Boston University
Institutional Biosafety Committee (IBC)
February 16, 2024 Meeting Minutes
Location: Zoom and/or by phone
Start time: 11:30 AM End time: 12:32 PM

Members Present:	R. Ingalls, B. Slack, E. Muhlberger (joined 12:20 PM), R. Davey, V. Gouon-Evans, X. Brown, P. Liou (left 11:59 AM), E. Loechler (joined 11:45 AM), T. Winters, R. Morales, C. Thurman, J. Keeney, R. Timmerman, V. Britton (joined 12:10 PM), S. Ghosh
Guests Present:	C. Fernald, J. Wood, A. Ahmad, A. Broos-Caldwell, M. Fitzgerald
Staff Present:	C. McGoff, L. Campbell

I. Review of January 23, 2024 IBC Meeting Minutes (R. Ingalls)
No concerns were voiced.
Motion: Approved
For: 11; Against: 0; Abstain 1; Absent: 3

II. Chair's Report:

III. New Business:
A. IBC Office Updates: Nothing to report.
B. Incident Report: No incidents to report.
C. Review of Research Occupational Health Program (ROHP) Report: Nothing to report.
D. Environmental Health and Safety (EHS) Report: Nothing to report.

Senior Research Clinical Veterinarian of the NEIDL, C. Thurman, informed members that in the next three months the ASC will be adding additional research space for BSL3 animal work.

IV. Protocol Review

1. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2286	Elke Muhlberger	Virology Services Core - Propagating BSL4 Pathogens	4	N/A	BUMC
Primary Reviewer: Rob Davey		Secondary Reviewer: Robin Ingalls Additional Reviewer: Jim Keeney			
Applicable NIH Guidelines: Section III-D-1-a, III-D-1-b, III-D-1-c					
Meeting Comments: The goal of this protocol is to perform general work for propagation of viruses in the BSL4 for other groups. The work covers growth of wild type viruses as well as evaluation of recombinant viruses. However, the recombinant nucleic acid work is described on a separate IBC protocol. Since last full review, new students were added. Training documentation is excellent and clearly describes path for new trainees. DURC aspects are described and while recombinant work is not expected to generate viruses of altered tropism or pathogenesis, they will look out for such and have an action plan in place: Stop work, contact EHS and if decided, destroy the material. Some consolidation of protocols was done to improve readability. One new-world arenavirus has been added. Overall, the work involves propagation of BSL4 and some BSL3 pathogens (SARS-CoV and SARS-CoV-2) at BSL4. Some new cell lines have been added. Work may involve infection of cells with recombinant viruses produced from reverse genetics systems containing plasmids encoding virus genomes. Nucleic acids are developed through a separate protocol but transfection of cells with this material occurs in the current protocol. Viruses are grown following well established SOPs that define work at BSL4 and how materials are inactivated so they can be safely analyzed or can be disposed of. Inactivation involves heat and/or chemical treatment using formalin or TRIzol or other treatment. For disposal, treatment uses 5% Microchem Plus which is routinely used at similar facilities for destruction of virus. Inside the laboratory, the virus is also autoclaved before disposal down the sewer. Solids are autoclaved. A system to study					

aerosolized virus is used to better understand how viruses survive in the air. The device is a closed system that is housed in a BSC in the BSL4 and so, personnel are protected from exposure. After experiments, it is decontaminated using Microchem Plus or gas such as vaporized hydrogen peroxide.

BUA Site Assessment: Biosafety trainings are updated for all members. All biosafety cabinets are duly certified which are all taken care of by the EHS on a semi-annual basis. There is no EHS concern for this lab.

PI was not present in the meeting during discussion or voting on this protocol.

Motion: Approve	For: 12	Recuse: 0	Against: 0	Abstain: 0	Absent: 3

2. rDNA/Bhz –New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2635	Samagya Banskota	New Molecular Tools for Advancing Genome Editing Technologies	2	N/A	CRC

