Boston University
Institutional Biosafety Committee (IBC)
March 16, 2021 Meeting Minutes
Location: Zoom and/or by phone
Start time: 12:02 PM End time: 1:30 PM

Members Present:	C. Abraham, R. Ingalls, E. Muhlberger, B. Slack, R. Davey, T. Winters, R. Varada, C. Thurman, J. Keeney, R. Timmerman, V. Britton, J. Barton (joined 12:05 PM), P. Liu
Guest Present:	A. Ahmad, P. Richmond, J. Wood, C. Bennett, T. Killeen, M. Fitzgerald, K. Tuohey, S. Benjamin
Staff Present:	S. Ghosh, L. Campbell, C. McGoff

I. Introduction: Committee was introduced to Dr. Pinghua Liu, the new IBC member. Dr. Liu is an Associate professor of Chemistry with active research program on identification of anticancer agents.

II. Review of February 23, 2021 IBC Meeting Minutes
Minor corrections made by the AVPRC were displayed on the screen. No comments or questions were voiced.
Motion: Approve
For: 12; Abstain: 1, Absent: 0

III. New Business

A. Safety & Quality Assurance Program (SQAP) Report

Guidelines on working with SARS-CoV-2 Variants

Sajal Ghosh presented new BU guidance on the research use of SARS-CoV-2 variants that was developed in response to City, State and University monitoring of these variants in local laboratories. The guidance was formed from discussions and input of the IBC Chair, Vice Chair, NEIDL members of the IBC, BSL4 BSO, LAI Subcommittee chair, Medical Director, NEIDL CSO and AVPRC, as well as some Investigators who conduct research with SARS-CoV-2 and its variants. The new guidance states:

"Since these variants are the same species as the original SARS-CoV-2, the containment level and biosafety practices for handling these variants are no different than those of the original SARS-CoV-2. Practices and procedures will be the same as will be the level of risk. The Biological Use Authorization application (the IBC application), with the review of the Biological Safety Officer (BSO), does not ask for information on strain variants unless there is a change in the biosafety level or other increased level of risk. The use of these variants does not constitute Dual Use Research of Concern (DURC) as they exist in nature."

Investigators will maintain an inventory of all SARS-CoV-2 mutants and variants used and/or identified in their labs and will notify the BSO (with a copy to the LAI and IBC offices), who will update the IBC at its monthly meetings and communicate the information to the BPHC.

The guidance will be sent to the IBC members for any additional comments after the meeting and will be posted on the website (along with an inventory template for investigators to complete), once final.

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

ROHP Report
Since the last IBC meeting on 2-23-21, ROHP had 5 incidents to report:

2-19-21: Researcher tested positive to SARS-CoV-2

One researcher tested positive for SARS-CoV-2 on asymptomatic screening, which later was deemed to be related to amplicon exposure.

2-23-21: Breach of BSL4 suit

A BSL4 researcher discovered a tear in his supplied air suit while in the shower exiting the BSL4 lab. The researcher noticed a hissing sound while in the shower, inflated the suit and discovered a tear by the head of his suit between a zipper and plastic section measuring about 3mm. The researcher had been pipetting Ebola virus into HeLa cells while working in the biological safety cabinet. Since the researcher was wearing a positive pressure suit while work was being performed in a biosafety cabinet and his head was not in the biosafety cabinet, this incident was not considered an exposure.

2-23-21: Laceration to finger

A medical student research assistant reported that he sustained a laceration to his finger from a microtome blade. He was wearing one pair of gloves, personal eye glasses and a lab coat when he tried to use a chemical wipe to wipe paraffin off of a microtome blade when he cut his left index finger. The student researcher was cutting paraffin blocks on the microtome to prepare slides of human melanoma cells that had been grown in mice. The student researcher was in training to use the microtome with his post-doc supervisor when the incident happened. The microtome machine and blade were disinfected with xylene prior to use. Further review of information on the cell line showed no risk for Hepatitis B, Hepatitis C or HIV. No post-exposure prophylaxis was needed.

