Boston University
Institutional Biosafety Committee (IBC)
August 15, 2023 Meeting Minutes
Location: Zoom and/or by phone
Start time: 12:00 PM End time: 2:01 PM

Members Present:	R. Ingalls, B. Slack, E. Muhlberger, I. Afasizheva, R. Davey, W. Lu, X. Brown, T. Winters, R. Morales, C. Thurman, S. Niemi, J. Keeney, R. Timmerman, V. Britton (Left 1:03 PM), N. Dey, S. Ghosh
Guests Present:	A. Ahmad, T. Killeen, J. Wood
Staff Present:	C. McGoff, L. Campbell

I. Review of July 18, 2023 IBC Meeting Minutes (R. Ingalls)
No concerns were voiced.
Motion: Approve
For: 16; Against: 0; Abstain: 0; Absent: 0

II. Chair Report: Chair had no IBC-related updates.

III. New Business:

A. IBC Office Updates: S. Ghosh reminded members of the IBC review process followed for BSL3 and BSL4 protocols. Members were also informed that the Laboratory Acquired Infectious Disease (LAI) subcommittee met earlier this month to review all new biological agents added to IBC protocols.
B. Incident Report: Nothing to report.
C. Review of Research Occupational Health Program (ROHP) Report: Nothing to report.
D. Environmental Health and Safety (EHS) Report: Nothing to report.

IV. Protocol Review

1. Bhz – Annual Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2548	Anthony Griffiths	Inactivation of SARS-CoV-2 using ultraviolet light	3	N/A	BUMC

Primary Reviewer: Elke Muhlberger	Secondary Reviewer: Sajal Ghosh
Applicable NIH Guidelines: N/A	

Meeting Comments: In this protocol the PI uses EHS-approved specialized instrument to generate aerosol with SARS-CoV-2 in BSL2 containment but the work is done entirely in Class III biosafety cabinet which is tightly secured in all direction. The protocol includes numerous SOP that are followed for the purpose of risk alleviation. They nebulize the virus aerosol in the chamber and then expose them to UV light to test if such exposure can kill the virus on the surface. The current submission is an annual renewal of the protocol where the only change made was to remove one personnel. The committee noted that one personnel listed in the protocol is an EHS member and asked if that is appropriate. IBC office clarified that this EHS personnel is also highly experienced in BSL3 research work and have recused herself from the EHS-related review of this protocol. The following will be communicated to the PI:

- Please complete the two additional questions at the bottom of the DURC section.
- Update BSC certification dates.
- VIII.8. Please add that 70% ethanol is used for cleaning sensitive equipment. It is not an approved disinfectant for SARS-CoV-2.

The committee recommended that annual renewal of this protocol will not be required until its next 3-year renewal. During this intervening time PI may submit amendments as needed whose review path will be determined based on the nature of the amendment.

Motion: Conditional Approval (Administrative Review)	For: 16	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

2. rDNA/Bhz – Annual Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1888	Elke Muhlberger	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 and Henipavirus infection and which cellular pathways involved in the antiviral defense are blocked or activated by filoviruses and Henipaviruses. In this annual renewal changes included are addition of CCHFV and Lassa viruses, both of which are BSL4 agents that have similar pathogenic outcomes as to Ebola virus. There is no difference in the way each will be handled.
Also in this update, protocols for inactivation have been expanded to include new approaches that were recently validated by the PI's group. A major addition is the use of dimethyl sulfate (DMS) for the use in studying RNA structure of viruses. Because DMS is toxic by oral, inhalation, skin and eye exposure, extensive PPE is described in the form of chemically resistant gloves, sleeve covers and apron to be used over the BSL4 suit. Disposal will be through mixing samples with TRIzol or Microchem to inactivate the virus and then to allow its removal from the BSL4 laboratory and subsequent disposal as a hazardous chemical. Since fume hoods are not available in BSL4 suits, the DMS work is being done in biosafety cabinet following specially written SOP in consultation with NEIDL EHS. IBC also have received independent confirmation of this SOP from the NEIDL EHS. The protocol remains well written from the aspects of personnel training and detailed description of the work being performed.

PI recused herself from voting.

