Boston University
Institutional Biosafety Committee (IBC)
July 16, 2024 Meeting Minutes
Location: Zoom and/or by phone
Start time: 12:00 PM End time: 1:44 PM

Members Present:	R. Ingalls, E. Muhlberger, R. Davey, I. Afasizheva, V. Gouon-Evans, W. Lu, P. Liu, T. Winters, R. Morales (joined 12:08), N. Dey, C Thurman, J. Keeney (joined 12:11), R. Timmerman, V. Britton (joined 12:05), S. Ghosh
Guests Present:	A. Ellis, A. Ahmad, J. Wood, P. Richmond, G. Madico, M. Fitzgerald, T. Killeen, C. Fernald
Staff Present:	C. McGoff, L. Campbell

I. Review of June 18, 2024 IBC Meeting Minutes

No concerns were voiced.

Motion: Approved

For: 12; Against: 0; Abstain: 1; Absent: 2

II. Member Training Session:

A. Presentation on Inactivation Procedures and Policies of BSL4 Viruses and Select Agents:
E. Muhlberger informed members on the BSL4 virus and select agent inactivation methods, workflow, timeline, and the challenges incurred along the way to the approval of the inactivation methods used.

III. New Business:

A. IBC Office Updates: Nothing to report

B. Research Occupational Health Program (ROHP) and Environmental Health and Safety (EHS) Report: Two (2) incidents from June 2024 report were presented to members for review.

IV. Protocol Review

1. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1888	[redacted]	Host Response to Filovirus and Henipavirus Infections	4	N/A	BUMC

Primary Reviewer: Rob Davey	Secondary Reviewer: Robin Ingalls
Applicable NIH Guidelines: Section III-D-1-c, III-D-1A	

Meeting Comments: The aim of this project is to study how cells react to filovirus, bunyavirus and henipavirus infection and which cellular pathways involved in the antiviral defense are blocked or activated by the infection In this 3-year renewal no new work has been added, only personnel training records have been updated and previous amendments have been reorganized to make them part of total project objectives. Other relevant aspects of the work are recombinant work using mutated virus genomes that incorporate fluorescent proteins and sequence changes in genes and promoter regions. This is built on work of the PI and others and is directed at understanding virus replication mechanism so that new therapies can be developed. As part of the recombinant work, some gene swapping experiments will be performed between Ebola virus and other filoviruses only. All work is performed in the BSL4 and any elevation of pathogenicity or tropism is not expected as the viruses being used are already highly pathogenic and have broad tropism. A list of all recombinant viruses will be made available to NEIDL EHS. Dimethyl sulphate (DMS) is used in this work to study RNA structure. Because of the toxic nature of this chemical, extensive PPE is described in the form of chemically resistant gloves, sleeve covers and apron to be used over the BSL4 suit which are appropriate precautions. Disposal will be through either mixing samples with TRIzol to inactivate the virus and passing the mixture out of the BSL4 lab for further processing or by mixing DMS directly with Microchem which would render the virus inactivated and allow its removal from the BSL4 laboratory and then disposal as a hazardous chemical. All viruses are inactivated through validated procedures that are approved by this IBC, BPHC and CDC. The protocol remains well written and the work appears to be performed appropriately. The following will be communicated to the PI:

- The title should be updated to include bunyaviruses.
- Please remove [redacted] from shared Laboratory locations on NEIDL level 2 as he has left BU. Add Nancy Sullivan as she now has staff working in the BSL4 in these spaces.
- In the description of CCHFV in the laboratory procedure section, it is stated that "Case fatality rates range between 1040%". This should be changed to "Case fatality rates range between 10 and 40%."
- In the Section VIII.5, BSC serial number 94341 should be 95341.

BUA Site Assessment: All personnel trainings are current. All biosafety cabinets are duly certified. PPE use in BSL4 suits is appropriate and is regularly monitored.

