Boston University
Institutional Biosafety Committee (IBC)
November 16, 2021 Meeting Minutes
Location: Zoom and/or by phone
Start time: 12:00 PM End time: 1:29 PM

Members Present:	C. Abraham, B. Slack, E. Muhlberger, I. Afasizheva, R. Davey, E. Loechler (Joined 12:50 PM), R. Morales, T. Winters, C. Thurman, V. Britton (Joined 12:05 PM), S. Niemi, J. Keeney, R. W. Timmerman, J. Barton (Joined 12:06 PM), S. Ghosh
Guests Present:	G. Madico, P. Richmond, A. Ahmad, J. Davis, T. Killeen, M. Fitzgerald, J. Wood
Staff Present:	S. Ghosh, L. Campbell, C. McGoff

I. Review of October 19, 2021 IBC Meeting Minutes

No comments or questions were voiced.
Motion: Approve
For: 13; Abstain: 0; Absent: 2

II. New Business

Dr. S. Niemi, the new Animal Science Center Director, was introduced as a new IBC member.

A. **Review of Training Requirement and SOPs for laboratories using BSL2 with BSL3 practices**
A revised BSL2+ laboratory practice guidance document created by the EHS was sent out to the committee members before the meeting for review. This document provides guidelines which needs to be followed when developing BSL2+ protocols. It will be made available on the EHS and IBC websites. In response to a question from one member on whether the guidance document includes a checklist that members could use when reviewing protocols, the SQAP Assistant Director informed members that an IBC checklist is being developed that would aid reviewers in reviewing IBC protocols.

B. **Safety & Quality Assurance Program (SQAP) Report**
Committee was informed that the IBC office is working with RIMS to ensure better communications to PIs and on internal processes to ensure that there are no pending protocols that may need further attention, such as protocols with requested revisions following IBC review that have not been responded to by the PIs. In addition, IBC office is also working with EHS to draft a non-compliance policy and procedure document, which will be reviewed at an upcoming meeting. Committee was informed that IBC office is also in the process of drafting updates to the biosafety manual and will include these changes.

III. Research Occupational Health Program (ROHP) & Environmental Health and Safety (EHS) Report

ROHP Report: **11/15/21:** A PI reported to the ROHP that a Master's student was bitten on their right thumb by a transgenic mouse earlier on that day. PI clarified that the transgene in the mouse involves modification of extracellular matrix protein and is not harmful to humans. ROHP advised the student to monitor area for signs and symptoms of infection-pain, redness, discharge or swelling. This incident will be reported to BPHC as the mouse is transgenic. ***EHS Report:*** EHS is actively investigating this incident and findings will be shared at the next meeting of the IBC.

III. Protocol Review

1. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2342		Identification of inhibitors of high containment virus infection	4	N/A	BUMC
Primary Reviewer: Elke Muhlberger		Secondary Reviewer: Guillermo Madico			

Applicable NIH Guidelines: Section III-D-1-c.

Meeting Comments: In this protocol the PI proposes to test variety of small molecules for their ability to block the infection of number of risk group 4 (RG4) viruses including filoviruses, arenaviruses, nipah viruses as well as coronaviruses like SARS-CoV-2 and MERS-CoV. This is a very well written protocol. All safety related issues are well described. All inactivation procedures are clearly written and are approved by the IBC and the EHS and are submitted to regulatory agencies. All members have appropriate training to handle RG4 agents. They will use liquid handler to add small molecules to the culture, which will minimize direct contact of the researchers to the pathogens. They will use human cell lines and primary cells. It was discussed that the use of small molecules in virus cultures may generate escape mutants which may become a dual use research of concern (DURC). This issue has been reviewed by the DURC subcommittee which previously determined that the work described in this protocols does not qualify to be a DURC. However, it was not clear whether any new procedure has been added since then which may require further review by the DURC subcommittee. The protocol clarifies that the proposed gamma irradiation method of inactivation has not been approved by the BPHC yet and the method will only be used after it is approved. Since the PI of this protocol was present in the meeting, on the Chair's request PI clarified that no new experiment has been added that require DURC subcommittee review and gamma irradiation SOP is currently being written for EHS approval. The following will be communicated to the PI:

- Please uncheck boxes and texts in the Overview and Grant Funding page that are for amendment and annual renews.
- Please correct "2019 nCoV" to current nomenclature SARS-CoV-2 in Section I.
- Heat inactivation – the current BSL4 SOP requires 10 minutes at 100°C (measured by external thermometer). Please revise accordingly.
- Biological safety Cabinet (BSC) certification dates for BSL-4 rooms need to be corrected: "Certification file with EHS": room expires Nov 2022, room expires 30 Sep 2022, room expires Aug 2022 and room expires Sep 2022.
- Remove Zaire Ebola virus from the list of hazardous agents because it is redundant.
- Add SW13 cells to the hazardous agents list.

