
New Employee	N/A	N/A
Annual Refresher Lab Biosafety	2	288
Select Agent-Initial	1	5
Select Agent- Refresher	N/A	N/A
Select Agent- Visitor	N/A	N/A
BSL-3 Laboratory Biosafety-Initial	1	1
Practical Training	1	1
BSL-4 Laboratory Biosafety-Initial	N/A	N/A
Suit Training	N/A	N/A
Checklist Training	2	2
BSL-4 Laboratory Biosafety-Refresher & SA Refresher	N/A	N/A
Laboratory Biosafety Support Staff-Initial	2	10
Laboratory Biosafety Support Staff-Refresher	N/A	N/A
Laboratory Biosafety Support Staff-Refresher & SA Refresher	N/A	N/A

C. Safety Audits and Inspections

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

D. Biological Incidents to Report
    a. Reportable incident occurred 11/29/23. Reported to OSP on 12/8/23, closed out 12/18/23 and no further information required.

E. Other Issues
    a. None

F. DURC-IRE Reviews
    a. Feldmann PRD 23-206 Alphaviruses
    b. Feldmann RD 22-452 Alphaviruses

NIH RML Institutional Biosafety Committee Meeting

Agenda for January 18, 2024

Location: Virtual via Zoom/Building A (b)(6)

Old Business

A. Draft minutes of December 21, 2023 meeting

New Business

A. Committee Business
    1) PRD 19-38 (Amend 01) PI: Hackstadt
    2) Draft BSL-3 (b)(6) SOP- Add SOP for removal of live Rickettsia spp.

B. BSO report (Dr. Becky Anderson)
C. Occupational Safety & Health Manager report (Seth Cooley)
D. IRFBSM report (Cmdr. Megan Brose)
E. Responsible Official Report (Cmdr. Megan Brose)
F. Associate Director Report (Dr. Marshall Bloom)
G. Comments from around the room

Next Meeting: February 15, 2024 virtual via Zoom/Building A (b)(6)

PRD- Pathogen Registration Document
RD- Recombinant DNA Registration Document
SOP-Standard Operating Procedures
BSO-Biosafety Officer
IRFBSM-Integrated Research Facility Biosafety Manager

NIH RML Institutional Biosafety Committee Minutes

January 18, 2024 (1:00 PM – 1:25 PM)
Virtual via Zoom/Building A (b)(6)

Members Present:

☒Sue Priola, Chair	☐Larry Brouwer	☒Scott Kobayashi
☒Andrea Marzi, Vice-chair	☐Marcie Caldwell (EO)	☒Jamie Lovaglio
☒Becky Anderson, Biosafety Officer (BSO)	☒Chad Clancy	☒Alida Merritt (NA)
	☒Seth Cooley	☐Alexandra Scranton (NA)
☒Paul Beare	☒Kendal Cooper	☐Brian Vickrey
☐Sonja Best (EO)	☐Frank DeLeo (EO)	☒Clayton Winkler
☒Chris Bosio	☐Heinz Feldmann (EO)	☒Todd Wohlman (NA)
☐Marshall Bloom (EO)	☒Erik Hoover	
☒Megan Brose	☐Josh Kellar (EO)	

(EO) *ex officio*
(NA) Members who are non-affiliated with RML

Guests: (b)(6)
(b)(6)

Announcements

I. None.

Old Business

I. Review of Past IBC Meeting Minutes
   a. December 21, 2023 Meeting Minutes
      i. Minutes were unanimously approved with minor changes:
         1. Correct typos

New Business

I. Registration of Material (Potentially) Infectious for Humans, Plants or Animals
   a. PRD 19-38 – (b)(6) (Amend 01)
      i. (b)(6) summarized the PRD. This is an amendment to request to lower the biosafety level from BSL-3 to BSL-2 with BSL-3 practices (BSL-2/3) for *R. rickettsii*
      ii. No animal work was discussed.
      iii. (b)(6) explained that the purification and characterization would continue to occur in BSL-3.
      iv. A committee member asked that the term "small scale" be quantified. According to the BMBL, 6th Edition, "Large scale" experiments are experiments of more than 10 L.
      v. A committee member asked what the definition of "non-propagative" work included. (b)(6) explained that the work in BSL-2/3 would not expand the *R. rickettsii*.
      vi. A committee member asked for rationale describing the specific organisms to be screened for to be included in the attached memo. (b)(6) explained that the specific organisms that the *R. rickettsii* will be screened for are present in the BSL-3 space that the *R. rickettsii* would be purified and removed from.

vii. The committee discussed the dual-use and ePPP potential of the studies. The committee agreed that there were no dual-use or ePPP concerns.
viii. A committee member asked if both wild type and recombinant strains are part of the request. (b)(6) confirmed that he would like to work with both at BSL-2/3. DOHS discussed that they need to review the NIH Guidelines to determine if there are more requirements pertaining to work with recombinant *R. rickettsii*.
ix. The committee unanimously approved the PRD with the following additions:
    1. Add language that experiments would be "dead end experiments."
    2. Explain the rationale for screening for the specific pathogens outlined in the amendment.
    3. Add language pertaining to work with recombinant strains of *R. rickettsii*, DOHS to look into additional requirements for such work.
        a. Only wild type strains were approved in this request. Recombinant strains will be submitted with the RD in a separate request.

