Boston University
Institutional Biosafety Committee (IBC)
February 14, 2023 Meeting Agenda
Location: Zoom and/or by phone
Start time: 12:00 PM End time: 2:26 PM

Members Present:	R. Ingalls, B. Slack, I. Afasizheva (left 1:54 PM), E. Muhlberger, R. Davey, W. Lu, T. Winters, E. Loechler (joined 12:04 PM), J. Keeney, R. Timmerman, V. Britton Z (joined 12:07 PM), J. Barton, N. Dey, S. Ghosh
Guests Present:	A. Ahmad, A. Broos-Caldwell, J. Wood, T. Killeen, M. Fitzgerald
Staff Present:	C. McGoff, L. Campbell

I. Review of January 24, 2023 IBC Meeting Minutes

No concerns were voiced.
Motion: Approve
For: 13; Against: 0; Abstain: 0; Absent: 1

II. Chair's Report:

Dr. Ingalls informed the committee that a meeting was held with the IBC office staff, the Chair and some members of the Dual Use Research of Concern (DURC) subcommittee, along with NEIDL Biosafety Officer, to discuss how the latest NIH NSABB Potential Pandemic Pathogen Care and Oversight (P3CO) pending recommendations be integrated into the current BU IBC review processes.

III. New Business:

A. SQAP Report:

- Update to DURC Committee
  Members were informed that the DURC subcommittee's scope will be expanded to more specifically address ePPP (enhanced potential pandemic pathogens) research; a working group of the current DURC subcommittee has made recommendations related to changes to RIMS IBC applications, and other administrative processes. Members also made other suggestions to help clarify the identification of viruses when completing an IBC application.

B. Review of Research Occupational Health Program (ROHP) & Environmental Health and Safety (EHS) Incident Report: No reportable incidents.

IV. Protocol Review

1. rDNA/Bhz – New Application

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: Rob Davey		Secondary Reviewer: Elke Muhlberger Additional Reviewer: Steve Niemi			
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 identify and characterize important virus-host interactions that regulate the virulence, host range and immunogenicity of several RG3 viruses, including members of the Flaviviridae and Coronaviridae family, and knowledge gained from the study of these interactions will be used to develop anti-viral countermeasures. In this current renewal they also are adding infection of mice with HIV-1, for which ready to use virus stock will be obtained from another BU colleague who has elaborated HIV-1 research program. The IACUC approval is indicated as pending. This renewal also adding human cell lines iPS-cell derived macrophages and the					

source of recombinant SARS-CoV-2 coronaviruses which will used in animal experiments. The HIV-1 infection work will be done in BSL2+ and ABSL2+ containment and processing of tissues infected with HIV-1 will be done in the BSL3 containment. The personnel list is updated to add new trainees. PPE appears appropriate for the work being done. Work is performed in BSL2 BSC with current certification date. Needles are used once and then disposed of appropriately in sharps containers. Transport of biohazardous materials will be in screw-capped tubes placed in shatterproof secondary container. The following will be communicated to the PI:

- Since [redacted] will no longer do any BSL3 work, please remove her as lab safety coordinator and include someone who will be working in the BSL3.
- ChemSafe training update required for Feitosa.
- The BSL2+ lab and the storage room for HIV on the [redacted] must be added to the research space information.
- It is stated that the work will be performed in BSL2+ and ABSL2+ containment. Please define these level 2+ practices that will be followed in this work.
- Please provide a statement on the purpose of adding proposed HIV-1 work to the protocol.
- It is proposed to generate recombinant viruses containing mutations or reporter gene insertions. Please add a statement that a list of all recombinant viruses will be compiled describing the insertions and mutations, and that this list will be made available to EHS/IBC upon request.
- State if the use of mutant viruses would require additional risk mitigation plan.
- Please add the source of the primary human cells and if they will be isolated from blood. It is not described what the primary human cells will be used for. This should be added.
- Please clarify if the proposed mutagenesis of the viral genomes and the in vitro transcription is covered by another BSL2 IBC protocol. If not, the respective BSL2 space, the cloning procedures, and the *in vitro* transcription processes must be added to this protocol.
- Hazardous material – HIV-1 should be indicted as "BSL2 with BSL3 practices" in the Hazardous Biological Agents list.
- Primary human cells (macrophages etc.) should be listed in the "Other Potentially Infectious Materials" section.
- The recombinant DNA section must be updated. The recombinant positive sense RNA viruses that will be generated or are already used according to the Laboratory Procedure section are not listed in the eukaryotic donor section. These viruses are replication-competent and genetically engineered and must be added in the Eukaryotic Experiment section.
- Use of recombinant viruses to infect animals must be added to the Animal Experiments section.