BUA Site Assessment: All trainings and medical clearances are current for all members. Boytz and Keiser are enrolled in the BSL-4 suit training and mentorship. Biosafety cabinets are all duly certified but dates stated in the application are incorrect. The certifications of the BSCs in NEIDL are done in rotation and are strictly maintained and those records are sent to BPHC on a regular basis.

PI recused himself from the voting.

Motion: Conditional Approval (Administrative Review)	For: 14	Recuse: 1	Against: 0	Abstain: 0	Absent: 0

2. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2345		Identification of host factors controlling virus infection.	4	N/A	BUMC

Primary Reviewer: Elke Muhlberger | Secondary Reviewers: Guillermo Madico

Applicable NIH Guidelines: III-D-1-a, III-D-2-a, III-E-1, III-F-8; Appendix F-8.

Meeting Comments: This protocol proposes to identify host cell proteins that act as antiviral proteins or support the growth of risk group 4 viruses. The protocol proposes two approaches – either to overexpress proteins of interest or to knockdown expression of specific proteins by either siRNA or by CRISPR/Cas9 technology. This is a cell culture only protocol and has no animal research component. Experimental details are nicely described. Viruses to be used in this work include many RG4 viruses and also SARS coronaviruses. They also use explants from non-human primates as well as from humans. Recombinant viruses will also be used but those will be only for SARS coronaviruses. This is a very well written protocol. All safety related issues are well described. All inactivation procedures are clearly written and are approved by the IBC and the EHS and are submitted to regulatory agencies. It was clarified that since it was reviewed last time, no new procedure has been added to the protocol that changes its non-DURC status. Work with

escape mutants is well described including preplan stop times if scape mutants increase cytopathic effect or enhance cell-to-cell transmission. The following will be communicated to the PI:

- Please uncheck boxes and texts in the Overview and Grant Funding page that are for amendment and annual renews.
- For heat inactivation – the current BSL4 SOP requires 10 minutes at 100°C (measured by external thermometer). Please modify accordingly**.**
- Biological safety Cabinet (BSC) certification dates for BSL-4 rooms need to be corrected: "Certification file with EHS": room expires Nov 2022, room expires 30 Sep 2022, room expires Aug 2022 and room expires Sep 2022.
- Remove *E. coli* K12 from hazardous agents list (because it is BSL1).
- Remove Zaire Ebola virus from the list of hazardous agents because it is redundant.
- Add primary human fibroblasts to the hazardous agents list.
- Add SW13 and Vero cells to the hazardous agents list.
- Add NHP skin explants to Other Potentially Infectious Material list and add source.

BUA Site Assessment: All trainings and medical clearances are current for all members. Boytz and Keiser are enrolled in the BSL-4 suit training and mentorship. Biosafety cabinets are all duly certified but dates stated in the application are incorrect. The certifications of the BSCs in NEIDL are done in rotation and are strictly maintained and those records are sent to BPHC on a regular basis.

PI recused himself from the voting.

Motion: Conditional Approval (Administrative Review)	For: 14	Recuse: 1	Against: 0	Abstain: 0	Absent: 0

3. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1728		New strategies to control hemorrhagic fever virus infection	2	2	BUMC

Primary Reviewer: Rob Davey	Secondary Reviewer: Colleen Thurman

Applicable NIH Guidelines: Sections III-D-2, III-D-3, III-E-1, III-F, App. B, App. G-II-B-3