Motion: Conditional Approval (Admin Review)	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

2. rDNA/Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2648	[redacted]	Elucidating the contribution of lung epithelial gain of function toxicity to AATD disease pathogenesis; Mechanistic studies of the genetic contribution of desmoplakin to pulmonary fibrosis in alveolar type 2 cells; Personalized therapy for AATD-associated liver disease via IPS modeling	2	2	BUMC

Primary Reviewer: Elke Muhlberger	Secondary Reviewer: Colleen Thurman

Applicable NIH Guidelines: November 2013. Appendix G-II-B-1: Standard Microbiological Practices (BL2). Section III-D-1: Experiments Using Risk Group 2, Risk Group 3, Risk Group 4, or Restricted Agents as Host-Vector Systems. Section III-D-4: Experiments Involving Whole Animals. Appendix B-II: Risk Group 2 (RG2) Agents. Appendix Q: Physical and Biological Containment for Recombinant DNA or Synthetic Nucleic Acid Molecule Research Involving Animals.

Meeting Comments: The goal of this protocol is to delineate the mechanisms underlying genetic liver and lung diseases using stem cell models. PI is a member of the stem cell laboratory of the Boston University. They use stem cells derived from patients with genetic diseases or in some cases from healthy individuals as well as using NIH-approved human embryonic stem lines to model features of disease that occur at the cellular level. Viral vectors such as lentivirus or AAV or CRISPR and variants of CRISPR are used at times to intentionally alter the expression of genes relevant to disease processes in order to understand their contribution to cellular homeostasis or disease. They complement their stem cell studies with animal models to investigate findings in vivo. This is a well-written protocol that provides a detailed description of the biosafety-relevant procedures for the proposed work. Procedures that ensure the safe handling of tamoxifen and isoflurane are described. The used systems and approaches are well described. The following will be communicated to the PI:

- Lab Inspection noted additional personnel working in the protocol may need to be added in the personnel list.
- Laboratory procedure and rDNA section state that lentivirus vectors are used in in vitro and in vivo experiments, but lentivirus is not listed in the hazardous biological agent list. Please lentivirus in this list and respond to all associated questions including animal work.
- Generally back fastening gowns and respirator are only used at ABSL3 or if there is no BSC used. Your proposed animal work would not need them.
- VIII. 6. Sharps should be closed and autoclaved when 75% full, right?
- VIII. 11. Please indicate that secondary container is leakproof and shatter proof.
- Add HepG2 cell in this list as well if you are using it.

- In rDNA eukaryotic experiments, the recombinant virus question is for creation of any recombinant infectious replication competent virus (not for viral vectors).
- IACUC approved 12/2023. AAV is in the protocol, but not lentivirus.

BUA Site Assessment: All trainings are current. Two additional personnel need to be added to the protocol. Biosafety cabinets are duly certified. A human cell line HepG2 cell line is used in the lab and it should be added to part IX section A of the protocol.

Motion: Conditional Approval (Admin Review)	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

3. Bhz –New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2657	[redacted]	Center for Translation Neuroscience Imaging Core	2	2	BUMC

Primary Reviewer: Robin Ingalls	Secondary Reviewer: Ron Morales Additional Reviewer: Colleen Thurman

Applicable NIH Guidelines: N/A

Meeting Comments: This protocol is for a new MRI core facility for imaging of both in vivo (mice, rats) and ex vivo (including fresh and fixed human samples, and fixed NHP tissues) samples. The in vivo imaging will be performed on mice or rats with no pathogen exposure. No in vivo scans will be done on NHPs. Anesthesia (isoflurane, oxygen tanks) will be available for live animal imaging. Unfixed tissues will be placed in a sealed container during the scan. The committee noted that this new MRI core facility is adjacent to another MRI facility that is exclusively used for live NHP work done by another PI. It was discussed the with the help of the IBC office PI will develop a Core Facility User form which MRI core PI should use to record users, type of materials to be scanned, and IBC approval information for the user. ROHP also clarified that users of MRI facility should be made aware not to have any metallic object on them that can be attracted by a magnet. The following will be communicated to the PI:

- Should this be ABSL-1? Or will they allow infected live animals? This is unclear because the layman's description states animals will not have any pathogen exposure, but the table of Biohazardous Agents states "any BSL2 pathogen" – so is that referring to infected tissues only? Please clarify. Ideally the protocol should be BSL2/ABSL1.
- The disposable scrubs, shoe covers, and double gloves seem to excessive PPE for this protocol. Please clarify or specify conditions when those will be used.
- Liquid waste should not be treated with 10% bleach but have bleach added to a final concentration of 10%.
- Please state that the 3T MRI located in [redacted] as described in question 2 is used for NHPs and humans and not part of this IBC approval. Refer which lab or which PI is involved in its use.
- VII.3. Briefly describe or refer to numbers of titles for core SOPs for PPE and safety procedures.
- VIII. 4. Describe or reference PPE for in vivo imaging (mice, rats, NHPs) if required by core. If that is described in users' IBC submissions, state that.
- Please request EHS to get a spill kit.
- Describe circumstances or types of samples that will require different disinfectants listed.
- IX. Section B. If unfixed primate tissue or primates are scanned, they should probably go in this section.
- Please clarify whether unfixed human tissues are put in sealed container in the MRI prep area or the customer PI put them in sealed container before bringing them to the core. If it is the first, the prep area decontamination procedure needs to be clearly mentioned.
- Mention what information the customer PI would be required to provide in the core user form.

BUA Site Assessment: All trainings are current. Add PPE: Safety glasses, Goggles. Remove PPE: Shoe cover, Double gloves. PPE for live animal work should also be mentioned in the protocol. No fume hoods or safety showers are available in the lab space. They should be installed in the space. The new user form for the core facility should be

created soon so that the users can use this core facility safely. While working with fresh NHP and human tissues ex vivo, the lab should ensure availability of a leak proof sealed container for the samples to be placed and imaged. Users from other labs should also bring their own sealed containers. This point must be emphasized in the new core user registration form. When there is liquid waste, the lab decontaminate them with bleach (final conc. 10%) and dump in Dr. [redacted] lab sink. The lab also stores its mouse samples in Dr. [redacted] lab.					
Motion: Conditional Approval (Admin Review)	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

4. rDNA/Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2658	[redacted]	Targeting gene expression in the mouse brain	2	2	BUMC

Primary Reviewer: Inna Afasizheva	Secondary Reviewer: M. Mazur
Applicable NIH Guidelines: Section II-D-4-a; Appendix B-V:	

Meeting Comments: This study aims to understand how substance use disorders (such as use of cocaine, alcohol, etc.) affects gene expression in brain in a persistent manner and often associated with symptom relapse. They plan to mouse model to study how dietary methionine affects histone methylation and chromatin structure. They will use AAV vectors to alter or knock-down specific genes of interest in different parts of the mouse brain and will try to correlate their findings with substance use disorder cases in humans. All viral vectors will be purchased commercially which will be aliquoted into vials and stored frozen until use. Viral particles are replication incompetent. All the animal work will be done in animal facilities in the W building. Few statements in the original submission was unclear and PI was contacted by the IBC office before the meeting to clarify those sections. This revised application was reviewed in the meeting. The following will be communicated to the PI:

- Please include response to PI's Overall experience, where and when and related experience question.
- Provide brief clarification about how the virus vector is made by the providers (just to know if helper adenovirus was used for the AAV stock preparation; protocol would be BSL2 in that case. If not, protocol stays as BSL1/ABSL1.
- Describe what are the downstream processes after brain surgery. What materials are collected from mice and what is done with them to complete the objective of the protocol? What is done with the unused AAV stock.
- Check animal inoculation.
- Remove shoe cover and head cover from the animal PPE section.
- Since biosafety cabinet (BSC) is being used for aliquoting AAV stock, please check Yes to BSC use question and complete other info on the BSC.

BUA Site Assessment: Biosafety cabinet is duly certified. Animal inoculation procedure needs to be checked. All trainings are current. The lab needs to add lab [redacted] to the protocol. The lab needs to elaborate the experiments in the protocol. They will conduct some behavioral studies on mice and will do tissue sectioning of mice brains. There is no need to autoclave the sharps container before their disposal into the Biowaste box. Ready to use AAVs are procured from the vendors.

Motion: Conditional Approval (Admin Review)	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent: 0