II. Registration of Recombinant DNA Experiments
    a. None.

III. Full Committee Review of Inactivation Procedures
    a. None.

IV. Standard Operating Procedures
    a. Draft BSL-3 SOP: *Coxiella burnetii, Rickettsia spp.* (Updates)
        i. The BSO summarized the updates to the SOP to the committee. The procedures outline methods for removing *Rickettsia rickettsii* from BSL-3.
        ii. A new SOP was added, "*Rickettsia rickettsii* Removal to BSL2/3."
        iii. The committee unanimously approved the updates to the SOP.

Reports

I. Biosafety Officer Report – Becky Anderson
    a. Becky Anderson presented the BSO report.
II. Occupational Safety and Health Manager Report – Seth Cooley
    a. Nothing to report.
III. IRF Biosafety Manager Report – Megan Brose
    a. Nothing to report.
IV. Responsible Official Report – Megan Brose
    a. Select Agent inspection week of March 11th will be a virtual inspection; there will be an in-person unannounced inspection of BSL-3 and BSL-4 in 2024.
V. Associate Director Report – Marshall Bloom
    a. Not present.

Around the Room

I. None

Other Issues

I. None

Next Meeting

I. February 15, 2024 virtual via Zoom/Building A (b)(6)

NIH RML Institutional Biosafety Committee Meeting

Biosafety Officer (BSO) Report

November 16, 2023

Business Conducted since the last IBC Meeting

A. BSO approvals
   a. None

B. Electronic business
   a. None

New business for IBC meeting

A. See agenda.

Biosafety Activities since the last IBC Meeting

A. Animal Study Protocols Review- Performed by Megan Brose, Rebecca Anderson, (b)(6)

ASP Title	Associated PRD	Associated RD	Reviewer
Prion disease progression in mice with an impaired integrated stress response	22-191	n/a	R. Anderson
Rapid Protection of VSV-KFDV in the Pigtailed Macaque Model	18-135 23-82	20-404	(b)(6)
Impact of obesity on the outcome of Klebsiella pneumoniae infection in mice.	19-218	n/a	M. Brose
Establishing an outbred challenge model for CCHFV	18-92	n/a	R. Anderson

B. Biosafety Training- Performed by Megan Brose, Rebecca Anderson, (b)(6)

Type of Training	Number of Sessions	Number of Employees Trained
New Employee	1	11
Annual Refresher Lab Biosafety	n/a	n/a
Select Agent-Initial	2	5
Select Agent- Refresher	n/a	n/a
Select Agent- Visitor	6	10
BSL-3 Laboratory Biosafety-Initial	1	3
Practical Training	2	3
BSL-4 Laboratory Biosafety-Initial	n/a	n/a
Suit Training	n/a	n/a
Checklist Training	n/a	n/a
BSL-4 Laboratory Biosafety-Refresher & SA Refresher	n/a	n/a
Laboratory Biosafety Support Staff-Initial	1	4
Laboratory Biosafety Support Staff-Refresher	n/a	n/a
Laboratory Biosafety Support Staff-Refresher & SA Refresher	n/a	n/a

C. Safety Audits and Inspections

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

D. Biological Incidents to Report
    a. None

E. Other Issues
    a. None

F. DURC-IRE Reviews
    a. None

NIH RML Institutional Biosafety Committee Minutes

February 15, 2024 (1:00 PM – 2:20 PM)
Virtual via Zoom/Building A (b)(6)

Members Present:

☒Sue Priola, Chair	☐Larry Brouwer	☒Scott Kobayashi
☒Andrea Marzi, Vice-chair	☐Marcie Caldwell (EO)	☒Jamie Lovaglio
☒Becky Anderson, Biosafety Officer (BSO)	☐Chad Clancy	☐Alida Merritt (NA)
	☒Seth Cooley	☐Alexandra Scranton (NA)
☒Paul Beare	☐Kendal Cooper	☐Brian Vickrey
☐Sonja Best (EO)	☐Frank DeLeo (EO)	☒Clayton Winkler
☐Chris Bosio	☐Heinz Feldmann (EO)	☐Todd Wohlman (NA)
☐Marshall Bloom (EO)	☒Erik Hoover (NA)	
☒Megan Brose	☐Josh Kellar (EO)	

(EO) *ex officio*
(NA) Members who are non-affiliated with RML

Guests: (b)(6)
(b)(6)

Announcements

I. None.

Old Business

I. Review of Past IBC Meeting Minutes
   a. January 18, 2024 Meeting Minutes
      i. Minutes were unanimously approved with minor changes:
         1. Correct typos

New Business

I. Registration of Material (Potentially) Infectious for Humans, Plants or Animals
   a. PRD 24-262 – Bosio (New)
      i. (b)(6) summarized the PRD. This is a new registration for work with *Coxiella burnetii* in BSL-3 (b)(6) The Bosio Lab will develop a pulmonary infection model of *Coxiella burnetii* in mice to determine the cellular and molecular components that contribute to disease.
      ii. Animal work with mice was proposed.
      iii. *Coxiella burnetii* is a Select Agent. All personnel with access to this agent must be authorized by the CDC Division of Select Agents and Toxins.
      iv. The committee discussed the dual-use and ePPP potential of the studies. The committee agreed that there were no dual-use or ePPP concerns.
      v. Work with *Coxiella burnetii* is approved at BSL-3/ABSL-3.
      vi. A committee member asked if a visiting scholar would be participating on this registration. Another committee member explained the process for adding visiting scholars to PRDs.