BUA Site Assessment: A different Laboratory safety coordinator needs to be listed. Training records for all but one members listed on the protocol are current. The Biosafety cabinets are duly certified. The labs listed in the protocol ([redacted], [redacted], and [redacted]) were last inspected January 2023.

Motion: Conditional Approval (Primary and Secondary Reviewer Review)	For: 14	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

2. rDNA/Bhz – Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2442	Mohsan Saeed	Investigating the role of viral proteins in disease pathogenesis	3	N/A	BUMC
Primary Reviewer: Elke Muhlberger		Secondary Reviewer: Robin Ingalls			
Applicable NIH Guidelines: Sections III-D-1-b, III-D-2-a, III-D-3-b; Appendix B-III-D and G-II-C for experiments described in this protocol					
Meeting Comments: The goal of this protocol is to analyze cell culture infection of several RG3 viruses including arboviruses, SARS and MERS coronaviruses, as well as SARS-CoV-2. They propose to infect human or non-human					

primate cell lines and iPS cell derived cells to study the interaction of virus proteins and host cell proteins. They also study recombinant SARS-CoV-2 viruses to understand attenuation mechanisms in SARS-CoV-2 Omicron variant using chimeric viruses. Virus stock cultivated in mammalian cells or generated by transfecting viral genomic RNA into mammalian cells. General lab practices including waste disposal follow approved BSL3 SOPs. Personnel experience and training seems adequate. This protocol has been reviewed by the IBC multiple times in recent months and the committee assessed that there are no additional biosafety concerns. However, it was recommended that there should be greater clarity of the work that is being performed with clear description of recombinant viruses being used in the protocol. The following will be communicated to the PI:

- The brief project description is too long. It needs to be significantly brief.
- Committee suggested the PI to review the entire write up and remove those statements that are no longer valid. Also remove all individual amendments paragraphs and merge them as part of broader research objective and state what is currently being done and what are immediate future plan. For example, it is stated that "We currently have no plans to insert mutations into the SARS-CoV-2 genome." However, subsequent amendments have been approved for such work. This sentence should be deleted and perhaps replaced with a statement such as "mutations in the genome are planned as detailed below" (or something like that).
- For clarity, please add a sentence to the effect of: "There are no animal studies directly carried out as part of this IBC protocol" (or something similar) on section where Dr. Douam's animal work is mentioned.
- This protocol describes the generation and use of many recombinant BSL3 viruses. It should be stated that a list of all recombinant viruses will be compiled describing the mutations, and that this list will be made available to EHS/IBC upon request.
- What is meant with "ancestral backbone"? Washington strain? Please clarify.
- What is the CPER platform? Please clarify.
- Since West Nile virus is no longer considered as RG3 virus according to BMBL6, downgrade the BSL level to BSL2.
- The generated recombinant viruses should be listed in the rDNA DONOR section.
- The BAC vectors must be added to the rDNA section. The BAC vectors are DNA-based.
- The rDNA section – Question 3 should be answered with yes since pathogenic polynucleotides or polypeptides (namely viruses) will be generated in this protocol.
- In the PPE section, please check the box for "other" since additional PPE is described in the free text box.
- Please update BSC certification date.
- In the disinfectant section, please add "fresh" or "freshly prepared" to the 10% bleach.

BUA Site Assessment: The listed laboratory safety officer needs to be replaced. All members listed on protocol are updated on their training records. Please add BSCs with serial numbers [redacted] and [redacted] to the protocol. The Biosafety cabinets listed are duly certified. The labs listed in the protocol ([redacted], [redacted], and [redacted]) were last inspected January 2023.

Motion: Conditional Approval (Primary and Secondary Reviewer Review)	For: 14	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

3. rDNA/Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2597	Meg Younger	The molecular basis of olfaction in mosquitoes	2	N/A	CRC
Primary Reviewer: Sajal Ghosh			Secondary Reviewer: Inna Afasizheva		
Applicable NIH Guidelines: Sections III-D-1-a, III-D-2-a					
Meeting Comments: The long-term goal of this protocol from a new faculty member in the Biology Department in CRC is to investigate how mosquitoes detect human smell and how that affects their search for a human to bite. Female mosquitoes rely heavily on human blood feast for reproduction. PI is particularly interested in identifying					

