Boston University
Institutional Biosafety Committee (IBC)
May 21, 2024 Meeting Minutes
Location: Zoom and/or by phone
Start time: 12:00 PM End time: 12:52 PM

Members Present:	R. Ingalls, E. Muhlberger, X. Brown, T. Winters, R. Morales, N. Dey, S. Niemi, C Thurman, R. Timmerman, V. Britton, S. Ghosh
Guests Present:	K. Tuohey, G. Madico, A. Ahmad, A. Broos-Caldwell, P. Richmond, J. Wood, M. Fitzgerald, T. Killeen, C. Fernald
Staff Present	C. McGoff, L. Campbell

I. Review of April 23, 2024 IBC Meeting Minutes (R. Ingalls)
No concerns were voiced.
Motion: Approved
For: 11 Against: 0; Abstain: 0; Absent: 0

II. Chair's Report: Members were informed that R. Davey has been appointed the new Vice Chair of the IBC.

III. New Business:
A. IBC Office Updates: Members were informed that the IBC is updating its DURC/P3CO policy and will be reviewing it with the members of that subcommittee.
B. Review of Research Occupational Health Program (ROHP) Report and Environmental Health and Safety (EHS) Report: No incidents for discussion.
C. Other updates: S. Niemi announced he will retire in June 2024 and Colleen Thurman has been appointed the new ASC Director.

IV. Protocol Review

1. rDNA/Bhz – Annual Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2375	Robert Davey	Evaluation of treatments for high containment viruses using animal disease models.	4	4	BUMC
Primary Reviewer: Elke Muhlberger		Secondary Reviewer: Colleen Thurman			
Applicable NIH Guidelines: Sections III-D-1-c, III-D-2-a, III-D-4-a, III-D-4-b and Appendix B-IV-D.					

Meeting Comments: This BSL4/ABSL4 protocol continues to work on identification of inhibitor of high consequence viral pathogens and to study their usefulness as a treatment option in animal models. There are number of changes in this annual renewal specifically the use of NHPs, the use of recombinant viruses for the infection studies, and the use of nanoparticles delivered by a nebulizer for treatment. However, this is a well-written protocol that provides a detailed description of the biosafety-relevant procedures for the proposed work. Risk-mitigating procedures that ensure the safe handling of animals and sharps etc. in BSL4 containment are described (for example, clear workflows, disinfection after procedure, 2-person rule when required, avoidance of sharps whenever possible, and appropriate PPE). The animal procedures covered in this protocol correspond with approved NEIDL SOPs. It is clearly indicated which steps are performed by the PI's lab and which steps are performed by the animal core via the animal core IBC protocol. The following will be communicated to the PI:

- Personnel – Since the animal core will be handling material generated under this protocol, key personnel of the animal core and pathology core should be listed in the personnel section ([redacted], [redacted], [redacted], [redacted], [redacted], [redacted]).
- Use of recombinant virus. It is proposed to use recombinant viruses with altered host tropism. It should be clearly stated that generation of these viruses is covered by IBC protocols [redacted] or [redacted].

