Boston University
Institutional Biosafety Committee (IBC)
May 23, 2023 Meeting Minutes
Location: Zoom and/or by phone
Start time: 12:00 PM End time: 2:17 PM

Members Present:	R. Ingalls, B. Slack, E. Muhlberger, R. Davey, I. Afasizheva, W. Lu, T. Winters, E. Loechler (joined 1:03 PM), R. Morales, C. Thurman, S. Niemi, R. Timmerman, V. Britton, N. Dey, S. Ghosh
Guests Present:	G. Madico, A. Ahmad, M. Fitzgerald, K. Tuohey, P. Richmond, E. Ercolino
Staff Present:	C. McGoff, L. Campbell

I. Review of April 25, 2023 IBC Meeting Minutes

No concerns were voiced.
Motion: Approve
For: 14; Against: 0; Abstain: 0; Absent: 1

II. Chair Report:

- The Chair did not have anything to report; suggestions were made to IBC staff on way to clarify project summaries when reviewing submissions and a proposal for updates to the rDNA section in RIMS. The Chair introduced E. Ercolino from BUMC Facilities who will be attending IBC monthly meetings as a guest until the new BUMC Facilities Management Executive Director is hired.

III. New Business:

A. IBC Office Update:
- Members were informed that a draft of the PC3O guidance is being reviewed by members of the Dual Use Research Review Committee (DURRC).
- Members were informed that the updated Research Compliance website has gone live and the link to the IBC section of the website will be sent to all IBC members.

B. Incident Report:
- Members were provided with a summary of an incident involving a small laceration/glove tear by EHS employee, who does biocontainment and decontamination work in the NEIDL. The NEIDL Chief Safety Officer informed the committee that the NEIDL after action report will be presented at Grand Rounds; the incident has been shared with the BPHC. IBC members requested that an after action report be shared with the committee when it is received.

C. Review of Research Occupational Health Program (ROHP) Report: Nothing to report.
D. Environmental Health and Safety (EHS) Report: Nothing to report.

IV. Protocol Review

1. rDNA/Bhz – Annual Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
875	[redacted]	Genetics of Host Resistance & Susceptibility to Tuberculosis	3	3	BUMC
Primary Reviewer: Rob Davey		Secondary Reviewer: Colleen Thurman Additional Reviewer: Aditi Broos-Caldwell			
Applicable NIH Guidelines: Sections III-D-1-a, III-D-1-b, III-D-2-a, III-E-1; Appendix B-III-A, G-II-C					
Meeting Comments: The protocol uses mouse model of tuberculosis to study anti-tuberculosis host defense mechanisms in the lung. They study gene mutations that make individuals susceptible to pathogen growth and ultimately the tuberculosis, with a long-term interest in developing better therapies for the disease. They study avirulent vaccine strain *Mycobacterium bovis* performed at BSL2. They also are working with other BSL2 Mycobacteria as well as *Francisella tularensis* vaccine strain. The protocol also include work with BSL3 strains of *M. tuberculosis*, some of which are recombinant stains that express fluorescent proteins. All work is done in a class II					

BSC, which is appropriate. Infection of mice is done by aerosol. Some nanoparticle work is also being done. Waste will be collected and treated with fresh 10% bleach or Vesphene (1%). Solid waste will be put into red bags. Mouse tissues are treated with formalin to inactivate bacteria. Recombinant work will involve expression of some non-oncogenic genes in Human HEK293 cells and primary mouse cells using 3rd generation pHAGE lentivirus vectors. The protocol remains well written from the aspects of personnel training and detailed description of the work being performed. In this current annual renewal application, only two new personnel are being added and two personnel are being removed. The following will be communicated to the PI:

- Please update description Suruchi Lata as it does not show where experience was obtained.
- III. 1. If ARS personnel will be helping with ABSL3 experiments with Mtb infected mice, please add to list. ARS Technicians with independent access to [redacted] include [redacted], [redacted], [redacted]. Additional ARS personnel with access include [redacted], [redacted]. If new veterinary pathologist [redacted] will help with necropsy in BSL3/ABSL3, please add her as well.
- Mice are housed in ventilated cages. Does this mean microisolated cages? If so, would be best to change to "microisolated cages with HEPA filters" to avoid confusion.
- VIII. 5. Update BSC certification
- Please note that PROTO[redacted] doesn't yet include *Franciscella tularensis* vaccine strain, as stated in Section A.4.