interaction of chemicals from human odor to the sensory receptors in mosquito brain and how it dictates biting behavior. This will be done by expressing wild type or mutant olfactory receptor genes from *Aedes aegypti*, some of which also encode fluorescent proteins like GFP or GCaMP in cell culture model as well as in transgenic mosquitoes and subjecting them to various odorants. They will create transgenic mosquitoes with mutant olfactory receptors by using CRISPR technology with the help of an off-site company. They clarified that their study has no concern for gene drive situation as they are not introducing any Cas9 gene, but only the protein and guide RNA in mosquito embryo and in fact, the new mosquitoes will not be able to survive or reproduce outside the lab. The biosafety risks in this protocol are use of human cell lines and regulatory requirements for the rDNA work. Liquid waste will be treated with bleach for 30 minutes and solid waste will be discarded in red biohazard boxes. No viral vectors will be used. Prokaryotic and Eukaryotic rDNA work has been clearly identified. The committee noted that a new insectary for mosquito work for the PI is under preparation, although PI has temporary arrangement for all her planned mosquito work. The committee wanted a detailed description of PI's current mosquito work facility and how exactly the live mosquito work will be done in that facility. Especially committee wanted to know what measures will be in place to confirm that no genetically modified mosquito can escape the workplace and make progenies. The following will be communicated to the PI:

Committee expressed concerns that the current description of laboratory procedure does not provide a clear view of the facility for working with live mosquito, especially the containment issues.

- Please describe in detail the facilities available to you to do the live mosquito work.
- Describe how the mosquitoes are grown and maintained in your lab.
- What safeguards are available to prevent escape of any mosquitoes from your current insectary space in the lab? This information is particularly required for risk assessment as some batches of mosquitoes will be recombinantly modified species.
- Please clarify if you have received clearance from the EHS for live mosquito work (including work with recombinantly modified mosquitoes).
- It is stated in the Laboratory procedure section that "We never generate mosquitoes that are dangerous or have increased fitness relative to wild-type mosquitoes. If anything, the animals we generate would be unlikely to be able to survive and reproduce outside the lab." Why would the recombinant mosquitoes not be able to survive or reproduce outside the lab? Please clarify.
- Section VII.3 – Clarify if live mosquitoes will be transported to other lab or facility for analysis (such as fluorescence microscopy or behavioral analysis). If so, provide more information about how they will be kept contained during the procedure.
- Section VIII.7a – Bleach concentration should be 10% final.

BUA Site Assessment: The mosquito work will be conducted in Arthropod Containment Level 2 (ACL2). The construction of a permanent ACL2 facility for the lab is under construction. The mosquitoes and associated waste are currently inactivated by freezing the waste for 24 hours and the resulting ice block is then allowed to thaw in the sink.

Motion: Conditional Approval (Primary and Secondary Reviewer Review and review by NEIDL investigator with ACL expertise)	For: 14	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

4. rDNA/Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2600	Stephanie Puig	Understanding the mechanism underlying opioid-mediated side-effects	1	1	BUMC
Primary Reviewer: Barbara Slack			Secondary Reviewer: Steve Niemi		
Applicable NIH Guidelines: III-D-4-a, III-E-1					

Meeting Comments: The goal of this protocol from a new investigator in BU is to study the brain neurological circuits that are involved in mediating the response to opioids including side effects and addiction. They specifically will study the characteristics of dopaminergic neurons in the brain as they are known to play a role in opioid addiction. They will use transgenic mouse model where activities of these neurons will be investigated by conditional expression of neurotransmitter receptor genes using *cre* recombinase and tissue-specific promoters. These genetic manipulations in the rodent brain will be done through the use of AAV8 vectors. In some cases, transgenic mice with appropriately positioned *flox* gene will be used in conjunction with *Cre*-expressing AAV vectors to ablate specific dopamine receptor. Opioid-mediated behavior and side-effects will be evaluated under these modified conditions. AAV virus particles will be obtained from Addgene. The post-doc who will perform the injections is experienced with this technique. The following will be communicated to the PI:

- Section VII.2- Project description mentions evaluating opioid-mediated behaviors, but no information is provided regarding the drugs that will be used. Please provide some information about which drugs will be used, if any, and how they will be handled and disposed of.
- Section VII.3 (Lab Procedures)- The paraformaldehyde should be handled in a fume hood. Please confirm that this is the case.
- Section VIII.4- check shoe cover for work in animal containment?
- Section VIII.5 - Verify certification date of BSC.
- Section VIII.8- The only disinfectant listed is 70% ethanol. Ethanol is not adequate for surface decontamination of non-enveloped viruses (such as AAV). 10% bleach would be more effective for this purpose.
- Section IX. Live animal used should be checked, since animals will be injected with AAV virus (and possible opioid compounds?).