3-1-21: Breach of BSL4 suit glove

A BSL4 researcher performing necropsy on a non-human primate infected with Ebola sustained a breach of his suit glove on the left index finger measuring a pinhole but two gloves under the suit glove were not compromised. After reviewing the incident with the biosafety officer and infection control, this case was deemed to be a non-exposure.

03-09-21: Researchers tested positive to SARS-CoV-2

Three researchers working with inactivated SARS CoV-2 in one lab tested positive for SARS-CoV-2 on asymptomatic screening and were likely related to amplicon exposure. An IBC member asked whether the research group was working with inactivated culture material, were using plasmid clones expressing viral genes or were using extracted nucleic acids for further amplification as it is unlikely that lab members could test positive if they were working with only inactivated material. The Senior Compliance Specialist clarified that this was not a NEIDL laboratory, rather a PI in a BSL2 laboratory who purchased inactivated cell culture material infected with SARS-CoV-2 and was amplifying RNA by RT-PCR for designing diagnostic reagents. Therefore, any contamination in the lab could result in positive detection of SARS-CoV-2 in screening tests.

All cases above have been reported to BPHC and a biologic research laboratory report form has been submitted.

EHS Report

A microtome laceration incident is being investigated and a full report will be presented at the next IBC meeting.

IV. Protocol Review

1. rDNA/Bhz – Annual Renewal

BUA	(PI)	Title	BSL	ABSL	Campus

2443		Investigating host-pathogen interactions regulating the pathogenesis and immunogenicity of BSL-3 viral agents.	3	3	BUMC

Primary Reviewer: Elke Muhlberger Additional Reviewer: Shannon Benjamin	Secondary Reviewers: Rao Varada
Applicable NIH Guidelines: Sections III-D-1-a, III-D-1-b, III-D-2-a, III-D-3-a, III-D-4-b, III-E-1; Appendix-B-II-D, Appendix G-II-B	
Meeting Comments: The goals of this project are to identify and characterize virus-host interactions that regulate the infectious cycle of multiple risk group 3 viruses, including members of the Flaviviridae and Coronaviridae family including SARS-CoV-2. They plan to use the knowledge gained in their research for developing anti-viral measures. The protocol also utilizes animal models to validate their findings. The protocol has been extensively reviewed in multiple amendments during the past year. In this annual renewal one member has been removed and a method to secure oxygen tank in the ABSL3 suite has been added. PI already addressed two minor issues that the reviewers pointed out (removing rodent cell line and biosafety cabinet certification date) before the meeting. ASC director indicated all the associated IACUC protocols are in good standing. *A motion was made not to require annual review of this protocol.* *For: 13; Against: 0; Abstain: 0; Absent: 0*	

Motion: Approve	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

2. Bhz – Annual Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2439		Storage, Propagation and Distribution of BSL-3 Emerging Pathogens	3	N/A	BUMC

Primary Reviewer: Rob Davey Additional Reviewer: Shannon Benjamin	Secondary Reviewer: Bob Timmerman
Applicable NIH Guidelines: N/A	
Meeting Comments: The goal of this protocol is to operate a risk group 3 virus stock repository in the NEIDL. This service receives stocks from BEI or other recognized source, stores them or makes limited expansion, characterize by sequencing and then stores them. Personnel have sufficient experience for the work (>3 years). Appropriate PPE (PAPR) and safety procedures (sealed centrifuge rotors, BSCs) and disinfectants (5% Microchem plus and 10% fresh bleach) are used. TRIzol and other approved inactivating reagents are used for material that will be removed from BSL3 (for sequencing) or other analysis. This annual renewal submission had no modifications except updates of training dates. Overall, the work appears to be appropriately performed by staff using approved handling and inactivation procedures that are compliant with the SOPs regarding pathogen inactivation and handling of the pathogens. *A motion was made not to require annual review of this protocol.* *For: 13; Against: 0; Abstain: 0; Absent: 0*	

