Boston University
Institutional Biosafety Committee (IBC)
January 25, 2022 Meeting Minutes
Location: Zoom and/or by phone
Start time: 12:00 PM End time: 1:26 PM

Members Present:	C. Abraham, B. Slack, E. Muhlberger, R. Davey, E. Loechler, R. Morales, T. Winters, C. Thurman, V. Britton, P. Liu (Joined 12:22 PM), X. Brown, S. Niemi, J. Keeney, R. W. Timmerman, J. Barton (Left 12:59 PM), S. Ghosh
Guests Present:	S. Benjamin, P. Richmond, A. Ahmad, J. Davis, T. Killeen, M. Fitzgerald, J. Wood, J. Penner-Hahn
Staff Present:	S. Ghosh, L. Campbell, C. McGoff

I. Review of December 14, 2021 IBC Meeting Minutes (C. Abraham)

No comments or questions were voiced.
Motion: Approve
For: 15; Abstain: 0; Absent: 1

II. New Business:

A. SQAP Report
Nothing to report

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

12/16/21: MD/PhD student reported experiencing low grade temperatures and other symptoms after he accidentally injured his thumb percutaneously on 12-6-21 while cleaning forceps that he had used to remove infected lungs from mice injected with NL63 virus. He cleaned the wound with soap and water and applied topical antiseptic medication. Discussion with ROHP suggested that the symptoms are consistent with community-based viral infection, possible influenza and not likely related to the reported forceps injury incident as NL63 is a respiratory virus that does not cause any symptomatic infection in human. Researcher was advised to stay home until afebrile for 24 hours without taking antipyretics and to isolate from his roommate who is asymptomatic. Advised to follow up with ROHP should symptoms worsen or not improve or as needed. BPHC has been notified. EHS Report: Safety specialist interviewed both PI and researcher. Root cause of the incident was attributed to not being conscientious. Steps to prevent reoccurrence included review of exposure control plan and procedures for reporting incidents. Advised on proper decontamination techniques and sharps safety practices. Online Sharps safety training was assigned as a reminder.

12/21/21: A fully vaccinated, asymptomatic PhD student tested positive for SARS-CoV-2 on 12/21/21. The student had been in the NEIDL office space prior to testing but denied entering lab spaces. She reports she has not worked in the BSL 2 lab for a couple of months and she does not work with SARS-CoV-2, but shares office space and break room with others that do. Repeat testing performed outside BU on 12/23/21 was negative, the student remained asymptomatic and was cleared to return to work 12/29/21. This student was educated on the importance scheduling routine SARS-CoV-2 testing prior to entering the work space. After this incident ROHP prompted Dr. Corley, NEIDL Director, to send out notification to NEIDL researchers to get routine surveillance testing prior to entering the lab. There have been no incidents since then. EHS Report: Results of samples collected for testing will be reported on when received. BPHC has been notified.

1/3/22: An asymptomatic postdoc researcher who works in the NEIDL, tested positive for SARS-CoV-2 on 1-3-22. He reported no known exposures, no recent travel, fully vaccinated, and received a booster shot. Released from isolation and deemed amplicon exposure. He denied working with SARS-CoV-2 but does work in shared

space that does perform SARS-CoV-2 work. ROHP deemed this positive case is deemed to be an Amplicon contamination. Amplicon prevention education was provided and the researcher is cleared to return to work. BPHC has been notified.

1/6/22: A fully vaccinated, asymptomatic PhD student tested positive for SARS-CoV-2. The student worked in NEIDL BSL2 in shared space where SARS-CoV-2 rDNA work is performed. Repeat testing performed was negative and the researcher was cleared from isolation on 1-10-22. Amplicon prevention education was provided by ROHP. Deemed amplicon contamination due to testing at the end day after being in the laboratory. Report will be submitted to BPHC.

1/12/22: Potential biological exposure to a BSL4 staff who entered a NEIDL BSL4 lab unsuited not realizing it was in use. The incident was reported to ROHP by the NEIDL Biosafety Officer and the NEIDL Response Team. The staff member also reported the possible exposure to EHS. After the exposure, she took a whole-body shower and was advised to remove her contacts and use the eye wash. However, it was deemed no-to-low risk incident of infection to the researcher, as there were no pathogens in the lab and no work was being done at the time of this incident. Employee was cleared to return to work but was escorted to ROHP for further evaluation and counseling. ROHP provided the employees with a medical surveillance wallet card with ROHP contact information and a thermometer. She was advised to call ROHP or NEIDL Control should she have any concerns and was cleared to return to full duty work with no restrictions. Report submitted to BPHC.