BUA Site Assessment: AAV waste and AAV contaminated surfaces should be disinfected with fresh 10% bleach with 30 minutes contact time. Cryotome SOP is not available in the lab. The lab doesn't have AAVs right now. The Biohazard waste box should be double lined. The liquid bio waste will be first disinfected by adding fresh bleach to final 10% Bleach.

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

5. rDNA/Bhz – Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
2231	Nelson Lau	Genomic and biochemical studies of Piwi proteins and piRNA regulation mechanisms	2	2	BUMC

Primary Reviewer: Sajal Ghosh	Secondary Reviewer: Ron Morales

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

Meeting Comments: The main goal of this protocol is to study how Piwi-pathway proteins interact with Piwi-interacting RNAs (piRNAs) and such interaction regulate and silence the activity of transposable elements. PI is already approved for such molecular biological studies with drosophila cells, mosquito and human cell lines as well as human tissues. He also had been using xenopus tropicalis frog before, but that is now replaced with Betta Splendens 'Koi' fish. He also wants to examine how virus infection of mosquito cells generate small piRNAs in them. In this amendment PI plans to infect mosquito cell lines with Dengue and Zika viruses in his K-building research lab and clarified that all safety concerns associated with this virus work will be reviewed by all researchers in PI's lab and other members who share the same laboratory rooms, biosafety cabinets and incubators. All hoods and work surfaces will be thoroughly disinfected as recommended. Other users of the TC room will be alerted when Dengue and Zika virus work will be performed and signage will be posted on the door. All members of the PI's lab and other users of the TC room will receive counsel from ROHP before they commence this project, and their PPE will include latex gloves, lab coats and safety goggles/glasses when conducting virus work. PI's lab will develop a Standard Operating Procedure for their virology work in consultation with the EHS. It was noted that one of the NEIDL

collaborator listed in the protocol no longer can actively participate in any protocol activities and also do not want to remain in the protocol. Since she is the only person listed with any experience and expertise with zika and dengue virus work, committee recommended that the person be removed from the personnel list and all proposed work with Zika and Dengue viruses be suspended until PI or his current lab members receives hands on training on working with these highly pathogenic viruses. The following will be communicated to the PI:

Committee requested and subsequently received clarification from the PI and the NEIDL investigator listed in the protocol that the NEIDL personnel can no longer collaborate or support the virological work described in the protocol at present. Based on this clarification IBC recommends that:

- Remove [redacted] from the personnel list.
- All proposed work with Zika and Dengue virus must be removed from the protocol for now (in Section VII and Section A). If you currently possess Zika and Dengue viruses, please make sure to mention that the virus stocks will NOT be handled in your lab until lab members have received appropriate training on working with those viruses.
- Add any new personnel that you may have plan to assign virological work responsibility and send that revision in RIMS. IBC will review and make approval decision on that personnel change revision.
- Separately, please arrange to get hands-on training on working with highly pathogenic viruses (including arboviruses/flaviviruses, if possible) from a lab that works these viruses. This should include basic procedures on virus growth, virus stock preparation and tittering them to be used in repeatable experiments, safe handling techniques of the virus infected cells, processing them for downstream experiments, disinfection of virus-contaminated liquid and solid wastes and their disposal, use of proper PPE during manipulation of virus-infected cells.
- After the above training has been received, please send a new amendment to add the zika and dengue virus work including detail description of the virology work and a letter from whom you might have receive the training. This submission will be subjected to further review by the IBC.
- Seek help from the IBC office if needed, in the submission of revised application with specific removal of any reference to Zika/Dengue work throughout the application.

Motion: Conditional Approval (Primary and Secondary Reviewer Review)	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

6. 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: Rob Davey	Secondary Reviewer: Tom Winters Additional Reviewer: Steve Niemi

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: The original protocol experiments with flaviviruses, studying disease models and immunity for Yellow fever, Dengue, Zika and Hepatitis C. This protocol also uses mosquitoes infected with virus to infect animals. In this amendment HIV-1 work in mice is added. This work is performed in the BSL3 lab. The virus will be obtained from BU Department of Microbiology collaborator Dr. Gummuluru. The IACUC is indicated as pending. Also added in this amendment is the mouse work with Dengue virus infected mosquitoes. Mosquitoes are handled in a specialized insectary that is set up to control escaped mosquitoes. It is unclear where the mice will be held while being bitten with the mosquitoes. Committee recommends that it should be in the insectary or in some other containment to prevent escape of mosquitoes. Human macrophage cells are added and listed in the hazards section. The amendment also updated personnel list to remove one and add a new trainee. Training will be done by Dr. [redacted], who is experienced with working with mosquitoes and arboviruses. PPE appears appropriate for work being done. Work is