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vii. The committee unanimously approved the registration with the following changes:
    1. Work with *Coxiella burnetii* can not start until Select Agent Program approval is obtained.

b. PRD 24-263 – Best (New)
    i. (b)(6) summarized the PRD.
    ii. These studies will 1) characterize the functional repertoires of alphaviruses, 2) determine host cell types that are permissive to infection and 3) evaluate host immune responses to infection. A primary objective will be to identify specific biochemical, cell biological, and/or immunological activities that promote infection of the nervous system. This registration is for Select Agent strains of Venezuelan Equine Encephalitis and Eastern Equine Encephalitis virus
    iii. Work with all listed strains of Venezuelan Equine Encephalitis virus (VEEV) and Eastern Equine Encephalitis virus (EEEV) is approved for work at BSL-3.
    iv. A committee member noted that the "Division of Select Agents and Toxins" had changed their name to the "Division of Regulatory Science and Compliance" and that, moving forward, references to DSAT are changed to DRSC. The recommendation section needs to be updated to reflect this change.
    v. A committee member asked if federal permitting was required to obtain shipments of EEEV and VEEV. The Biosafety Officer stated that permits will depend on where they are obtaining the viruses.
    vi. A committee member noted that the question in the eukaryotic cell section regarding foreign gene expression needs to be changed from no to yes.
    vii. A committee asked if an additional Point of Contact for the research was necessary. The committee agreed that an additional Point of Contact was not necessary.
    viii. The committee discussed the dual-use and ePPP potential of the studies. The committee agreed that there were no dual-use or ePPP concerns.
    ix. The committee unanimously approved the registration with the following changes pending review from the DURC-IRE.
        1. Update DSAT to DRSC in the recommendation section.
        2. In the eukaryotic cell section, the foreign gene expression question needs to be changed from no to yes.
        3. Work with Select Agent strains of VEEV and EEEV can not start until Select Agent Program approval is obtained.
        4.

c. PRD 24-212 – Best (Renewal)
    i. (b)(6) summarized the PRD. This is a renewal of PRD 19-212, there is no new work being added. The Best Lab would like to understand how different flaviviruses escape recognition by the early (innate) immune response. The Best lab has three major aims: 1) Understand how type I interferon is induced in response to flavivirus infection, and how viruses antagonize the signaling events to evade type I interferon 2) Determine how various ISGs restrict flavivirus replication and how viruses escape the antiviral functions of these cellular proteins 3) Determine how these events affect virus pathogenesis in vitro and in vivo using mouse models of infection.
    ii. A committee member noted that the question in the eukaryotic cell section regarding foreign gene expression needs to be changed from no to yes.
    iii. The committee discussed the dual-use and ePPP potential of the studies. The committee agreed that there were no dual-use or ePPP concerns.

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iv. A committee member asked if the viruses listed on the registration needed to be explicitly named. The committee agreed that using "various" strains was sufficient.
v. The committee unanimously approved the registration with the following changes:
    1. In the eukaryotic cell section, the foreign gene expression question needs to be changed from no to yes.

d. PRD 24-135 – Best (Renewal)
    i. (b)(6) summarized the PRD. This is a renewal of PRD 18-135. The proposed work is to study the mechanisms of immunopathology in-vitro and in-vivo. In vitro studies will focus on examining the cellular innate immune responses to viral infection, and how the virus is able to antagonize and evade the immune responses. In vivo experiments will be aimed at describing the innate and adaptive immune responses to infection, and how augmenting these responses changes the outcome of disease.
    ii. Work with mice and non-human primates was proposed.
    iii. The committee discussed the dual-use and ePPP potential of the studies. The committee agreed that there were no dual-use or ePPP concerns.
    iv. The TBEVs are Select Agents. All personnel with access to this agent must be authorized by the CDC Division of Regulatory Science and Compliance. Work with the listed TBEV is approved at BSL-4/ABSL-4.
    v. The committee unanimously approved the registration.

II. Registration of Recombinant DNA Experiments
a. RD 24-505 – de Leo (New)
    i. A committee member summarized the RD. The de Leo Lab will develop a gene knockout system in *Klebsiella pneumonia* in antibiotic resistant strains, which will facilitate efforts towards identifying putative virulence factors and candidate vaccine antigens.
    ii. A committee member pointed out that work included the expression of foreign genes, and as such, the related question should be answered "yes" in the Eukaryote Cell section. The foreign genes should be listed in the Research Product section.
    iii. A committee member asked if Dual-use question 3b being marked "yes" was accurate. The committee agreed that the answer was accurate for the work described.
    iv. Work with mice was proposed.
    v. Work with *K. pneumonia* is approved at BSL-2/ABSL-2.
    vi. Research using prokaryotic cells is approved at BSL-2 under sections III-D-1-a and III-D-2-a of the NIH Guidelines.
    vii. Research using eukaryotic cells is approved at BSL-2 under sections III-D-1-a of the NIH Guidelines.
    viii. The committee discussed the dual-use and ePPP potential of the studies. The committee agreed that there were no dual-use or ePPP concerns.
    ix. The committee approved (Scott Kobayashi abstained) the registration with the following changes:
        1. Update the Research Product section to include the foreign genes being expressed.
        2. In the eukaryotic cell section, the foreign gene expression question needs to be changed from no to yes.

b. RD 24-506 – Best (New)
    i. A committee member summarized the RD. This study will investigate the pathogenesis of Alphaviruses during acute infection of mammalian host organisms and identify mechanisms that promote successful infection of the host nervous system.