Motion: Approve	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

3. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2286		Biomolecule Production Core - Propagating BSL4 pathogens	4	N/A	BUMC

Primary Reviewer: Rob Davey	Secondary Reviewer: Nadya Yun
Applicable NIH Guidelines: Section III-D-1-a, III-D-1-b, III-D-1-c	
Meeting Comments: This core protocol is responsible for storage and handling of BSL-4 viruses. The service of the core is to provide viruses to NEIDL BSL-4 researchers for their experiments and to perform BSL-4 infection studies for	

the research community. The group handles filoviruses (ebolaviruses, marburgviruses, cuevaviruses), henipaviruses (Hendra virus, Nipah virus), arenaviruses (Lassa, Lujo, Guanarito, Junin, Sabia, Machupo viruses) and Crimean-Congo hemorrhagic fever virus (CCHFV), which belongs to the group of bunyaviruses, as well as risk group 3 agents, SARS-CoV-2, MERS-CoV and now SARS-CoV. Work is done using appropriate PPE (biocontainment suit), BSCs, sealed centrifuge rotors and other procedures for preventing exposure to these viruses. All work is performed within the BSL4 laboratory in the NEIDL with state of the art engineering controls to protect the community. A number of analytical approaches are done. Each is designed around the same principles of containing the viruses. Virus is inactivated by multiple, validated inactivating approaches. Most of the validations were performed by the PI's group and personnel training is documented. Personnel description is excellent and describes very well the experience of each person. They appear appropriately qualified for the work. Records are maintained for the inactivated material allowing efficient tracking. Disinfectant used is mostly 5% Microchem plus which is an approved for use in BSL4. This three-year renewal added SARS-CoV and 2 bat cell lines but no changes in procedures. Procedure section has been edited to make more succinct and to update training records. Overall, the work appears to be appropriately performed by staff using approved handling and inactivation procedures that are compliant with the SOPs relating to BSL4 work.
PI recused herself from voting.

BUA Site Assessment: All personnel listed in the protocol are up-to-date with their training. Work with SARS-CoV in BSL4 is approved by the CDC.

Motion: Approve	For: 12	Recuse: 1	Against: 0	Abstain: 0	Absent: 0

4. Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1487		CLASSIFICATION OF STUDIES: 1. Human Studies-NIH, industry and internally sponsored 2. IACUC/Animal Protocols *Specific titles are listed in Section VII.	2	2	BUMC

Primary Reviewer: Robin Ingalls	Secondary Reviewer: Colleen Thurman

Applicable NIH Guidelines: N/A

Meeting Comments: The broad objective of this protocol is to study ear infection (known as Otitis Media) and vaccine response to this disease that involve both human research and animal research. The human research part includes immunization of human study participants and analyzing their blood for immune responses. Phlebotomy for this study is done in the clinic and blood is processed in their laboratory to do flow cytometry and protein analysis. Other observational studies in the protocol investigate Hepatitis C virus (HCV) infection in pregnant women and mother-to-infant transmission of HCV. In their animal model studies they use chinchillas to investigate how bacteria overcome the host defense system in establishing otitis media. They also use the same animal model to evaluate new vaccine candidates and passive immunization to block experimental otitis media. With regard to biohazardous procedures, the protocol involves handling of human specimens, such as spinning and shipping, some ELISA, flow cytometry and phagocytic assays for fluorescently labelled bacteria, as well as handling small volume of bacterial culture. The Medical Director confirmed that members in this group are current on their flu vaccinations.

- Please check Animal Handling in section VIII.1.
- Clarify in section VIII.7A that liquid waste is treated with bleach to a 'final' concentration of 10%.
- Update IACUC protocol numbers with new numbers (14726=PROTO201800075, 14826=PROTO201800091, 14776=PROTO201800082, 14982=PROTO201800128).

BUA Site Assessment: The lab has exposure control plan. All members have appropriate medical clearance. Some members need update of their safety training. Biosafety cabinet and fume hood are duly certified. Their use of PPE is appropriate.