1/22/22: An Animal Care Technician sustained an ABSL1 transgenic mouse bite on the right finger near to middle knuckle. The PI of the study reports that the Adipo-cre transgenic mice involved in the incident, express a protein called Cre recombinase (exclusively in their fat cells). This incident took place in ABSL1 and the mouse contained no hazardous agent. There is no hazardous concern regarding this transgenic mouse other than the potential for infection or local allergic reaction with a mouse bite. ROHP discussed the importance of washing for full time period (10-15 min) following a bite and risk of infection from own skin flora. She could apply antibiotic ointment over the site of the bite marks until they are resolved. Instructed to monitor for signs of infection. A report will be submitted to BPHC. EHS Report: More information will be provided on this mouse bite incident at the next IBC meeting.

III. Protocol Review

1. Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2352		Propagation and characterization of viruses	BSL4	NA	BUMC
Primary Reviewer: Elke Muhlberger		Secondary Reviewer: Guillermo Madico Shannon Benjamin			
Applicable NIH Guidelines: N/A					
Meeting Comments: The goal of the study is to understand the biology of viruses to facilitate the development and licensure of therapeutics and vaccines. They will study multiple risk group 4 (RG4) hemorrhagic fever viruses, henipaviruses and SARS coronaviruses. They will receive small amounts of virus from other laboratories and then amplify these viruses to generate virus stocks. They will determine the characteristics of the viruses to verify the authenticity of the stock and quantify by plaque assay. They will also perform inactivation of RG3/RG4 viruses using approved and validated inactivation procedures. All safety measures for working in a BSL4 laboratory are described in great detail. Waste disposal plan BSL4 lab and special PPE requirements for working with RG4 agents are nicely described. Following initial review of the protocol, PI was reminded that NEIDL is not approved to bring inactivated SARS-CoV material out of the containment as SARS-CoV is a select agent and the genomic RNA of this virus is capable of producing infectious virus upon transfection. PI promptly revised this information. PI also updated personnel list and biosafety cabinet certification dates. No other concerns were noted for this protocol.					

BUA Site Assessment: Exposure control plan and all other safety documents are available in the lab. All biosafety cabinet certification dates are current and all required safety training are current with all members.					
Motion: Approve	For: 16	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

2. rDNA/Bhz – Annual Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2442		Investigating the role of viral proteases in disease pathogenesis	BSL3	N/A	BUMC

Primary Reviewer: Rob Davey	Secondary Reviewer: Shannon Benjamin
Applicable NIH Guidelines: Sections III-D-1-b, III-D-2-a, III-D-3-b; Appendix B-III-D and G-II-C	

Meeting Comments: This protocol investigates how viral proteases remodel host cells and create favorable environment for their replication. In particular, they will investigate how proteases of risk group 3 (RG3) viruses contribute to disease mechanisms. They also study SARS-COV-2 interaction with cells and to develop treatment therapies. In this annual review, new procedures are being added to make SARS-CoV-2 chimeric viruses containing the spike protein of different variants. They will use a reverse genetics system that has the virus genome on a plasmid. The spike gene from different viruses will be substituted into this genome and virus made by transfection of the plasmid into cells. The viruses will then be characterized for cell specificity (tropism). The Washington/Wuhan strain will be used as the base genome and variant spike proteins added. Since most of the changes in variants are in the spike protein, this is much like making any virus that is in current circulation except that the few other changes in the genome are being made constant so that the function of the spike can be studied as the single change.
DNA will be made in the BSL2 lab and then transferred to BSL3 where it will be transfected into cells. Transfer is in a shatterproof, sealed container, which is appropriate. While it is not expected that these chimeric viruses will exhibit higher transmissibility, as the spike genes are the same as found in circulation, any aberrant behavior will be reported to EHS if identified and work will be stopped. The work has been previously reviewed by the dual use research of concern (DURC) subcommittee and was determined to be a non-DURC protocol. The work is being performed appropriately and the appropriate containment levels are being used. Overall, the new changes do not alter the risk of the work.

Motion: Approve	For: 16	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

3. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2355		Characterization of cellular proteins cleaved during virus infection	BSL2	ABSL2	BUMC

Primary Reviewer: Barbara Slack	Secondary Reviewers: Steve Niemi
Applicable NIH Guidelines: Sections III-D-1-a, III-D-2-a, III-D-3-a, III-D-4-a, and III-E-1	