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ii. The committee discussed the dual-use and ePPP potential of the studies. The committee agreed that there were no dual-use or ePPP concerns.
iii. A committee member reiterated that chimeric viruses would not be made and gene swaps would not be performed under the work proposed.
iv. A committee member noted that III-D-2 should be III-D-2-a in the Research Product section.
v. No animal work was proposed.
vi. Research using prokaryotic cells is approved at BSL-2 and BSL-3 under sections III-D-2-a, III-E-1, III-D-1-b, III-D-3-b of the NIH Guidelines. Protein expression work is approved at BSL-2.
vii. Research using eukaryotic cells is approved at BSL-3 under sections III-D-1-b, III-D-3-b and III-E-1 of the NIH Guidelines. Protein expression work is approved at BSL-2.
viii. In the Eukaryote Cell section, the answer to "if a viral vector is to be used, will an infectious virus be generated" should be changed from yes to no.
ix. In the Eukaryote Cell section, the answer to the expression of foreign genes should be changed from no to yes.
x. The committee unanimously approved the registration pending select agent approval and review by the DURC-IRE, and with the following changes:
    1. Change III-D-2 to III-D-2-a in the Research Product section.
    2. Clarify in the Prokaryote and Eukaryote Cell section that protein expression work can be performed at BSL-2.
    3. In the Eukaryote Cell section, the answer to "if a viral vector is to be used, will an infectious virus be generated" should be changed from yes to no.
    4. In the Eukaryote Cell section, the answer to the expression of foreign genes should be changed from no to yes.

c. RD 24-454 – Best (Renewal)
i. A committee member summarized the RD. This is a renewal for work with Yellow Fever Virus and its amendments.
ii. A committee member asked the Best Lab to change all references of "flaviviruses" to Yellow Fever Virus specifically.
iii. A committee member asked for clarification on the use of "chimeric" viruses. Another committee member explained that proteins would be switched between a virulent and avirulent strain of YFV, and not between flaviviruses or other viruses.
iv. A committee member asked if this RD could be added to the Best Lab's RD pertaining to general flaviviruses. The BSO mentioned that perhaps this could be done in the new system, but that this RD should be kept as YFV-specific.
v. The committee discussed the dual-use and ePPP potential of the studies. The committee agreed that there were no dual-use or ePPP concerns.
vi. The committee unanimously tabled the registration. The Best Lab will be asked to clean up the registration in the new Electronic Registration System. Work submitted prior to this renewal is still approved.

III. Full Committee Review of Inactivation Procedures
a. None.

IV. Standard Operating Procedures
a. Draft BSL-3 (b)(6) SOP – SOP for Corona-, Alpha-, and Flaviviruses (New)

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NIH RML Institutional Biosafety Committee Meeting

Biosafety Officer (BSO) Report

February 15, 2024

Business Conducted since the last IBC Meeting

A. BSO approvals
   a. Feldmann PRD 22-83 Amend 04
      i. Add permits

B. Electronic business
   a. None

New business for IBC meeting

A. See agenda.

Biosafety Activities since the last IBC Meeting

A. Animal Study Protocols Review- Performed by Megan Brose, Rebecca Anderson, (b)(6)

ASP Title	Associated PRD	Associated RD	Reviewer
Myeloid-Lymphoid Dysfunction in Lassa Virus Infection and Therapeutic Development in Cynomolgus Macaques	18-94	n/a	(b)(6); (b)(3):42
Evaluating monoclonal antibodies against CCHFV infection in mice	18-92	n/a	M. Brose
Small rodent trapping in subsaharan Africa	n/a (Field study)	n/a	R. Anderson
Further characterization of the Hartley Guinea Pig as a disease model for Lassa Fever	18-94	n/a	(b)(6); (b)(3):42
Protective pulmonary T cell responses to bacterial pathogens in mice	18-71 18-73 17-195	n/a	R. Anderson

B. Biosafety Training- Performed by Megan Brose, Rebecca Anderson, (b)(6)

Type of Training	Number of Sessions	Number of Employees Trained
New Employee	1	3
Annual Refresher Lab Biosafety	n/a	n/a
Select Agent-Initial	2	8
Select Agent- Refresher	n/a	n/a
Select Agent- Visitor	1	5
BSL-3 Laboratory Biosafety-Initial	1	6
Practical Training	2	4
BSL-4 Laboratory Biosafety-Initial	1	6
Suit Training	n/a	n/a
Checklist Training	n/a	n/a
BSL-4 Laboratory Biosafety-Refresher & SA Refresher	n/a	n/a
Laboratory Biosafety Support Staff-Initial	1	3
Laboratory Biosafety Support Staff-Refresher	n/a	n/a
Laboratory Biosafety Support Staff-Refresher & SA Refresher	n/a	n/a

C. Safety Audits and Inspections

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

D. Biological Incidents to Report
    a. Report of incident submitted to NIH OSP on 1/26/2024. Awaiting a response.

E. Other Issues
    a. None

F. DURC-IRE Reviews
    a. None

NIH RML Institutional Biosafety Committee Meeting

Agenda for March 21, 2024

Location: Virtual via Zoom/Building A (b)(6)

Old Business

A. Draft minutes of February 15, 2024 meeting

New Business

A. Committee Business
    1) PRD 23-103 (Amend) PI: Peterson
    2) Draft SOP-4-28-66 Prairie Dog Procedures in Level 4 Biocontainment-update anesthesia and cage change frequency

B. BSO report (Dr. Becky Anderson)
C. Occupational Safety & Health Manager report (Seth Cooley)
D. IRFBSM report (Cmdr. Megan Brose)
E. Responsible Official Report (Cmdr. Megan Brose)
F. Associate Director Report (Dr. Marshall Bloom)
G. Comments from around the room

Next Meeting: April 18, 2024 virtual via Zoom/Building A (b)(6)