Motion: Conditional Approval (Administrative Review)	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

5. Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2012		1. Lacosamide effects on alcohol self administration and craving in heavy drinkers 2. The Effects of Exenatide, a GLP-1 Agonist, on Alcohol Self-Administration in Heavy Drinkers 3. Calibration study of a wearable noninvasive blood alcohol monitor 4. The effects of the histamine-3 receptor inverse agonist pitolisant on alcohol self-administration in heavy drinkers	2	N/A	BUMC

Primary Reviewer: Carmela Abraham	Secondary Reviewer: Tom Winters

Applicable NIH Guidelines: N/A

Meeting Comments: This study evaluates the effect of two drugs for treating drinking and craving of alcohol by heavy drinkers. One of the drugs is an anti-seizure medication lacosamide and the other one is a GLP 1 receptor antagonist exenatide that is used for treating type 2 diabetes. The protocol also includes a wristband blood alcohol concentration measurement study that allows monitoring and reduction of and harm from alcohol as a research tool. In this three-year renewal they are adding Pitolosant, a H-3 receptor inverse agonist approved for treatment of excessive daytime sleepiness in people with narcolepsy. They will test this drug on people with craving alcohol habits and heavy consumption of alcohol to help them lower their alcohol intake. They will collect blood and urine for analysis, including pregnancy tests. Urine will be collected at each clinic visit. Samples will be used for inclusion/exclusion in studies. GCRU is used for injecting exenatide to the study participants. All procedures are performed under BSL-2 precautions and using appropriate protections for working with blood-borne pathogens.

- It is stated that Ms. Reid has had 3 years experience working with bodily fluids and she will be under the direct supervision of the lab manager, Laurie Colaneri. But Laurie is not a listed as personnel in the protocol. Please clarify.
- How is COVID-19 contraction risk mitigated in breath testing procedures?
- It is described that blood and urine will be collected. However, there is no description of what will be done with these materials afterwards. Will they be tested in the PI's lab?
- Will the same heavy drinkers be used in all follow-up experiments?
- If blood and urine will be pipetted or centrifuged, please check the "Pipetting infectious liquid" and "Centrifugation and ultra centrifugation" boxes In Table VIII.1.
- In Section VIII.6, the response should be "Yes" since blood is being drawn.
- In Section VIII.11, instead of marking N/A, please state briefly how the blood will be transported from one room to another.
- In Section B, please also list human blood and provide source information.

BUA Site Assessment: The lab has updated exposure control plan. All members have ROHP clearance. Required safety trainings are current for all members and they are using enhanced PPE. There are no issues with the lab.

Motion: Conditional Approval (Administrative Review)	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

6. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1522		Virus - Host interactions during HIV-1 pathogenesis	2+	2	BUMC

Primary Reviewer: Robin Ingalls	Secondary Reviewer: Rao Varada

Applicable NIH Guidelines: Sections III-D-1, III-D-2, III-D3: App G-II-C, B-III-D

Meeting Comments: The lab has long-standing interest in the study of HIV immunity and recently they have also added some SARS-CoV-2 work in the protocol. For the HIV studies, their goal is to identify the mechanisms by which the virus is transmitted to a new host and the role various immune cells (such as dendritic cell, macrophages and CD4+ T-cells) play in establishing an infection. They generate virus by transfecting plasmids that carry full-length viral genome or use lentivirus or AAV vectors, which express HIV-1 envelope protein. They use the generated virus or a concentrated stock obtained by ultracentrifugation, for infection of host cells for various experiments. In some other experiments they also use virus-like particles on which they express surface proteins of other RNA viruses for comparison. They also work on macaque blood samples obtained from collaborators who work with HIV-2 and SIV-infected animals. They have a plan for developing an *in vivo* model for nanoparticle-mediated delivery of antiretroviral drug into lymphatic tissues but it was not clear whether the study is still ongoing or ended as the animal PPE section of the application is blank and the IACUC approval for that study has expired. However, disposal of nanoparticle waste is clearly described. They are developing single-cycle replication competent HIV particles that express SARS-CoV-2 spike proteins that will be used to study the mechanism of virus infection. The project involves handling of lots of biohazardous material but management of these wastes are well described.