Primary Reviewer: Barbara Slack	Secondary Reviewer: Sajal Ghosh

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

Meeting Comments: This new protocol from a new investigator proposes to develop and design drug delivery approaches that works better than existing approaches. They want to use new scientific knowledge and advanced procedures in genome editing technology together with synthetic biology and protein engineering techniques in their approach. The other goal of their work is to develop genome and epigenome editing techniques to study the function of transposable elements that consists almost half of the human genome. Their laboratory work will include use of human cell lines, production of lentiviral, retroviral, and AAV particles, and sgRNA templates to target disease-related genes, CRISPR/Cas9 or CAs12 technology, and cellular imaging using immunochemistry or fluorescence staining. The rDNA sequences of interest will include regulatory regions and coding regions of nonpathogenic fungi, bacteria and viruses, and human, and animal DNA sequences. Vectors will be propagated in E. coli. Retroviral, lentiviral and AAV vectors will be packaged in HEK293 cells. Lentiviral and retroviral vectors will be packaged with the VSVG envelope protein. All viral vectors are replication-incompetent. The protocol carefully and extensively describes safety concerns for each individual laboratory procedure that they will be using. The need for the use of biosafety cabinets, sharps and engineering control to avoid risks of exposure to biohazardous materials are provided in great detail. Source of cell lines and viral vectors (AAV or lentiviral) are clearly described. The following will be communicated to the PI:

- Please include a list of the genes that will be targeted using CRISPR-Cas editing in the lab procedures section. Also, please add a broad statement on how various laboratory procedures described in the protocol are connected to the goal of developing better drug delivery tool or to the elucidation of function of transposable elements.
- Section A. Use of retroviral particles is mentioned in Lab Procedures, but they are not listed in the table.
- Section H (rDNA). If neuro-2A cells will be transfected or transduced with viral vectors, they should also be listed as host cells in the Eukaryotic section.

BUA Site Assessment: This is a new lab and still is being set up. All safety trainings are current. Biosafety cabinet is certified until June 2024. 3rd generation lentivirus system will be used in the lab.

Motion: Conditional Approval (Administrative Review)	For: 12	Recuse: 0	Against: 0	Abstain: 0	Absent: 3

3. rDNA/Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2634	Thomas Clarke	Identifying chromatin factors required for DNA repair using a novel, high-throughput screening methodology.	2	2	BUMC

Primary Reviewer: Valerie Gouon-Evans	Secondary Reviewer: Steve Niemi
Applicable NIH Guidelines: Sections III-D-1, III-D-2-a, III-D-4-a, III-E-1; Appendix B-II-D, G-II-B	
Meeting Comments: The goal of this project is to understand the impact of a particular cellular gene for DNA damage repair in human cells. The PI has just set up his lab in January 2024. He is the only person in his lab. All his bioraft trainings are up to date and his ROHP approval pending. They will achieve this by reducing levels of this protein in cells or increasing the level of protein gene in cells and assessing the effects this has on the ability of cells to repair DNA damage generated by various chemotherapeutic agents *in vitro* and *in vivo* in mice model. Using a novel high throughput screening methodology, this proposal aims to identify key chromatin factors required for (1) the repair of DNA damage and (2) the re-establishment of chromatin structure and function following DNA repair. They will use mouse embryo fibroblast, as well as several human cancer cell lines obtained from ATCC. Genetic manipulations of cells *in vitro* will be done by knockdown or overexpression of gene of interest using lentiviral vectors. The protocol also involves significant rDNA work in the lab involving rDNA cloning, transformation in E. coli and plasmid extraction. In some cases cell lines will be irradiated using multi-rad350 X-ray irradiator. Xenograft tumor models using engineered cancer cells will also be used to test efficacy of treatment with chemotherapeutic agents. Protocol also involves FACS analysis, cellular imaging and proteomic analysis. Overall, this was a nicely written protocol. The following will be communicated to the PI: • Please include brief statement of your plan of use of lentivirus vectors. Provide name, source, generation number, what they express and a broad statement of why you want to use them. • Remove the N95 PPE; not required for your work. • Provide certification date of the biosafety cabinet that you plan to use currently. You should provide the certification information for the new one, once you get it. • Remove E. coli from the hazardous biological agent list. • Since the protocol involves, cloning, and transformation, please complete the prokaryotic experiment section (host-vector-donor information) • Complete the Vector Packing information again in Eukaryotic Experiments section. • Since you will be injecting human cell lines as well as rDNA-modified cell lines in animals (xenograft experiments), you must complete the animal experiments section as well. • Your revise your response to questions 15 and 16. They be the opposite of what is stated now. • For the response to question 19, just state 'Section III-D-1-a, III-D-2-a, III-D-4-a and III-E-1'. BUA Site Assessment: The lab is currently being set up. 3rd generation lentiviral vectors will be used by the lab. The lab has a shared liquid nitrogen dewar at lab # [redacted] in the same larger space. N-95 respirator not needed. A new BSC is coming soon for the lab.	