PRD- Pathogen Registration Document
RD- Recombinant DNA Registration Document
SOP-Standard Operating Procedures
BSO-Biosafety Officer
IRFBSM-Integrated Research Facility Biosafety Manager

NIH RML Institutional Biosafety Committee Minutes

March 21, 2024 (1:00 PM – 1:45 PM)
Virtual via Zoom/ (b)(6)

Members Present:

☒Sue Priola, Chair	☐Larry Brouwer	☒Scott Kobayashi
☒Andrea Marzi, Vice-chair	☐Marcie Caldwell (EO)	☒Jamie Lovaglio
☒Becky Anderson, Biosafety Officer (BSO)	☒Chad Clancy	☒Alida Merritt (NA)
	☒Seth Cooley	☐Alexandra Scranton (NA)
☐Paul Beare	☒Kendal Cooper	☐Brian Vickrey
☐Sonja Best (EO)	☐Frank DeLeo (EO)	☒Clayton Winkler
☒Chris Bosio	☐Heinz Feldmann (EO)	☐Todd Wohlman (NA)
☐Marshall Bloom (EO)	☒Erik Hoover	
☒Megan Brose	☐Josh Kellar (EO)	

(EO) *ex officio*
(NA) Members who are non-affiliated with RML

Guests: (b)(6)
(b)(6)

Announcements

I. Bosio Lab concerns regarding a Select Agent exempt strain of *Francisella tularensis*.
   a. (b)(6) from the (b)(6) Lab presented data suggesting that a Select Agent Exempt strain of *F. tularensis* (SchuS4ΔclpB, a proposed vaccine strain) is not as attenuated as suggested in previous literature. This strain is currently approved for work at BSL-2/ABSL-2 in Canada, but data compiled from the (b)(6) Lab and presented by (b)(6) proposes that this strain is more lethal in mice than data recently published. All work with this strain of *F. tularensis* at RML was treated as a select agent and was performed in the BSL-3/ABSL-3 (b)(6) presented her concerns to the committee:
   b. Criteria for exemption as select agent and (at least in Canada) reclassification as BSL-2/ABSL-2 pathogen are not reproducible.
      i. SchuS4ΔclpB not as attenuated in Balb/c and C57Bl/6 mice as previously reported
      ii. Data showing superior protective efficacy reported for SchuS4ΔclpB was generated by comparing to vaccination with poorly efficacious strain of LVS
   c. Attenuation is not consistent.
      i. 2021 manuscript reported that 5 passages in chemically defined medium resulted in shift from 100% to 60% survival and further expansion in fermenter dropped survival to 40% following IN inoculation of 10^4 bacteria
   d. Straight forward complementation using standard, published protocols and equipment easily obtainable or readily available would result in fully virulent SchuS4
   e. With the assistance of the Responsible Official, we have asked for an opinion of our findings from the Federal Select Agent Program and we are suggesting SchuS4ΔclpB be reclassified as a select agent

Old Business

I. Review of Past IBC Meeting Minutes
    a. February 15, 2024 Meeting Minutes
        i. Minutes were unanimously approved with minor changes:
            1. Correct typos

New Business

I. Registration of Material (Potentially) Infectious for Humans, Plants or Animals
    a. PRD 23-103 – Peterson (Amendment)
        i. (b)(6) summarized the PRD. This is an amendment to PRD 23-103. This amendment adds the Orthobunyavirus Oropouche virus to the registration.
        ii. No animal work was proposed.
        iii. The committee discussed the dual-use and ePPP potential of the studies. The committee agreed that there were no dual-use or ePPP concerns.
        iv. Work with Oropouche virus is approved at BSL-2/ABSL-2. Care should be taken to prevent worker exposure to aerosols, such as working in a certified Class II BSC and using gasketed bucket covers when centrifuging infectious material.
        v. The committee approved the amendment to the registration, Clayton Winkler abstained from the vote.

II. Full Committee Review of Inactivation Procedures
    a. None.

III. Standard Operating Procedures
    a. Draft SOP# 4-28-66 Prairie Dog Procedures in Level 4 Biocontainment
        i. Jamie Lovaglio summarized the changes to the SOP. Changes were made to the way in which the prairie dogs are anesthetized and handled. Prairie dogs will be anesthetized in their home cage and kept sedated for transport to the procedure corridor. Another change was made to the timeframe of cage changes. Route of inoculation were also added to the SOP simulating sexual transmission studies.
            1. A committee member asked if there was any chance of occupational exposure during anesthetization in the prairie dogs' home cages. Jamie Lovaglio indicated that there was no chance of occupational exposure to isoflurane for the procedures outlined in the BSL-4 facility, and that the anesthetization procedures are performed on a downdraft table in BSL-4.

Reports

I. Biosafety Officer Report – Becky Anderson
    a. Becky Anderson presented the BSO report.
    b. Becky Anderson informed the committee that on March 25th, the new ERS system will go live. Beginning in April, the committee will see documents in the new format.

II. Occupational Safety and Health Manager Report – Seth Cooley
    a. Nothing to report.

III. IRF Biosafety Manager Report – Megan Brose
    a. Nothing to report.

IV. Responsible Official Report – Megan Brose
    a. Select Agent inspection week of March 11th will be a virtual inspection; there will be an in-person unannounced inspection of BSL-3 and BSL-4 in 2024.