performed in BSL2 BSC with current certification date. Needles are used once and then disposed of appropriately in sharps containers.
Transport of biohazardous materials will be in screw-capped tubes placed in shatterproof secondary container.
The Medical Director clarified that men or women of reproductive age are required to review the Zika Virus-specific Agent Training module in BioRAFT. A confidential medical reproductive hazard consultation can be requested at any time by contacting ROHP. If accommodation in the work environment is being considered, a consultation and referral to the Equal Opportunity Office can be made. The following will be communicated to the PI:

- What is the scientific objective of adding HIV-1 work in this amendment (put in VII.1 and VII.2)
- Specify if monocyte-derived macrophages are being prepared in PI's lab or are received already prepared by another PI or source. If it is the first, clarify if the blood received for preparing macrophages was screened for presence of infectious agents like HIV1, HepB etc.
- If room [redacted] is being used for HIV1 infection of mice, please state what "ABSL2 with ABSL3 (ABSL2+)" practices are being followed.
- State where exactly the infection of mice with viruses (via mosquito bite) is being done. Is it in [redacted] insectarium or [redacted] animal room? Please emphasize prevention of mosquitoes escaping with the mice by providing more description on experimental set up. If a specific SOP is being followed for this experiment, please cite the SOP number.
- Please make sure that members of the protocol (men or women of reproductive age) take the Zika virus agent-specific training module in BioRAFT. Please also add this statement in the "A. General Laboratory practices in BSL2" section of the lab procedure (Section VII.3).

Motion: Conditional Approval (Administrative Review, BSL3 BSO will check the resubmission)	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

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

List of protocols (below) that are currently being reviewed by DMR was displayed in the meeting.

1. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2190	Mary Dunlop	Feedback, Noise, and Dynamics in Synthetic and Natural Gene Circuits	2	N/A	CRC
Primary Reviewer: Ed Loechler		Secondary Reviewer: Bob Timmerman			
Applicable NIH Guidelines: Section III-F (exempt experiments); Appendix B-I and C-II					

2. Bhz – Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1782	Xin Zhang	Cell Force Sensing siRNA Loaded Hydrogel Nanoparticles Impedance Sensing Fabricated Computed Tomography Contrast Agents Scalable Nanomanufacturing	2	N/A	CRC
Primary Reviewer: Pinghua Liu		Secondary Reviewer: Valeda Britton			
Applicable NIH Guidelines: N/A					

3. Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus

2426	Elizabeth Stier	H-33380: ANCHOR Study: Anal Cancer/ High-grade squamous intraepithelial lesions (HSIL) Outcomes Research Study. H-36335: AMC 088: A Randomized, Phase III Study of Intra-Anal Imiquimod 2.5% vs. Topical 5-Fluorouracil 5% vs. Observation for the Treatment of High-Grade Anal Squamous Intraepithelial Lesions in HIV-Infected Men and Women. H-35739: AMC 092: A multicenter observational and feasibility study of excision of superficially invasive squamous cell carcinoma (SISCCA) of the anal canal and perianus in HIV-infected persons.	2	N/A	BUMC
Primary Reviewer: Tom Winters		Secondary Reviewer: Jim Keeney			
Applicable NIH Guidelines: N/A					

4. rDNA/Bhz – Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2437	Mark Grinstaff	Relaxin-2 as a treatment for hypertrophic and keloid scar formation	2	1	CRC
Primary Reviewer: Barbara Slack		Secondary Reviewer: Steve Niemi			
Applicable NIH Guidelines: Sections III-D-1-a, III-D-2-a, III-D-4-a, III-E-1; Appendix G-II-B					

5. Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1136	Naomi Hamburg	Research Program in the Coronary Health Unit	2	N/A	BUMC
Primary Reviewer: Inna Afasizheva		Secondary Reviewers: Jim Keeney			
Applicable NIH Guidelines: N/A					

6. Bhz – Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
964	Michael Sorenson	Molecular Systematics and Population Genomics of Birds	2	N/A	CRC
Primary Reviewer: Robin Ingalls		Secondary Reviewer: Ron Morales			
Applicable NIH Guidelines: N/A					

VI. List of approved Protocols since last IBC meeting (since the 1/24/23 Meeting)

A complete list of protocols approved by the IBC since the last IBC meeting on 1/24/23 was provided to the members before the meeting and also was displayed in the meeting.