Motion: Approve	For: 15	Recuse: 1	Against: 0	Abstain: 0	Absent: 0

3. rDNA/Bhz – New Project

BUA	(PI)	Title	BSL	ABSL	Campus
2616	Nancy Sullivan	Role of viral glycoproteins in virus pathogenesis	2	N/A	BUMC

Primary Reviewer: Rob Davey	Secondary Reviewer: Sajal Ghosh

Applicable NIH Guidelines: Sections III-D-1-a, III-D-2-a

Meeting Comments: The goal of this new protocol is to study the role of viral glycoproteins in the attachment and internalization of the virus and viral genome in the host cells. They are particularly interested in studying the viruses that are associated with deadly diseases. However, instead of growing the deadly viruses in the lab (which require BSL3 and BSL4 containment), they want to use lentivirus or vesiculostomatitis virus (VSV) backbone-pseudotyped viruses that will express glycoproteins from filoviruses, arenaviruses, paramyxoviruses, coronaviruses, alphaviruses or influenza viruses. For making the lentivirus pseudotypes, they will transfect cells with lentivirus backbone devoid of env glycoprotein and most of the other proteins (gag, pol, rev, tat) but containing a reporter gene. For the VSV pseudotypes BSR-T7 or HEK293T/T7 cells will be transfected with full-length antigenome VSV DNA clone containing heterologous glycoprotein along with expression plasmids for VSV N, P and L proteins that are required for virus replication. In some cases, transfection will be done in other permissive cell lines and T7 polymerase will be provided through infection with vaccinia virus that expresses T7. Prepared viruses will be quantified by plaque assay and used as stock. These viruses will then be treated with test antibodies or monoclonal antibodies, NHP or human serum to test neutralization potential of those serum during cell culture infection. They will use various glycoprotein expression plasmids from their previous studies or will be purchased commercially for making the pseudotyped viruses. Lentiviruses to be used are 3rd generation vectors. The committee requested that for risk evaluation, the origin of the VSV strain and the name of the vaccinia virus be stated. Cell culture work will be done in class II BSCs using appropriate PPE such as lab coat, gloves, and eye protection. However, because of the tropism of Nipah virus glycoprotein towards brain cells, it was suggested that the work with Nipah virus glycoprotein-pseudoviruses be done in BSL2+ containment. Liquid waste generated will be disinfected by adding 10% bleach (final) for 30 minutes before disposal down the sink. The following will be communicated to the PI:

- To be consistent, please provide Dr. [redacted]'s experience description in greater detail, as is done for Dr. [redacted].
- Because Nipah F+G glycoproteins have tropism towards brain cells, the committee recommended that VSV-pseudotyped viruses expressing Nipah F+G glycoproteins or G alone should be used in BSL2+ or higher containment level. Please clarify and modify the application appropriately (recommendation is to add N95 and faceshield and restrict access to space to others when being worked on Nipah glycoprotein pseudotypes, along with other standard BSL2 precautions).
- VIII.5. Correct SterilGrad to SterilGard.
- VIII.8. Should be 10% freshly made bleach.
- VIII.10. In the statement of where viruses are stored in plastic tubes, it is recommended to add that aliquots of virus be stored in plug cap or o-ring sealed tubes to prevent leakage.
- VIII.11. For transportation of virus stocks, please indicate a shatterproof secondary contain will be used.
- Section A. Clarify if the VSV Indiana strain is the weakly pathogenic lab adapted strain or the original strain.
- State here or in the rDNA section that the lentivirus system is a 3rd generation vector system.
- Please indicate the vaccinia virus strain (vTF7-3) and identify its origin (Western Reserve or modified Ankara, etc.) so that ROHP can evaluate the need for vaccination of the research personnel.
- Check all boxes in the agreement policy.

BUA Site Assessment: Room [redacted] should also be added. Biosafety cabinets are duly certified. Lab is appropriately set for the described work.

Motion: Conditional Approval (Administrative Review)	For: 16	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

4. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1957	Vyacheslav Labunskyy	Molecular mechanisms of translational regulation in aging	2	N/A	BUMC

Primary Reviewer: Barbara Slack	Secondary Reviewer: Weining Lu

Applicable NIH Guidelines: Section III-F-8

Meeting Comments: The goal of this protocol is to characterize molecular mechanisms of aging, and role of iron and heme homeostasis in aging. The models they use for their work include *S. cerevisiae*, *C. elegans*, mouse embryonic fibroblasts, and primary human skin fibroblasts. They use ribosome profiling and next generation sequencing to analyze transcriptional and translational changes that occur in yeast cells with aging; identify genes that are translationally regulated in response to iron deficiency in wild-type yeast and deletion mutants. They will use live-cell microscopy using fluorescent protein reporters and microfluidic technologies to track heme levels and cellular changes with aging in yeast and in normal and mutant *C. elegans.* Protocol proposes analysis of gene expression and protein translation in specific gene knockout mouse embryonic fibroblasts and human skin fibroblasts lacking the mammalian TIS11 homolog using RNA-Seq and ribosome profiling. PPE used appear appropriate. However, it was not clear what would be the source of TIS 11 deleted primary normal human dermal fibroblasts or the mouse knockouts. The following will be communicated to the PI:

- Section III.1- Please provide experience for Dr. [redacted] (who will assist with training to two other lab members).
- Section III.2- No LST dates for Dr. [redacted].
- Section III.3- some ROHP clearance dates are missing.
- Section VII.3- How will the TIS11 knock-out human primary dermal cells and mouse TTP-KO embryonic fibroblasts be obtained/generated?
- Section VIII.2- Engineering controls including use of centrifuges with sealed rotors (plasmid propagation in bacteria); HEPA and hydrophobic protection for vacuum line (cell culture) should be added/checked.