V. Associate Director Report – Marshall Bloom
    a. Not present.

Around the Room

I. None

Other Issues

I. None

Next Meeting

I. April 18, 2024 virtual via Zoom/Building A (b)(6)

NIH RML Institutional Biosafety Committee Meeting

Biosafety Officer (BSO) Report

March 21, 2024

Business Conducted since the last IBC Meeting

A. BSO approvals
   a. None

B. Electronic business
   a. None

New business for IBC meeting

A. See agenda.

Biosafety Activities since the last IBC Meeting

A. Animal Study Protocols Review- Performed by Megan Brose, Rebecca Anderson (b)(6)

ASP Title	Associated PRD	Associated RD	Reviewer
Efficacy analysis of different COVID-19 vaccines administered via various approaches.	22-143	22-410	(b)(6)
Combined remdesivir/dexamethasone treatment in Nipah virus-infected Syrian hamsters	18-91	n/a	R. Anderson
Generation of Prion Infected Brain Material from Various Mouse and Prion Strains for Experimental Use	22-51 22-191	n/a	(b)(6)

B. Biosafety Training- Performed by Megan Brose, Rebecca Anderson, (b)(6)

Type of Training	Number of Sessions	Number of Employees Trained
New Employee	3	4
Annual Refresher Lab Biosafety	n/a	n/a
Select Agent-Initial	1	3
Select Agent- Refresher	n/a	n/a
Select Agent- Visitor	4	7
BSL-3 Laboratory Biosafety-Initial	1	3
Practical Training	2	2
BSL-4 Laboratory Biosafety-Initial	n/a	n/a
Suit Training	1	1
Checklist Training	1	3
BSL-4 Laboratory Biosafety-Refresher & SA Refresher	n/a	n/a
Laboratory Biosafety Support Staff-Initial	n/a	n/a
Laboratory Biosafety Support Staff-Refresher	n/a	n/a
Laboratory Biosafety Support Staff-Refresher & SA Refresher	n/a	n/a

C. Safety Audits and Inspections

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

D. Biological Incidents to Report
   a. Report of incident submitted to NIH OSP on 1/26/2024. Closed out 2/23/2024.

E. Other Issues
    a. None

F. DURC-IRE Reviews
    a. Best PRD 24-263
    b. Best RD 24-506

NIH RML Institutional Biosafety Committee Meeting

Agenda for April 18, 2024

Location: Virtual via Zoom/Building A (b)(6)

Old Business

A. Draft minutes of March 21, 2024 meeting

New Business

A. Committee Business
   1) PRD 23-253 (Amend) PI: Long
   2) 24-RML-001 (New) PI: Long
   3) 24-RML-002 (New) PI: Long
   4) RD 23-225 (New) PI: Peterson Reviewers: Sue Priola, Kendal Cooper
   5) Draft ABSL-3 Bunyavirus SOP (Update) add option for N95 or PAPR
   6) Draft BSL-3 (b)(6) (Update) add procedures for prion infected samples
   7) Draft BSL-3 (Update) add procedures for prion infected samples

B. BSO report (Dr. Becky Anderson)
C. Occupational Safety & Health Manager report (Seth Cooley)
D. IRFBSM report (Cmdr. Megan Brose)
E. Responsible Official Report (Cmdr. Megan Brose)
F. Associate Director Report (Dr. Marshall Bloom)
G. Comments from around the room

Next Meeting: May 16, 2024 virtual via Zoom/Building A (b)(6)

PRD- Pathogen Registration Document
RD- Recombinant DNA Registration Document
SOP-Standard Operating Procedures
BSO-Biosafety Officer
IRFBSM-Integrated Research Facility Biosafety Manager

NIH RML Institutional Biosafety Committee Minutes

April 18, 2024 (1:00 PM – 1:51 PM)
Virtual via Zoom/Building A (b)(6)

Members Present:

☒Sue Priola, Chair	☐Larry Brouwer	☒Scott Kobayashi
☐Andrea Marzi, Vice-chair	☐Marcie Caldwell (EO)	☐Jamie Lovaglio
☒Becky Anderson, Biosafety Officer (BSO)	☒Chad Clancy	☒Alida Merritt (NA)
	☒Seth Cooley	☐Alexandra Scranton (NA)
☐Paul Beare	☒Kendal Cooper	☐Brian Vickrey
☐Sonja Best (EO)	☐Frank DeLeo (EO)	☒Clayton Winkler
☒Chris Bosio	☐Heinz Feldmann (EO)	☒Todd Wohlman (NA)
☐Marshall Bloom (EO)	☒Erik Hoover	
☒Megan Brose	☐Josh Kellar (EO)	

(EO) *ex officio*
(NA) Members who are non-affiliated with RML

Guests: (b)(6)
(b)(6)
(b)(6)

Old Business

I. Review of Past IBC Meeting Minutes
   a. March 21, 2024 Meeting Minutes
      i. Minutes were unanimously approved with minor changes:
         1. Correct typos, Andrea Marzi should have been marked present.