Meeting Comments: The overall goal of this proposal is to identify the repertoire of host proteins targeted for cleavage upon infection. A large number of risk group 2 viruses such as, coxsackievirus, poliovirus, human rhinoviruses, enteroviruses, sendai virus, human corona viruses including SARS-CoV-2 cDNA and replicons, herpes simplex virus and murine hepatitis virus (MHV) will be used in the protocol. Human and NHP cell lines will be used to grow these viruses and standard assays such as immunofluorescence, western blot, DNA/RNA analysis, flow cytometry and mass spectrometry will be used for data analysis. Genes of interest will be knocked down or knocked out using shRNA or CRISPR-Cas9 (guide RNA and Cas9 on the same plasmid). SARS-CoV2 DNA from collaborators will be propagated in bacteria or yeast, and subjected to in vitro transcription to generate RNA, which will be transported to NEIDL BSL3 space for cell transfection experiments. Only subgenomic replicons will be used for transfection experiments in the BSL2 laboratory. A chemical screen to identify compounds that inhibit viral proteases will be carried out using mouse hepatitis virus (MHV) and human coronavirus infection system. Animal experiments involving infection of mice with BSL2 viruses are described in detail, but the PI states that the IACUC application has not yet been filed. No animal work will be done until approval is received. This is a well-written and detailed application. The safety precautions to be taken are described in detail. One reviewer expressed concern that PI's reference of MHV as a RG2 agent may not be appropriate as BMBL does not refer such risk group assignment.

However, another member commented that this virus is a serious pathogen for mouse and if the PI wants to use it at a higher containment (BSL2), he may be allowed to do so. However, review of the ATCC website during the meeting confirmed that MHV is recommended to be used at BSL containment as their determination of the assignment is based on BMBL information. The committee ultimately determined that PI may use it in BSL2 containment. The following will be communicated to the PI:

- Please consider rewriting the Layman's description omitting any scientific jargons and making it easily understandable to non-scientific non-technical individual.
- Section VIII.1- please check 'animal handling, cage changing'.
- Verify that BSC certification is up-to-date.
- Section VIII.7A- please specify that liquid waste brought up to 10% bleach will be allowed to sit for at least 20 minutes before disposal in the sink.
- Section A. The table lists some viruses (dengue, Zika) that are not described in the proposal. Please reconcile this list with the proposed experiments. THP-1 cells should be added to the table.

BUA Site Assessment: The lab has appropriate exposure control plan and other emergency control plans. Safety trainings are complete for all members and their medical clearances are current. Biosafety cabinet and fume hood are duly certified.

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
1540		Aldolase Genes in Normal and Fructose Intolerant Humans & Metabolic Pathways and Defects in Fructose Metabolism	BSL2	ABSL1	CRC

Primary Reviewer: Carmela Abraham	Secondary Reviewer: Pinghua Liu

Applicable NIH Guidelines: Sections III-D-1-a, III-D-2-a, III-D-4-a, Section III-E-3 (transgenics); Appendix B- 1, C-I,II,III Appendix E-II-A; Appendix E-III-A,B; Appendix Q-II-A,B, Appendix G-II

Meeting Comments: In this project the PI will use recombinant DNA techniques to understand the structure, function and mechanisms of eukaryotic aldolases, fructokinases, and deaminases, which are enzymes involved in carbohydrate metabolism. They will characterize recombinantly expressed enzymes and their variants, compare similar enzymes from other distantly related species and will also generate aldolase B "knock-out" and/or "knockin" mouse and analyze their behavior. Human blood, tissues, and/or saliva containing buccal cells from subjects suspected or known to suffer from hereditary disorders due to mutation(s) in the aldolase genes will be used. DNA isolated from these specimens will be analyzed for known and unknown mutations. Biohazards used in the protocol include handling of human blood and tissues, use of viral vectors, use of radioisotopes and X-ray diffraction studies. All members handling rDNA materials are trained on NIH guidelines and each have access to the BU Biosafety Manual. All work with biohazardous materials are done in biosafety cabinet wearing lab coats, gloves and eye-protection. However, members noted that it was not clear what is being done currently and what has been already completed. The following will be communicated to the PI:

It was not clear which experiments are being done currently and what has been already completed. Please consider this concern when responding to the meeting comments.

- It is stated in section III.1 Lab experience for the PI: All have >40 years experience working in the laboratory as well as prior experience at other labs. Please correct this typo.
- Room should be BSL2 because of Storage of Biohazardous Materials, storage of cell lines in liquid nitrogen freezer.
- Please add bleach concentration in this statement "The spill is neutralized with dilute bleach and absorbed with absorbent paper". It should be dilute freshly made 10% bleach. This should also be changed in the next paragraph.

- Where are the human blood, buccal cells and liver biopsies coming from? How are they transported to the PI's lab?
- When and how is radioactivity used in this protocol (32P, 35S, 3H and 14C)? Section G states that their use is stated in Section VII but no information is available there.
- Protocol states use of multiple human cell lines and lentivirus vectors. Their use in the current protocol needs to be briefly described.
- There is no description of any animal work in the lab procedure. If this is from previous version of this protocol, please clarify accordingly.
- VIII. 3. Do you use all the checked PPEs in your regular BSL2 lab work? If not, please check only those PPEs that are used in your lab.
- VIII.7. Liquid waste should be treated with 10% bleach final volume for 30 minutes, not 5 minutes.
- VIII.8. There is no need to decontaminate with bleach solid waste with bleach before discarding into biohazard waste containers, but if you do, change the concentration to 10%.