- DURC question. It is proposed to use recombinant rodent-adapted viruses. This falls into the following potential DURC category: Alters the host range or tropism of an agent or toxin. The PI should clarify if generation of these viruses was reviewed by the DURC committee (either for this protocol or for protocols [redacted] or [redacted]).
- Preparation of inoculum – to be consistent across different BSL4 animal IBC protocols, please revise as follows: "The virus stock used for infection will be pipetted into a sterile small trough. A blunt-ended oral gavage needle will be attached to the syringe, and the viral inoculum will be carefully and slowly drawn up. The syringe will be capped with a syringe cap, carefully wiped down with a paper towel soaked with 5% Microchem Plus and placed into a plastic bag. The plastic bags containing the syringes will be placed into a shatterproof, leak-proof container with a lid marked with a biohazard symbol and contents clearly stated and transported to the site of animal handling."
- Please clarify the use of recombinant material for treatment. Is there an SOP for use of a nebulizer? Is it always pre-exposure treatment at BSL-2? Are animal core personnel trained in this procedure? Which BSL-2 rooms will be used for the procedure? A more detailed explanation would be helpful. Also, if use of the nebulizer is strictly BSL-2, the PI may wish to remove it from the BSL-4 protocol.
- "All virus stocks will be obtained from the Biomolecule Production core (NEIDL), from BEI resources (ATCC) or the NEIDL Biological Agent Repository is through Dr. [redacted]. Is the highlighted statement still accurate?
- "Each procedure requires prior approval through the IBC before it can be used….". Please add that "BPHC also approves the inactivation procedures."
- "The vessel is completely immersed for at least 10 minutes contact time before material is retrieved from the dunk tank." The SOP (SAF-SOP-0023) states that the time is 15 minutes, so please change it accordingly for consistency.
- PPE section, 2. Should "Gasket blenders/homogenizers" be checked?
- IX. check other potentially infectious materials (NHP material)
- Hazardous Biological Agents section – Add recombinant viruses as source of viruses.
- Hazardous Biological Agents section – NHPs must be added to table (live animals with agent).
- Following details and clarifications have been provided by the ARS. Please use or add the information as appropriate.
  - VII. 3. 2. NHPs and larger rodent species, such as guinea pigs, are handled on a downdraft table instead of a BSC.
  - VII. 3. 4. If NHP cages need to be changed on study, they will be transferred during a scheduled sedation event. Normally, only pans are changed and grates cleaned while animals are out for scheduled study activities.
  - VII. 3. 6. For NHPs, most common mode of sedation is ketamine IM followed by isoflurane by mask as needed.
  - VII. 3. 12. Carcass handling: for larger animals, such as NHPs, they are usually autoclaved in large sharps containers with absorbent material at the bottom.
- Relevant SOPs for ARS work:
  - Receipt of NHPs WD-SOP-0098
  - "Procedures for Daily Husbandry, Care and Environmental Monitoring for NHPs in the NEIDL ABSL-2, -3, and -5 Laboratories (NSU-SOP-517).
  - "NHP Cage Changing Procedures in the ABSL-2 and -4 Laboratory" NSU-SOP-519
  - "Movement of NHPs within the ABSL-4 Laboratory" NSU-SOP-516
  - SAF-SOP-0168 "Autoclave Use Procedures in ABSL-2, -3 and -4 Laboratories"
  - NSU-SOP-503 Procedures for Inoculation and/or Administration of Substances to NHPs in the NEIDL ABSL-2, -3 and -4 Laboratories.
  - NSU-SOP-518 "Procedures for Sedation and Handling of NHPs in NEIDL ABSL-2, -3, and -4 Laboratories"
  - NSU-SOP-505 Procedures for NHP Blood Collection in NEIDL ABSL-2, -3 and -4 Laboratories
  - NSU-SOP-511 Clinical Chemistry Analysis using the VetScan VS2 and Piccolo Xpress Analyzers

- NSU-SOP-512 Hematology Analysis Using the VetScan HM5 Analyzer
- NSU-SOP-513 Coagulation Analysis using the VetScan VSPro Analyzer
- NSU-SOP-507 Procedures for Visual Observations, Clinical Examination and Body Weight and Temperature Measurement of NHPs in NEIDL ABSL-2, -3 and -4 Laboratories
- NSU-SOP-700 Procedures for Conducting Necropsies in the NEIDL ABSL-2, -3 ,and -4 Laboratories
- OPS-SOP-0313 Operation and Maintenance of Non-ducted Downdraft Tables in ABSL-2, -3, and -4 Laboratories.

Motion: Conditional Approval (Admin Review)	For: 11	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

2. rDNA/Bhz – Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2331	Robert Davey	Transfer of materials for storage at NEIDL	2	N/A	BUMC

Primary Reviewer: Sajal Ghosh	Secondary Reviewer: Tom Winters

Applicable NIH Guidelines: Section III-D-1-a, III-D-2-a, III-E-1.

Meeting Comments: This protocol is intended for the storage of various research reagents that are either rDNA materials or cell lines or inactivated biological samples. It also include storage of plasmids, cell lines, crisper, third generation lent virus, library, SIRNA libraries, fix cells and tissues. These materials are generated from PI's other protocols or from investigators outside of Boston University. In this submission new inactivated virus-infected cell lines have been added that are in accordance to approved inactivation procedures. Further, the protocol title has been modified to indicate specific storage location (NEIDL). Collection and storage procedures are clearly described. All are stored in sub 80°C freezers and are materials from BU and outside BU. Transfers are done in secondary containers. Inactivation of material is done using inactivation SOP's. BSL-2 level with blood-borne pathogen standard is evoked. The personal protective equipment is appropriate. No sharps are used. Liquid waste, solid waste, and disinfection are appropriate. The shipping of cryovials is done in shatter proved containers and boxes. Commercial third generation Lentivirus system with three plasmids is explained. Overall, biosafety risks have not changed in this submission.

BUA site Assessment: Biosafety cabinets are certified (not needed for this protocol), O-rings and safety cups are available for centrifuges. Freezers are hooked up to building alert system. Two members have taken the shipping biologicals training.