New Business

I. Registration of Material (Potentially) Infectious for Humans, Plants or Animals
   i. PRD 23-253 – Long (Amendment) *Naegleria fowleri, Naegleria australiensis, Acanthamoeba spp.* (b)(6) summarized the PRD. This is an amendment to PRD 23-253. This amendment adds two species of Amoeba that may be present in environmental samples, this includes *Naegleria australiensis* and *Acanthamoeba spp. Naegleria australiensis* is also a "free-living" amoeba found in geothermal water sources (including mud from 25 to 43 degrees Celsius) capable of causing Primary amebic meningoencephalitis (PAM) in both humans and animals. The difference between *N. Fowleri* and *N. australiensis* is that *N. australiensis* has a lower pathogenic potential and requires a longer incubation time to develop neurological symptoms. *Acanthamoeba spp.* cause Granulomatous Amebic Encephalitis. The amoeba is a "free-living" amoeba found in soil and warm, often stagnant, fresh water including lakes, rivers, hot springs, marshes and sea water. It is a facultative parasite, causing infection and disease when entering the body through cuts, inhalation, or mucus membranes and generally infects individuals with compromised immune systems. Symptoms progress over several weeks and occur slower than PAM caused by *Naegleria fowleri*. Most natural cases of infection

are after recreational activities. The primary lab hazards are generation of aerosols and splashes to mucous membranes.

ii. No animal work was proposed.

iii. The committee discussed the dual-use and ePPP potential of the studies. The committee agreed that there were no dual-use or ePPP concerns.Work in the lab with *Naegleria fowleri* and *Acanthamoeba spp*. is approved at Biosafety Level 2, with Biosafety Level 3 practices (BSL-2/3). BSL-2/3 includes enhanced practices in a BSL-2 facility: fastidious adherence to proper microbiological techniques, decontaminating all potentially infectious waste prior to moving to MPW waste boxes for incineration, working in a BSC wearing proper PPE- double gloves, full eye protection and mucus membrane protection, tie-back gown, use of gasketed safety cups for centrifugation procedures, and minimizing the use of sharps, among other considerations to minimize worker exposure to aerosols, such as only working in a certified Class II BSC for any procedures that may generate aerosols.

iv. A committee member asked for more information to be added to clearly specify what would be co-cultured

v. A committee member suggested that the registration be updated to include that pathogenic amoeba species can infect animals, such as mice.

vi. The committee unanimously approved the amendment to the registration with the following changes:

1. Add more detail to specify what will be co-cultured.
2. Add that mice can be infected by the listed amoeba species.

b. 24-RML-001 – Long (New) *Naegleria fowleri, Naegleria australiensis, Acanthamoeba spp*. including Field work

i. (b)(6) summarized the new registration. This registration covers work with *Acanthamoeba spp*. and *Naegleria fowleri* (risk assessment for these amoeba described above). The registration also proposes field work by the (b)(6) lab in Yellowstone National Park in which they may identify these amoeba species. Researchers will conduct field work through direct collection with pre-determined water sampling sites. Water samples will be brought back to the lab for analysis.

ii. Within the field, researchers will collect samples with a “fishing pole” apparatus. While in the field, researchers will wear a face mask, sterile gloves, eye protections (safety glasses). For outdoor concerns, researchers will bring sunscreen, water food, and appropriate clothing including rubber boots. Teams will work in groups for “buddy system safety” for accidents, wildlife, and navigation purposes. Water samples will be packaged and shipped to RML for analysis.

iii. A committee member suggested that the registration be updated to include that pathogenic amoeba species can infect animals, such as mice.

iv. A member of the committee asked for clarification on how unregistered agents in field collected samples would be identified and dealt with. The BSO indicated that as soon as samples are identified to contain additional pathogens, amendments to the registration will be submitted. (b)(6) will also update the current registration with other known potential bacteria that are likely to be found in the samples.

v. No animal work was proposed.

vi. Work in the lab with *Naegleria fowleri* and *Acanthamoeba spp*. is approved at Biosafety Level 2, with Biosafety Level 3 practices (BSL-2/3). BSL-2/3 includes enhanced practices

in a BSL-2 facility: fastidious adherence to proper microbiological techniques, decontaminating all potentially infectious waste prior to moving to MPW waste boxes for incineration, working in a BSC wearing proper PPE- double gloves, full eye protection and mucus membrane protection, tie-back gown, use of gasketed safety cups for centrifugation procedures, and minimizing the use of sharps, among other considerations to minimize worker exposure to aerosols, such as only working in a certified Class II BSC for any procedures that may generate aerosols.

vii. The committee discussed the dual-use and ePPP potential of the studies. The committee agreed that there were no dual-use or ePPP concerns.

viii. The committee unanimously approved the registration with the following changes:

1. Add that mice can be infected by the listed amoeba species.
2. Update the registration with other bacteria that are likely to be found in the field samples.

c. 24-RML-002 – Long (New) *Burkholderia pseudomallei*

i. (b)(6) summarized the new PRD. The Long lab seeks to characterize *Burkholderia pseudomallei*. *B. pseudomallei* is a tier-1 Select Agent. Work with *B. pseudomallei* is approved at BSL-3/ABSL-3. This registration will be reviewed by the DURC-IRE prior to approval. Approval will also be pending CDC select agent program approval.

ii. A committee member asked for clarification on what kind of samples would be obtained. (b)(6) indicated that the samples would be collected from patient blood in Cambodia by a collaborator.

iii. A committee member pointed out a minor spelling error for ceftazidime.

iv. A committee member asked that the IRB number be included

v. The committee discussed the dual-use and ePPP potential of the studies. The committee agreed that there were no dual-use or ePPP concerns.

vi. *Burkholderia pseudomallei* is a Select Agent. All personnel with access to this agent must be authorized by the CDC Division of Regulatory Science and Compliance.

vii. All individuals listed on this registration and all those with access to the laboratory must be enrolled in and meet all health and security requirements of the NIH Biosurety Program and complete the RML BSL-3 and/or BSL-4 Biosafety Training Program.

viii. IBC approved validated inactivation procedure(s) must be followed when inactivating and removing samples to a lower containment level. Inactivation certificates are required for all samples that are inactivated.

ix. The committee unanimously approved the registration with the following changes pending DURC-IRE review and CDC Select Agent Program approval:

1. Correct spelling error for ceftazidime
2. Indicate IRB number for clinic samples.

II. Registration of Recombinant DNA Experiments

a. RD-23-225 – Peterson Recombinant California Serogroup viruses (Amendment)

i. Sue Priola summarized the amendment to the RD. The amendment is to add Oropouche virus to the registration.

ii. A committee member indicated that DURC question 7B be changed to “yes.”

iii. A committee member asked for clarification on which of the NIH Guidelines would be applicable to the amendment. Another committee member suggested that the applicable NIH Guidelines be made specific. The specific guidelines for this amendment are III-D-1-a; III-D-2-a, and III-E-1.

iv. A committee member pointed out a typo, "studies" should be "studied" in the Eukaryote Cell section.
v. A committee member asked if the registration should also indicate that it includes a pathogen. The committee discussed that this is the way the registrations transferred from HealthRx into the new ERS system. The BSOs noted that registrations can be returned to PIs to fill in this information which in some cases would allow us to deactivate redundant registrations. This registration could be updated to include the pathogen section.
vi. The amendment to the RD was approved, Clayton Winkler abstained, with the following changes:
    1. Change DURC Question 7B to "yes"
    2. Indicate the use of animal cells in the Eukaryote Cell section
    3. Indicate that the proposed work would include a pathogen.
    4. Correct typo in the Eukaryote Cell section for "studies"

III. Full Committee Review of Inactivation Procedures
    a. None.

IV. Standard Operating Procedures
    a. Draft ABSL-3 Bunyaviruses SOP (updates)
        i. Becky Anderson summarized the changes to the SOP. The PPE section was updated to allow for the option to use an N-95 mask or a PAPR. Minor changes were made to offer flexibility in PPE particularly for those performing health checks.
        ii. The committee unanimously approved the changes to the SOPs.
    b. Draft SOP (b)(6) Updates)
        i. Becky Anderson summarized the changes to the SOPs. Changes include updated disinfectant methods for handling prions.
        ii. A committee member indicated that samples could not be removed from BSL-3 to lower containment without the use of an approved inactivation method.
        iii. The committee unanimously approved the changes to the SOPs.
    c. Draft SOP (b)(6) (Updates)
        i. Becky Anderson summarized the changes to the SOPs. Changes include updated disinfectant methods for handling prions.
        ii. A committee member indicated that samples could not be removed from BSL-3 to lower containment without the use of an approved inactivation method.
        iii. The committee unanimously approved the changes to the SOPs.
    d.

Reports

I. Biosafety Officer Report – (b)(6)
    a. (b)(6) presented the BSO report.
II. Occupational Safety and Health Manager Report – Seth Cooley
    a. Nothing to report.
III. IRF Biosafety Manager Report – Megan Brose
    a. Nothing to report.
IV. Responsible Official Report – Megan Brose
    a. Select Agent inspection week of March 11th was a virtual inspection; there will be an in-person unannounced inspection of BSL-3 and BSL-4 in 2024.
V. Associate Director Report – Marshall Bloom

a. Not present.

Around the Room

I. None

Other Issues

I. None

Next Meeting

I. May 16th, 2024 virtual via Zoom/Building A (b)(6)

NIH RML Institutional Biosafety Committee Meeting

Biosafety Officer (BSO) Report

April 18, 2024

Business Conducted since the last IBC Meeting

A. BSO approvals
   a. None

B. Electronic business
   a. None

New business for IBC meeting

A. See agenda.

Biosafety Activities since the last IBC Meeting

A. Animal Study Protocols Review- Performed by Megan Brose, Rebecca Anderson, (b)(6)

ASP Title	Associated PRD	Associated RD	Reviewer
Innate immune regulation of Jamestown Canyon Virus (JCV) infection in mice	23-103 23-184	n/a	R. Anderson
Assessing the cross-protection of the VSV-LASV vaccine in the cynomolgus macaque model of Lassa virus infection	18-94 23-82	20-404	(b)(6); (b)(3):42 U.S.C. 262a(b)
Rapid protection of the VSV-based Bundibugyo virus vaccine in cynomolgus macaques	18-90 23-82	20-404	R. Anderson
Protective efficacy of VSV-based Bombali virus vaccine in ferrets.	18-90 23-82	20-404 21-407	(b)(6)

B. Biosafety Training- Performed by Megan Brose, Rebecca Anderson, (b)(6)

Type of Training	Number of Sessions	Number of Employees Trained
New Employee	2	2
Annual Refresher Lab Biosafety	n/a	n/a
Select Agent-Initial	2	5
Select Agent- Refresher	n/a	n/a
Select Agent- Visitor	n/a	n/a
BSL-3 Laboratory Biosafety-Initial	2	4
Practical Training	1	2
BSL-4 Laboratory Biosafety-Initial	2	4
Suit Training	1	2
Checklist Training	5	3
BSL-4 Laboratory Biosafety-Refresher & SA Refresher	n/a	n/a
Laboratory Biosafety Support Staff-Initial	n/a	n/a
Laboratory Biosafety Support Staff-Refresher	n/a	n/a
Laboratory Biosafety Support Staff-Refresher & SA Refresher	n/a	n/a
BSL-4 Medical Emergency Egress Training	2	34

C. Safety Audits and Inspections

Settlement Item 14: NIH agrees to provide a copy of safety audits and inspections to a local health officer or designee (list under each item, a-b, indicates audit or inspection submitted)

D. Biological Incidents to Report
    a. None

E. Other Issues
    a. NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules were updated, current date is April 2024. Email sent to committee.

F. DURC-IRE Reviews
    a. None