- Section IX. Primary normal human dermal fibroblasts from a commercial vendor will be used, so "Other potentially infectious materials" should be checked.

BUA Site Assessment: They have not planned the experiment on how to make TIS11 knock out human primary dermal fibroblasts, although MEFs from knockout mouse will be obtained from collaborators. PPE used are adequate and two biosafety cabinets in the lab are duly certified.

Motion: Conditional Approval (Administrative Review)	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

5. rDNA/Bhz – Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1399	Maria Dominguez	Control of embryonic development by CK2: CK2 as a core Wnt/beta-catenin component Effect of CK2 Dysregulation on Heart Morphogenesis Cardiac proliferation: Role of Protein Kinase CK2 Characterization of CSNK2A1 variants in Okur-Chung Neurodevelopmental Syndrome	2	1+	BUMC

Primary Reviewer: Inna Afasizheva	Secondary Reviewer: Steve Niemi

Applicable NIH Guidelines: Section III-D-2-a, Appendix B-II-D, G-II-B, Section III-D-4

Meeting Comments: The goal of this protocol is to study Wnt signalling pathways that are essential for embryonic development and homeostasis. Project focuses on two kinases (CK2 and GSK3) that are regulated by Wnt. Experiments are designed to study the mechanism of CK2/GSK3 action in Wnt signaling by activation of the transcription of beta-catenin. These are done by using kinase inhibitors including chemicals, induced protein expression and siRNA/shRNA for blocking Wnt signaling. All experiments are performed on Xenopus model. Laboratory procedures include molecular cloning using prokaryotic vectors and *E.coli* strains INVF and DH5. Plasmids will be utilized in Xenopus frog embryos and oocytes. Animal protocol is approved but needs update. PI is the only personnel listed in the protocol. The committee enquired whether any animal/human cell lines described in the previous renewal are still stored in the lab. The committee also recommended that the ABSL1+ designation be removed. The following will be communicated to the PI:

- Since the lab has been moved to [redacted], please add this room to the location list. Keep X-building lab location as well if any biological material is still being stored there.
- Please clarify if any of the human and non-human primate cells line listed in previous approval of this protocol are being stored or are destroyed. If so, the protocol no longer requires BSL2 containment and may be changed to BSL1 as the current work is entirely on Xenopus model.
- Please change the ABSL status to ABSL1 (not ABSL1+).
- Update Animal protocol approval date in the rDNA/animal experiments section.

BUA Site Assessment: Not completed yet.

Motion: Conditional Approval (Administrative Review)	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

6. rDNA/Bhz – Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2389	Matthew Kulke	Cancer and Hematology Clinical Research Program and Translational Research Core	2	N/A	BUMC

Primary Reviewer: Xin Brown	Secondary Reviewer: Jim Keeney

Applicable NIH Guidelines: Section III-E-1

Meeting Comments: The protocol essentially is an umbrella protocol that includes at least 90 IRB protocols related to Cancer and Hematology Clinical Research Program and Translational Research Core protocols, so that patient

specimen from these IRB protocols can be collected and stored. These samples will either be analyzed in the central lab [redacted], [redacted], or be shipped to sponsor's lab. Another goal is also to create and maintain a repository of human blood, tissue, and microbiome material (oral, nasal and stool samples). As part of one particular IRB protocol, they will also characterize human primary T cells to define functional properties of chimeric antigen receptor (CAR) T-cells from newly diagnosed multiple myeloma cases. CAR T-cells will be generated from primary T cells using lentiviral or retroviral vectors. DNA and protein from these cells will be analyzed using electrophoresis method, mRNA will be analyzed using qRT-PCR, and cell surface antigens will be analyzed using FACS. Safety measures for both components are described clearly. The following will be communicated to the PI:

- The PI must have updated rDNA/IBC Policy training for the approval of the protocol.
- As stated in the IBC training requirement document, all members of a protocol involving rDNA work must also complete rDNA/IBC policy training. Personnel those who do not enter or work inside the wet research lab, may be excused from this requirement.
- Provide experience of [redacted]. If all members other than [redacted] also are involved in collecting clinical samples, the response to Infectious Agents question should be "experienced" for all. Please clarify what exactly are their role in the protocol.
- Please state clearly in the laboratory procedures section which individuals will be doing the rDNA work.
- Section VIII.1. Uncheck 'Animal Inoculation'.
- Section VIII.5. Update biosafety cabinet certification date.
- Section A. Under Hazardous Biological Agents, remove DH5-alpha and plasmids from the list. For the 'IRB for agent' question leave as blank instead of 'pending'.
- Section F. None of the chemical listed on are high hazard. They can be deleted. First delete all the text, then save. Then go back to Section IX and uncheck High Hazard Chemicals.
- Section H: The protocol include significant prokaryotic rDNA work (cloning, transformation, plasmid preparation, etc.). The prokaryotic experiment section (host-vector-donor) must be completed.
- Applicable NIH guidelines should be changed to 'Sections III-D-1-a, III-D-2-a and III-E-1.'

BUA Site Assessment: Not completed yet.

Motion: Conditional Approval (Administrative Review)	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

7. 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: Robin Ingalls	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: This protocol investigates how members of the Flaviviridae family such as Hepatitis C Virus, Dengue virus, West Nile Virus or Zika virus interact with their host and vectors, and how these interactions regulate virus replication, cellular tropism, host range, disease and immune response. They also investigate how immunodeficiency, such as the one induced upon HIV-1 infection, can compromise these interactions and immunoregulation. In this amendment they are adding commercially purchased human fetal tissues (BSL2) from elective abortions and survival surgery to implant it into mice. IRB approval is not required for the use of discarded fetal tissues but the committee recommended that PI provide detail information about the source of these fetal tissues and donor consents. The amendment also include removal of one personnel and addition of new research space. It was noted that PI's IACUC application has not been updated yet to include implantation of human fetal tissues into the mice. The following will be communicated to the PI:

The committee acknowledges that use of deidentified, discarded tissue is IRB exempt. However, as research that utilizes fetal tissue can be controversial, the committee recommends inclusion of documentation of what PI is

receiving from the company also the PI states very clearly in the application about consent from donors, etc. IBC office may be able to help in uploading the document in RIMS, if needed.

- IV. Please leave [redacted] vivarium space as "[redacted]vivarium" rather than specifying suites. [redacted] is still being used, but [redacted] isn't.
- VII. 2.3.14 Microchem isn't an appropriate surgical disinfectant to clean the animal's skin. Povidone iodine or dilute chlorhexidine should be used along with isopropyl alcohol. Sterile (autoclaved) packs should be used every 5 mice if >5 mice are having surgery in a day. Glass bead sterilizers may be used in between mice up to 5 animals per IACUC policy. It is noted that survival surgery is not described in the approved IACUC protocols yet.
- VII. 3.A. The ABSL2+ work in Room [redacted] with HIV-1 in particular (a blood borne pathogen) does not require N-95. Work with other respiratory pathogen may require N-95. Please clarify this in the text.
- VII 3. C. 70% ethanol is not a good disinfectant, so recommend Microchem as primary disinfectant for instruments with ethanol to follow to remove residue.
- VII. 3. C. 2.3.1 [redacted] is no longer being used. Please broaden to include any [redacted] vivarium ABSL2 space in case of change in space allocation.
- VIII. 4. Are N95s being used? All animals are handled in a BSC. They are not readily available at the PPE station, nor necessary for bloodborne pathogen work in a BSC.
- IX. PROTO[redacted] approved through 01/12/2024; PROTO[redacted] approved through 6/13/2026

Motion: Conditional Approval (Administrative Review)	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

8. rDNA/Bhz – Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
2332	Anthony Griffiths	Investigations of negative-strand virus and alphaherpesvirus biology	2	N/A	BUMC

Primary Reviewer: John Connor	Secondary Reviewer: Robin Ingalls

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

Meeting Comments: The goal of this protocol is to study molecular pathogenesis of viruses that causes severe or fatal human disease such as herpes viruses or filoviruses with special interest to understand how these viruses replicate in and interact with host cells. In this amendment they are adding Semliki Forest Virus-based hybrid pseudo-alpha virus platform to study virus replication and transcription. In these hybrid viruses the structural protein coding genes have been replaced by reporter genes and structural gene of the test virus. These construct are cotransfected with other viral genes of interest to create infectious but non-replicating virus-like particles (VLPs). The finished VLPs will not be generated at BU but instead will be provided ready for use by a commercial company. No concerns were noted.

Motion: Approve	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent: 1