Meeting Comments: The goal of this protocol is to develop better treatment strategies for Ebola and related hemorrhagic fever viruses. They will engineer Vesicular Stomatitis Virus (VSV)-based vectors to express ebolavirus (EBOV) surface glycoproteins and will use this system to improve immune reactivity to Ebola and related viruses and to study immune responses against these viruses. A minigenome system, that involves transfecting plasmids into cells that encode the virus RNA polymerase, will be used to study how the virus replicates its genome. The system will also be used to identify small molecules that interfere with it, which may be used as therapeutics. No live risk group 4 viruses will be used although a recombinant vaccinia virus (Western Reserve) is used to make cells express high levels of T7 RNA polymerase. The virus will be handled by vaccinated personnel. Vaccine potential of their r-VSV constructs will be tested in guinea pigs, although it appears that the animal work is not being done at this time. The Medical Director of the ROHP clarified that researchers working with vaccinia virus are immunized every 10 years and vaccination efficacy is verified by 'scratch and scar' test. Additional work proposed include evaluation of primary cell model systems using Draper Laboratory's Predict-96 platform which allows testing of treatments in human primary cell culture and a human vein-on-chip model. All work will be performed in biosafety cabinets with eye protection, double gloves, and lab coat, which is appropriate PPE for this work. Use of sharps involve microscope slides for examining cells from cultures and animal work and razors for cutting gels for recombinant DNA work. Each is disposed in glass and sharps containers, respectively. Bleach at a final concentration of 10% is used for the treatment of waste for 30 minutes before sewer disposal. Virus stocks are stored in O-ring sealed tubes in -80°C freezer. Personnel will be trained by the PI and senior postdoc in the lab, both of whom has more than 5 years of experience with viral or recombinant DNA system. The following will be communicated to the PI:

- NEIDL 624 for ABSL2 experiments: if live animal work or necropsy is to occur, list all NEIDL 6th floor ABSL2 rooms for live animal work since they all have the same health status (suites). Rooms and can be the necropsy rooms. If no animal work is to occur, remove areas that are not needed.
- The donor tissue material to be used in the vein-on-chip model must be done using standard precautions for human pathogens. Please provide additional language to this effect.
- There is no live animal use proposed at this time. The described guinea pig study is complete, and no active IACUC protocols are available for the PI. Please clarify and modify the animal work description appropriately.
- Update biosafety cabinet certification date.
- Highest ABSL is checked in as ABSL2, but there is no live animal work at this time. Modify as appropriate.
- Section A. Vaccinia virus Western Reserve strain is a non-attenuated vaccine strain. Please modify your response in section A.2.

BUA Site Assessment: Not completed yet.

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

4. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2092		Analysis of small regulatory RNA biogenesis and function	2	1	BUMC

Primary Reviewer: Barbara Slack	Secondary Reviewer: Colleen Thurman

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

Meeting Comments: The protocol investigates mechanisms of post-transcriptional regulation, focusing primarily on the study of RNA-binding proteins, microRNAs, and RNA modifications. They use zebrafish, and RNA viruses as model systems. For the zebrafish studies they inject zebrafish embryos with mRNA to transiently express wild-type or mutant forms of RNA-binding and regulatory proteins of interest or CRISPR/Cas9 and analyze the effect by northern or western blot as well as by mass spectroscopy. For the virus infection model, they analyze RNA and protein derived from human and animal cells infected with filovirus, nidovirus (including SARS-CoV-2 and Mouse Hepatitis Virus (MHV). All materials are inactivated by inactivation procedures approved by NEIDL EHS and BU IBC. Inactivated material are obtained from BU NEIDL PI or outside collaborators. Hazards involved in the protocol include use of human cell lines, recombinant viral vectors including lentivirus and adenoviral vectors, gene-editing by CRISPR/Cas9 and the use of radioactive material. They will also use SARS-CoV-2 replicons to generate RNA which will be given to NEIDL PIs to transfect in human cells. Inactivated lysates (all done in the NEIDL) from those cells will be used for the study of transcriptional regulation. SARS-CoV-2 culture work will only be done by collaborators in the NEIDL. No member of the PI lab will work in the NEIDL. Waste decontamination, disposal and PPE use plan are appropriate. The lab will strictly follow EHS guidelines on working with genomic materials from SARS-CoV-2. IBC program manager clarified that inactivated materials from RG3 or RG4 agents are no longer considered biohazardous and as such does not need to be included in the hazardous biological agent list. It was discussed whether zebrafish should be considered animals. Veterinary experts explained that zebrafishes are considered animals after they are hatched. If they are maintained from the embryo stage to until they are adult, then all animal work related checkboxes should be checked. The following will be communicated to the PI:

- Section III.1- Training for Park - please specify who will do the training.
- Section III.3- ROHP clearance for Kretov is overdue.
- Section VII. 3- Update IACUC (AN-15558) to new number format. Provide more information on how long the micro-injected zebrafishes will be maintained for the proposed experiments.
- Section VIII.1- Should check animal handling and inoculation for zebrafish handling and injection of embryos.
- Section VIII.3,4- Check surgical mask to conform to Covid19 guidelines
- Section A. Inactivated virus-infected samples do not need to be in this table as they are no longer biohazardous.