Members voted that this protocol be reviewed at the three-year renewal and will not require an annual review.
Vote: For: 14; Recuse: 0; Against: 0; Abstain: 0; Absent: 1

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

2. rDNA/Bhz – Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
2352	[redacted]	Propagation and characterization of viruses	4	N/A	BUMC

Primary Reviewer: Robin Ingalls	Secondary Reviewer: Guillermo Madico

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

Meeting Comments: The goal of this study is to receive and then grow variety of risk group 4 viruses, including Filoviruses (including Ebola, Sudan, etc.), Lassa, CCHF, etc. Additionally, they will investigate the biology of coronaviruses with a view to developing medical countermeasures. In this amendment they request to obtain Lloviu virus, a filovirus isolated from bats with unknown disease capability in humans. This virus will be handled at BSL4 containment, similar to other filoviruses. This is not a new virus in the Boston University as work with this virus has already been approved for other investigator in the NEIDL. The amendment also is adding procedures for the use of glass coverslips to be used with chamber slides (plastic/glass) which are handled only with forceps, fixation and subsequent immunofluorescence analysis. Four new members are also being added to the protocol. The following will be communicated to the PI:

- It was noted that the coverslip use procedure in the NEIDL-BSL4 is covered by a specific SOP. Please provide that SOP number and statement that this SOP will be used in your protocol.

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

3. Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2607	[redacted]	Automation for Organoid Culturing and Development	2	N/A	CRC

Primary Reviewer: Barbara Slack	Secondary Reviewer: Ron Morales

Applicable NIH Guidelines: N/A

Meeting Comments: The goal of this project is to develop a protocol to culture organoids from cell lines with fibroid or myometrial characteristics with the goal of automating the process using robotic instrumentation. The long term goal is to develop a model to test therapies for fibroid diseases. Biohazards in the protocol are human cells lines and primary human fibroid and myometrial cell lines purchased from ATCC. Standard manual cell culture techniques will be used. The later steps will be carried out by a robotic instrument. Cells will be fixed and stained for imaging. This will be done both manually and by robot. Imaging will be done by confocal microscopy in the imaging core facility. Analysis of live or dead cell will be done by Cell Viability assay kit (Millipore) and assay by fluorescence microscopy. This is a simple straightforward protocol. The following will be communicated to the PI:

- Section III.3- Personnel: ROHP clearance needed for [redacted]. The PI BSL1/2 training lapse on 5/23/23
- Section VII.3-Lab Procedures: How will the cells be fixed? If paraformaldehyde will be used, please describe safety precautions: (use of fume hood/ disposal as hazardous waste).
- Section VIII.3- PPE: safety glasses should be checked.
- Section VIII.7A- liquid waste. Please add that liquid waste that does not contain hazardous chemicals will be handled of by adding fresh bleach to a final concentration of 10%, and allowing solution to stand for 30 minutes (not 20 minutes), before being disposed of in the sink. (Note- this is indicated in the Lab procedures section, but not in Section VIII.7).
- Section VIII.7A- Please provide a brief description of robotic system and what is meant by “contained system”.
- Section VIII.7A- Please provide a brief description of the process for routine cleaning of the robotic equipment and frequency.
- Section VIII.7B-solid waste: please specify that biohazardous waste will be disposed of in cardboard boxes double-lined with red biohazard bags, the bags taped or tied shut when 3/4 full, and the box closed and taped shut for pick-up by custodial staff.
- Section IX. The human uterine fibroblasts and smooth muscle cells are primary cells isolated from donors, so should be listed as ' Other Potential Infectious Materials". The box should be checked and related information added to the table (Section B) that will appear once the box is checked.
- Section A/B. The cell lines and primary cells listed in the tables should designated BSL2 and handled accordingly. [It is noted that the ATCC website lists all of these as BSL1; nevertheless, because of the potentially infectious nature of human cells, the BMBL recommends that "At a minimum, human and other primate cells should be treated as potentially infectious and handled using BSL-2 practices, engineering controls, and facilities" (Appendix H, p. 468; 6th edition)]. Further, it is BU’s policy that all human or NHP cell lines or any primary materials be handled in BSL2 containment.

BUA Site Assessment: Both biosafety cabinet and fume hoods are duly certified, although flow speed in one fumehood is low. Facilities have been notified and it will be fixed soon. Eye protection is recommended for the work.

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

4. Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2604	[redacted]	Tailoring Mechanical Microenvironments in Bone Regeneration	1	1	CRC