Motion: Conditional Approval (Administrative Review)	For: 12	Recuse: 0	Against: 0	Abstain: 0	Absent: 3

4. rDNA/ Bhz – Annual Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2443	Florian Douam	Investigating host-pathogen interactions regulating the pathogenesis and immunogenicity of BSL-3 viral agents.	3	3	BUMC

Primary Reviewer: Sajal Ghosh	Secondary Reviewer: Colleen Thurman
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 goal of this protocol is to study how risk group 3 (RG3) viruses interact with their target cells and how such interactions cause disease in the host. The protocol hopes to use this knowledge of virus-host cell interactions in developing antiviral countermeasures. This is a nicely written protocol that provide details of each procedure and risk mitigation plans and has been reviewed multiple times during the past year for number of	

amendments. In this annual renewal PI is adding new personnel and removing personnel those are no longer in the lab. They are clarifying that the yellow fever virus (YFV) strains used in the study are Asibi and Dakar. Additionally, they are proposing to test in mice model the pathogenicity of number of chimeric viruses between YFV 17D vaccine strain and the pathogenic varieties (Asibi and Dakar) created in the laboratory of collaborator in the Princeton University in mice. Committee expressed concerns that this submission does not provide details of the genomic segments exchanged in these chimeras. It was recommended that for the purpose of proper risk assessment the protocol must provide clear plan in the event any of the chimeras display enhanced pathogenicity than the parental viruses. The following will be communicated to the PI:

Committee reiterated that use of recombinant form of any pathogenic viruses or any other pathogenic microbes must be approved by the IBC prior to their use in the laboratory. Since Yellow Fever Virus (YFV) has the potential to cause serious disease in humans, and the pathogenicity of the requested chimeras are yet unknown in animal models, approval of request to use recombinant YFV may be subjected to review by the DURC/P3CO subcommittee at the recommendation of the IBC. Committee recommends that the following must be addressed with sufficient clarity:

- In the laboratory procedure section describe the nature of gene swaps in all the chimeric viruses that will be received from the collaborator.
- Please provide a safeguard statement of when the lab would pause if variants start showing more virulence.
- The committee felt putting Asibi/Dakar gene segments in 17D backbone, as stated in the application, may raise serious safety concerns. Please clarify that it is indeed the plan. If so, please justify why that is needed.
- If there are published data on *in vitro* pathogenicity of the exact clones that will be received, please provide them.
- Complete the DURC Section of the IBC application (specifically questions 3, 4, 5, and 6). State what is unknown, what could happen and how would you deal with the worst possible scenario. Depending on your response, we may send the revision to the DURC/P3CO subcommittee for their review.
- Will the lab be doing any retro-orbital (RO) injections? If IV administration will be done via retroorbital method (not just tail vein), it should be described in Experimental injections in Mice (VII. 3. VII. 1.). This method has not yet been added to [redacted] under Intravenous injection.
- Does the lab intend to do viral infections using the mosquitoes using the insectary at this time (ACL2 or ACL3) or if this project continues to be injection only?
- Update Biosafety Cabinet certification date (if all have same certification date, indicate so. If not, state the dates individually).

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

5. Bhz – Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
2356	Anthony Griffiths	Testing medical countermeasures against high consequence pathogens in non-human primates.	4	4	BUMC

Primary Reviewer: Elke Muhlberger	Secondary Reviewer: Colleen Thurman

Applicable NIH Guidelines: N/A

Meeting Comments: The overall goal of this protocol is to test the efficacy of vaccination and antiviral countermeasures for risk group 4 (RG4) pathogens in animals. Since outbreaks caused by RG4 pathogens are sporadic and unpredictable, human clinical trials for those diseases are difficult to conduct and could be unethical. Animal studies could therefore be the only alternative for development and refinement of medical countermeasures. This is a nicely written protocol that has been reviewed multiple times by the IBC in last few years. In the current amendment PI is only adding one recombinant virus, called Lloviu virus. No live virus has been isolated yet for this virus. But all available information available so far indicate that it is related to filovirus but with minimal pathogenicity. Nevertheless, PI proposes to work with this virus in BSL4 containment in the same way as with other

filoviruses from a biosafety perspective. The NEIDL animal research service (ARS) section will perform all animal experiments on behalf of the PI. ARS has their own IBC approval for handling animals infected with RG4 agents. No additional concerns noted.					
Motion: Approve	For: 14	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

V. List of Protocols reviewed by DMR (not discussed in the meeting)

A list of protocols that were reviewed by DMR was displayed in the meeting.