BUA Site Assessment: Safety training for all members are current. ROHP clearances are being updated. Emergency control plan and other documents are in place. The lab has duly certified biosafety cabinet.

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

5. rDNA/Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2535		Molecular Mechanisms of PTEN and USP7 Regulation	BSL2	NA	BUMC

Primary Reviewer: Xin Brown	Secondary Reviewer: Jim Keeney

Applicable NIH Guidelines: Section III-E-1; Appendix B-1

Meeting Comments: The goal of this protocol is to investigate how post-translational modification of proteins influence their biological functions. They will use two well-known proteins PTEN (phosphatase and tensin homolog on chromosome 10) and USP7 (ubiquitin specific peptidase 7) as model in their study. The protocol provides a very general description of procedures they will use, such as peptide synthesis, protein expression and purification, recombinant DNA manipulation and transfection of human cancer cells, but no detail is provided. It is not clear how these procedures will be carried out and how will they contribute to the overall objectives of the protocol. Committee wanted to know more detail of the work so that a better risk assessment can be done. However, despite lack of details, the protocol does include information on all hazardous materials, personal protection measures, appropriate plan for material storage and waste disposal, which assures PI's clear understanding of the safety protocols. The following comments will be sent to the PI:

Committee expressed concerns that the application lacks details on the actual work to be done. Committee members requested that a brief description of each of the procedures be provided, and to note that the PI should contact IBC office for further clarification and direction on what specific information needs to be included in the application.

- Please remove all technical terms in the Layman's description and replace PTEN and USP7 with simpler biological language.
- What kind of peptides will be synthesized and what will they be used for?
- Which proteins will be expressed and purified?
- What kind of experiments will be set with those purified proteins?
- What will the cancer cells be transfected with and what will be done to the cells after the transfection
- The protocol states that "All biohazardous materials will be transported in a container that is resistant to leaking and breaking. Please indicate what is the primary container for transportation and then mention that the secondary container will be a leak-proof and shatterproof container.

- Baculovirus, Sf9 and Sf21 insect cell lines are RG 1 agents. Similarly, *B. subtilis,* BL21, JM101,DH10, DH5-alpha ExpiSF9, High Five cells, all can be maintained in BSL1. These agents do not need to be added to the Hazardous Biological Agent table (Section A).

BUA Site Assessment: The lab has exposure control plan and chemical hygiene plan in place, Safety Trainings are complete for all members. ROHP clearances are being renewed. Duly certified biosafety cabinet and fume hood are available to the lab.

Motion: Conditional Approval (Primary and Secondary Reviewer Review)	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

6. Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2537		Novel Linkers and Conjugation Methods for Generating Antibody-Drug Conjugates with Improved Properties.	BSL2	NA	BUMC

Primary Reviewer: Sajal Ghosh	Secondary Reviewer: Bob Timmerman

Applicable NIH Guidelines: N/A

Meeting Comments: This goal of this protocol is to create conjugates of biologically active but toxic compounds with tumor specific antibody molecules. The conjugate is then applied on to cancer cells in vitro to test cell killing potential of the toxic compound. The biohazard aspect of this protocol is the use human cell lines which they use to test the efficacy of their conjugate. They provided extensive detail of laboratory procedure for maintenance of cell lines, treatment of the conjugate and colorimetric evaluation of the effect of the treatment. These are all simple and standard analytical assays. The use of PPE seems appropriate for BSL2 work. Liquid waste are treated with bleach at 10% final concentration for 30 minutes and solid wastes are disposed of in red biohazard bag which are all appropriate. Cells are stored in locked room with card key access. However, it was not clear what is the nature of the toxic compound and how they are being handled. The following will be communicated to the PI:

- The research project description section states that biologically active toxins are used to make toxin-antibody conjugate. Please provide more information about the toxins that are being used.
- Are these select agent toxins? If so, please confirm that are being used at or below permissible level. Check select biological toxin box in Section IX and complete the Section D.
- If the toxins are something other than those listed in select toxin list, state the nature of the toxin and discuss the safety issues that lab workers must follow while handling them.
- State how the toxins are inactivated and how they are disposed of safely.
- State if antidotes are available for any accidental ingestion/inhalation of those toxins.
- Please keep ROHP updated about the toxins you use in your study.
- ROHP clearance is required for all members of the protocol.

BUA Site Assessment: The lab has certified biosafety cabinet. Training is complete. Lab members are working on updating their ROHP clearances.

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