- Please clarify if the animal work for sustained delivery of anti-retrovirals to the lymphatic tissue is still in progress.
- Note that the IACUC approval for this animal work (PROTO201800455) expired on 8/21/2020. If the animal work is to be continued, the IACUC approval needs to be re-instated.
- The animal PPE section is currently blank. To make this question visible, first check the animal handling and cage changing' box in question VIII.1. Then complete the Animal PPE section (Section VIII.4) by checking the use of lab coats, disposable gloves, face shield, surgical mask, shoe cover and head cover.

BUA Site Assessment: Not done, scheduled for Thursday (3/18/21).

Motion: Conditional Approval (Administrative Review)	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

7. Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2111		Behavior, Physiology, and Genomics of Development in South African vervet monkeys (*Chlorocebus pygerythrus*)	2	2	CRC

Primary Reviewer: Ed Loechler	Secondary Reviewer: Colleen Thurman

Applicable NIH Guidelines: N/A

Meeting Comments: The goal of this study is to understand how obesity is influenced by long-term development and growth. The PI's group investigate non-human primates, mainly the vervet monkeys that are both captive and in the wild to understand how diet and body size affects obesity, along with the role of genetic factors. Project goals include: a) characterization of the genetic and developmental etiology of obesity in captive vervet monkeys, both phenotyping and genotyping (in Vervet Research Colony, Wake Forest University School of Medicine), where obesity genes and co-variables such as diet, maternal diet, microbiome, are studied; and b) characterization of postnatal growth and development in both captive and wild populations of vervet monkey. Wild animals are trapped in their South African natal home ranges and samples are collected for microsatellite and mitochondrial DNA sequencing on next generation sequencing platforms available with the collaborators. Behavioral observations are made in the wild to assess food-related and dietary behavior. Samples will be collected and air shipped to the U.S. according to CDC and the International Air Transport Association (IATA) guidelines. Samples are placed in a leak-proof primary receptacle, surrounded by absorbent material in a leak-proof secondary package. Appropriate PPE will be worn (sterile nitrile or latex gloves, face masks, and sterile gowns). Work in the BU Vervet Research Colony (VRC) will be conducted by the PI, assistants and undergraduate students. DNA will be extracted from fecal and tissue samples. Hair samples, blood dots and microbiome swabs will also be collected. All samples will be stored in the -80C lab freezer until they are sent out to collaborators for further analysis. It was noted that physical location of the Vervet Research Colony has not been indicated in the protocol. It was also not clear how the samples will be transported from PI's lab to other BU collaborators.

- Please clarify where the BU Vervet Research Colony is located physically and how monkey biological samples from this colony are brought to the BU research facility.
- Check Biological Agents due to the proposed new project that include handling of potentially infectious samples from yellow-tailed woolly monkeys (New World Primate species) in the lab.
- Please discuss briefly if exposure to herpes B virus is a concern while handling the primary biological samples from the monkeys in this study (wild or captive).
- Revisit the statements in various sections of the Research Project Description and remove ALL statement that refer to previous iteration of the protocol (for example 'Sample collection in the VRC will not be done until 2018').
- If studies are being done with samples collected from captive vervet monkey's, please describe those activities also.

BUA Site Assessment: Biosafety cabinet is duly certified. Training of members are all current. A few members need update on their ROHP clearance and they all have been notified.

Motion: Conditional Approval (Administrative Review)	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

8. rDNA/Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2511		Dynamic determinants of co-transcriptional gene regulation: Insights for Cancer Dysfunction	2	N/A	CRC

Primary Reviewer: Barbara Slack	Secondary Reviewer: Jim Keeney

Applicable NIH Guidelines: Sections: III-D-1-a, III-D-2-a, III-F-8; Appendix C-1

Meeting Comments: The goal for this project is to explore how human gene transcription is regulated by the activities of gene promoters and messenger RNA splicing machinery. For these studies they are transfecting HEK 293 cells with bi-fluorescence reporter genes that are driven by human gene promoter libraries to screen for splicing of interest. Identified genes will be incorporated in HEK 293 cell genome and further analyzed to understand splicing mechanism. It is not clear what method they are using to knock-in genes in HEK 293 cells. However, no major safety concerns were noted in the protocol.