- Section A. Human cancer cell lines (K562, U2OS) and Vero cells (NHP) should be listed as possible causes of human disease.
- Section H. 2. Update IACUC protocol information - PROTO201800373 through 3/3/2022 and zebrafish breeding protocol PROTO201900008 through 3/18/2022.

BUA Site Assessment: They have bloodborne pathogen exposure control plan. Training for all members are current. One member needs to update the ROHP clearance. Their biosafety cabinet has been certified earlier this month. Fume hood is duly certified. Lab confirmed that they are not doing any COVID-19 related work at this time.

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

5. rDNA/Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2524		Testing and target validation of novel antimicrobials.	2	2	BUMC

Primary Reviewer: Sajal Ghosh Additional Reviewer: Tom Winters	Secondary Reviewer: Colleen Thurman

Applicable NIH Guidelines: April 2019 NIH guidelines: Section III-D-1-a, III-D-2-a, III-F-8, Appendix BI, BII, and CII

Meeting Comments: This is a new protocol from a BU tenant company. These companies perform independent research work but follow all safety guidelines and standards of the Boston University. The goal of the protocol is to design novel antimicrobial agents that are more potent against recurrent infections or that easily gain resistance to multiple drugs. They test multiple derivatives of their test drugs on the growth of multiple bacteria or fungi either on agar plates/broth cultures or *in vivo* by variety of mouse models of infection. They will determine typical drug development data parameters like pharmacokinetics and pharmacodynamics to evaluate the potential of their lead compounds in future clinical studies. The biohazards in the study include about 30 risk group 2 bacteria and fungi which they obtain from ATCC. Their study include bacterial protease activators and characterization of drugs that are specific for H. pylori infection. Only five specific bacterial strains will be used in animal model studies of infection and test efficacy of their antimicrobials. They provided detail information on individual microbial agents in their list that have the potential to cause laboratory acquired infections (LAI) and discussed what safety measures they practice for handling those agents in the lab. These include small volume culture, restricted access to the lab and wearing gloves and lab coats at all times, working in a biosafety cabinet, and disinfecting work surfaces with freshly prepared 10% bleach for a minimum contact time of 10 minutes. Also included is the vaccination of the lab workers whenever available. ROHP will provide PV-23 vaccination for the use of *S. pneumoniae*. The ROHP Medical Director clarified that the agents with potential LAI concerns are already included in BU LAI list. Other new agents identified in this application do not cause serious disease in humans and do not qualify as LAI agents. One member suggested a need for the IBC to reevaluate if *H. pylori* should be added to the current LAI list. The lab also will perform standard rDNA work to manipulate bacteria and study the genes involved in their virulence, antibiotic resistance, or to facilitate antibiotic discovery and development. Liquid wastes are treated with bleach at a final concentration of 10% and solid wastes are collected in red biohazard bags for sterilization by third party vendor. The Secondary Reviewer informed the committee that she is the PI on record for the IACUC work associated with this protocol. However, she has no role in the management of this IBC protocol. The following will be communicated to the PI:

- ROHP clearance for Chumbler and Russell need to completed before they may start lab work.
- Add ASC room in the Research Laboratory Facility information for the ABSL2 animal work.
- Provide more information on the purpose of use of human cell lines.
- Describe transport of microbial agents to the ASC and bringing back the infected animal organs in laboratory procedure section as well.
- EHS indicated that one of the research lab as an IACUC approved space for some animal injection and post-monitoring activities. Please add those activities appropriately in the laboratory procedure section.
- Please clarify whether *Neisseria meningitidis* will be used in this study and if so, which strain will it be.
- If any recombinantly modified microbial agent is to be injected in to the animals, complete the animal experiment sections in the Recombinant DNA section of the application. Add the following information in the

laboratory procedure and rDNA section (as appropriate): PROTO201800204 H pylori infection approved through 3/25/2024; PROTO201800666 Novel antibiotic therapy approved through 2/4/2022.