Motion: Approve	For: 11	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

3. rDNA/Bhz – Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
2591	Shawn Lyons	Regulation of Translation Initiation	2	N/A	BUMC

Primary Reviewer: Robin Ingalls	Secondary Reviewer: Xin Brown

Applicable NIH Guidelines: Sections III-D-1-a; III-D-2-a and Section III-E-1 and Appendix B-II-D

Meeting Comments: The goal of the project is to study translation initiation of mRNA in greater detail. In this protocol third generation lentiviral system will be used in addition to lipofectamine mediated transfection method. CRISPR/Cas9 will be used to knock out specific proteins or to add tags to the endogenous protein in human cell lines. Various chemicals will be used to inhibit translation. Cell extracts will be used for in vitro translation of RNA synthesized via T7-mediated in vitro transcription. Vesicular Stomatitis virus (VSV) has been used as model system to study translation initiation. Additionally they are using Human Parainfluenza virus 3 (HPIV3) to validate their VSV findings. This amendment add methods to insert additional translational regulatory elements to the RSV and VSV genome. They also will also generate replication incompetent glycoprotein-deleted rabies virus vector for gene delivery experiments. The following will be communicated to the PI:

- The detail of the construction of RSV, VSV and delta-G rabies virus needs to be removed from the rDNA section and added to the Laboratory procedure section. The rDNA section should only contain what recombinant virus you plan to use in the protocol.
- State briefly the purpose of use of delta-G rabies virus in your protocol.
- Provide updated biosafety cabinet certification date.
- The delta G rabies virus should be marked as “attenuated”.
- Since VSV (Indiana strain) can disease in humans, please mark it accordingly in the table.
- HeLa cells are just human cell lines. Please mark it accordingly.
- In the rDNA recombinant virus question, please only state what recombinant viruses will be used in this protocol . Please move the construction details to the laboratory procedures section.

Motion: Conditional Approval (Admin Review)	For: 11	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

4. rDNA/Bhz – Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
2397	Florian Douam	Host and viral determinants regulating Flaviviridae pathogenesis and immunogenicity	2	2	BUMC

Primary Reviewer: Rob Davey	Secondary Reviewer: Colleen Thurman

Applicable NIH Guidelines: Sections III-D-1-a, III-D-2-a, III-D-3-a, III-E-1; Appendix-B-II-D, Appendix G-II-B

Meeting Comments: The described work investigates molecular mechanisms by which host factors regulate infection by flaviviruses such as Yellow fever, Dengue, Zika and Hepatitis C. In this amendment, few non-flaviviruses, Respiratory syncytial virus and Influenza virus are added. These viruses have similar biological containment requirements to the flaviviruses. The amendment further adds the use of mosquitoes infected with virus to study infection of animal hosts. The work will look at interactions between viral proteins/RNA and how these host factors regulate innate immune responses and host tropism. Pathogenicity models using mice engrafted with human tissues is used to study virus spread in tissues and immunogenicity in vivo. Materials from animals are treated with formalin to inactivate the viruses. In this amendment changes are also made in virus genes that control pathogenicity. It is expected that such changes will likely attenuate the virus but will typically reduce pathogenicity, making the work unlikely to be DURC related. However, IBC will be notified if at any time the research produces or can reasonably produce previously unanticipated experimental effects, or if there is a potential for the research project to become DURC.
Mosquito work is performed in a specialized insectary laboratory that is screened to prevent mosquito escape. Mosquitos are infected with virus and dissected later on. Mice that were fed on by infected mosquitos are held in ABSL2 space after removal of mosquitoes. Plasmids encoding the genomes of Ross River Virus, Sindbis virus, Babanki virus, Barmah forest virus, Middelburg virus, Ndumu virus will be stored in a freezer but will not be used until further amendments are approved for work to develop recombinant virus systems. The processes to decontaminate materials are well documented and compatible with what is already approved. Fresh 10% bleach or 1% vesphene is used. Personnel will work with disposable labcoats, sleeve coverings and shoe coverings as well as N95 and other face protection as needed. Personnel are warned when Zika is being used by signage as it is of higher risk for exposure to pregnant women. Overall, the amendment adds new viruses that are handled with similar precautions to what was previously approved. Committee noted that the original mention of specific animal work rooms was not appropriate. But PI corrected those animal work spaces in a revision before this meeting. The following will be communicated to the PI:

- In the laboratory procedure section that describes ‘Experimental injections into mice’ tail vein injections are described. Please clarify if retro-orbital injections will also be done in this protocol as with the other ABSL IBC protocol of the PI.

Motion: Conditional Approval (Admin Review)	For: 11	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

V. List of Protocols reviewed by DMR (not discussed in the meeting

A list of protocols that were reviewed by DMR was displayed in the meeting