- Lab Procedures section: please specify the transfection method that will be used.
- Please clarify if CRISPR/Cas9 or related methodologies are used in integrating promoters into the HEK 293 genome. If so, describe briefly the technology being used, how it is being delivered to the cells (transfection or lentiviral vector, etc.) and how any associated risks are mitigated.
- Section H. rDNA table
  - Please specify the *E. coli* strains and plasmid vector(s) that will be used.
  - The 'Eukaryotic Experiments' section of the table should also be completed for host-vector-donor information, since the application describes transfection of HEK 293 cells.

BUA Site Assessment: Few members need updated ROHP clearance and they have been informed. Training is current for all members. Their biosafety cabinet is certified. Their PPE use plan is appropriate.

Motion: Conditional Approval (Administrative Review)	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

9. rDNA/Bhz – Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
2363		Exploring molecular mechanisms of the immune system	2	2	BUMC

Primary Reviewer: Elke Muhlberger	Secondary Reviewers: Rao Varada

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

Meeting Comments: The original goal of this protocol is to understand how the body's immune system responds to various threats. In variety of laboratory and animal work cultured cells or animals are exposed to immune stimulating agents which are then analyzed by cellular and molecular biological techniques. In this amendment, they are adding two viruses (respiratory syncytial virus [RSV] and influenza virus H1N1/H5N1] and one adenoviral vector that expresses human ACE2 protein. The committee expressed concerns that the group does not have experience in respiratory virus work and did not clarify where will they get appropriate training. Further, some H1N1/H5N1 virus work requires higher containment level, but the application does not specify which strains they will use. PI was informed about these concerns before the meeting. PI's email response to these concerns was displayed in the meeting. It was further noted that even though PI's IACUC approvals are all current, the plan of work with RSV or influenza virus is not included in them. EHS confirmed that BSL2 level biohazard wastes maybe disposed of directly in the red biohazard boxes without prior disinfection. The Committee recommended that these concerns be addressed properly in the actual application.

- PI needs to be added to personnel list.
- It is not clear if anyone in the lab is experienced in handling respiratory BSL2 viruses. Please indicate who will provide training in RSV and influenza A virus cell culture and animal studies.
- Which adenoviral vectors will be used?
- Please provide more details regarding the experimental procedures involving RSV and influenza A virus. The procedure section of the amendment seems to only refer work with bacteria. For example, viruses do not form colonies.
- Is there an accompanying IACUC protocol covering the mouse work with RSV and flu? Details of amendments describing the use of viruses RSV and H1N1/H5N1 in animal experiments need to be included in the laboratory procedures.
- Will the viruses be propagated in the PI's lab? Will virus stocks be provided by collaborators and only used for animal work?
- Using a fume hood to handle biohazards is not acceptable. Fume hoods are not equipped with HEPA filters. Work with BSL2 biohazards must be done in a biosafety cabinet.
- Solid material that was in contact with RSV or influenza A virus (e.g. pipette tips) should be decontaminated before disposing of in the red waste bag. If 10% bleach is used for decontamination please indicate that the exposure time will be at least 30 minutes.
- It must be specified which H5N1 will be used. Only low pathogenic avian influenza virus (LPAI; North American H5N1) could be added to this protocol if they are classified as BSL2. Highly pathogenic HPAI H5N1 is classified as BSL3 and cannot be added to this protocol.
- It must be specified which H1N1 virus will be used.
- How can RSV be used to induce septic shock? This should be clarified in the procedure section.
- Adenoviral vectors must be added to recombinant DNA section.

Motion: Conditional Approval (Primary and Secondary Reviewer Review)	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 0