- Section VIII.1 – Check Animal Handling/Cage changing
- Section VIII.4 – Check double gloves for all ABSL2 animal work PPE
- Section VIII.6 – Describe how instruments used for surgery or animal tissue collection will be sterilized.

BUA Site Assessment: Their biosafety cabinet certification is current. All trainings are current as well. ROHP clearance of new members are being processed.

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

6. Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2532		Deciphering isogenic APOE isoform dependent neurodegenerative response in human glia	2	2	BUMC

Primary Reviewer: Carmela Abraham | Secondary Reviewer: Colleen Thurman

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

Meeting Comments: This new protocol investigates the contribution of different forms of the APOE genes in the development of Alzheimer's disease (AD), in particular the APOE4, as this is already known to be a major risk factor for this disease. The PI will receive de-identified human fibroblasts and will prepare iPS cells that will be differentiated into glial cells. She will then use CRISPR/Cas9 to produce different ApoE genotypes and ApoE knockout cells which will be tested in response to disease modifying conditions and to determine causative pathological mechanisms of the disease. She will also perform RNA sequencing analysis on each culture to understand ApoE genotype contribution to particular cell types. The goal of the project is to identify how the gene expression networks and cellular functions are governed by various APOE genotype in the presence or absence of disease relevant environment to pinpoint the earliest and potentially most treatable mechanisms involved in AD pathogenesis. The following will be communicated to the PI:

- Provide more information on the Federal Funding information (name of the funding agency and what type of grant).
- Make sure to secure ROHP clearance before starting any lab work.
- Are all of the Core Facilities be used for this protocol? If so provide more information for the purpose of core facility use. If not, keep check mark only on those that will be used.
- "Lab personnel will wear lab coat while handling cells." Not enough PPE. Either remove this sentence from section VII. 3 or add all PPE to be used.
- Please add clarification after the sentence "As a future plan, I will inject iPSC-derived astrocytes and microglia into immunodeficient mice brain (commercially available through Jackson Laboratory) to study APOE4 risk effect in the context of in vivo brain environment." - that no animal work will be done at this time. When ready, I will amend the IBC protocol to provide more detail of the animal work and apply for IACUC approval before initiation of the animal work.
- Provide Biosafety Cabinet information and date of last certification.
- Check "Yes" for use of sharps.
- For Liquid waste – state that waste will be treated with bleach at a FINAL concentration of 10% for 30 minutes before sink disposal.
- How will the biohazards be stored? Is the freezer or the room locked?
- How will the cells be transported to core facilities?
- Mark "Other potentially infectious materials" for primary human cells and complete Section B.
- Uncheck "Synthetically derived nucleic acid molecules". This does not apply in your application.
- Uncheck "Live animal use" and highest ABSL2 from the Table as no animals are used (check N/A).

BUA Site Assessment: The lab is under minor renovation and some of the proposed work are future plans, particularly the animal work. IACUC protocol will be submitted when PI is ready to start animal work. IBC protocol will be amended to include more detail. All trainings are current. ROHP clearance is actively being followed up. Safety measures and PPE use plan are all appropriate.					
Motion: Conditional Approval (Administrative Review)	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

7. Bhz – New Application (previously deferred)

BUA	(PI)	Title	BSL	ABSL	Campus
2527		Molecular characterization and therapeutic targeting of Protein Kinase D2 in t(4;14) multiple myeloma	BSL2	N/A	BUMC

Primary Reviewer: Inna Afasizheva			Secondary Reviewer: Carmela Abraham		
Applicable NIH Guidelines: N/A					
Meeting Comments: This new application was previously reviewed in the October 2021 meeting and was deferred because reviewers expressed concerns that there was very little description of what biologically hazardous materials will be used and what safe handling procedure will be used or how the wastes will be disposed of. The protocol seeks to investigate the role and function of the Serine/Threonine protein Kinase in t(4;14) chromosomal translocation observed in high risk patients with Multiple Myeloma (MM) and to identify drug targets in MM. PI's revised application was re-reviewed by the primary reviewer and the IBC chair. Reviewers both indicated that the revised submission addressed each of the previous concerns and recommended approval of the protocol.					
Motion: Approve	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent: 0