Primary Reviewer: Weining Lu	Secondary Reviewer: Steve Niemi

Applicable NIH Guidelines: N/A

Meeting Comments: This new IBC protocol aims to study how mechanical microenvironment of bone marrow stromal cells regulates various aspects of bone healing and aging affects the process. The 3D-printed hydroxyapatite scaffolds will be used to create mechanical microenvironment for young and aged mouse cells. They plan to identify which microenvironments are most beneficial to osteogenesis in order to inform future scaffold designs. A collaborator will provide mouse marrow stromal cells (MSCs) and 3d printed hydroxyapatite scaffolds. The mouse marrow stromal cells will be seeded onto the scaffolds and cultured in a bioreactor system inside the BSC. Periodic media changes will

be performed within the BSC. Following culture of these stromal cells, the scaffolds will be fixed in 4% paraformaldehyde solution, imaged using micro-computed tomography, and processed for histological and fluorescence immunohistological analysis. 10% bleach will be used to sterilize liquid waste. 10% bleach or 70% ethanol will be used to clean/sterilize contaminated equipment and surfaces when necessary. All procedures will be performed using appropriate PPE. The protocol did not appear to involve use of any biohazardous materials or recombinant DNA material. The committee determined that IBC approval is not required for proposed activities. However, the protocol is being approved in case PI wants to use any human cells or other biohazardous material in near future. No renewal will be necessary if the current research plan does not change in future.

BUA Site Assessment: The lab is using cryotome in Gerstenfeld lab, where they use cut resistant gloves. The lab members will be trained by a histologist. It was noted that the lab picks up frozen mouse primary cells from BUMC and transports them to CRC for work.

Motion: Approved	For: 14	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

5. rDNA/Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2611	[redacted]	Cellular Mechanisms of Antidepressant and Opioid Drug Actions in Models of Chronic Pain	1	1+	BUMC

Primary Reviewer: Robin Ingalls | Secondary Reviewer: Steve Niemi

Applicable NIH Guidelines: Sections III-D-4-a, III-E-1

Meeting Comments: The goal of this new protocol is to study the behavioral and biochemical effects of opioids in mouse models of chronic pain and analgesia. They will compare clinically used opioids, such as oxycodone, methadone, fentanyl and morphine, and investigates their brain specific actions. They will use viral gene transfer methodologies to knockdown genes of interest by infection of specific brain regions with AAV2Cre vectors that express various regulators of G protein and epigenetic modifiers. Sufficient detail is provided in the description but not always in the correct section. Layman's description was too long and contained significant amount of scientific detail. Similarly, scientific project description section contained excessive procedural detail. However, the protocol provided clear description of all procedural detail and personnel safety and risk mitigation plans were well described. The following will be communicated to the PI:

- There is duplication of PI's name in the personnel list. Please remove one.
- The [redacted] is room for elevator. Please put correct Vivarium room number.
- Layman's description is too long and technical. Please shorten the section to 3-4 sentences and simplify. Should be similar to the "narrative" of an NIH grant. There is no need to list all the specific genes and opioids of interest, and should not list the technical names of the behavioral assays being performed (Von Frey, locomotor activity, etc.) or phrases like "nucleus accumbens" and "viral mediated gene transfer". Also, training does not need to be described here. What is written is actually more appropriate for Q2, overview of scientific objectives.
- Similarly, the description of exact procedures, as currently written in VII.2 (scientific objective), should be moved to Section VII.3 (laboratory procedures).
- Do you use double gloves in the lab all the time? If not, describe in laboratory procedure section for which experiments do you use double gloves.
- Please complete the Biosafety Cabinet Information details, including recent certification date (must be less than one year old).
- Liquid waste treatment should say bleach added to achieve a final concentration of 10% (not 10% solution of bleach added to the liquid waste).

BUA Site Assessment: The containment level should be ABSL1 instead of ABSL-1+. The sonicator in [redacted] will be used inside a fume hood. The red biohazard boxes need to have double-lined red bags. Microtome blades used are disposable. Cut resistant gloves are available and lab is working on an SOP on how to use cryotome.					
Motion: Conditional Approval (Administrative Review)	For: 14	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

6. rDNA/Bhz – Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2455	[redacted]	Transcription Factor Profiling for SARS-CoV2 Tolerance/Symbiosis Regulation	2	N/A	CRC
Primary Reviewer: Elke Muhlberger		Secondary Reviewer: Bob Timmerman			
Applicable NIH Guidelines: Sections III-D-1-a, III-D-2-a; Appendices B-II-D, G-II-B					

Meeting Comments: This protocol attempts to characterize metabolic pathways in bat cell lines that make them permissible to hosting certain types of viruses that can emerge and cause harm to other species, including humans. This project will use bat cell line models to investigate differences in cellular transcription factors that are differentially active in different cell line models, and to study the effects that immune-stimulating factors and SARS-CoV-2 proteins have on host cell protein activity have on host cell protein activity. Protocol involves use of biochemical analysis (Western blots, EMSAs, proteomics) and molecular analysis (protein-binding microarray, cell transfection). All cell culture experiments will be carried out in BSL2 lab and gloves, lab coats, and safety glasses will be worn when performing tissue culture and cell lysis procedures. Solid waste will be disposed of in red biohazard boxes and liquid waste will be decontaminated with 10% bleach, allowed to sit for 30 minutes before sink disposal. Needles used to disrupt cells during lysis will be disposed of in designated sharps containers. Areas in the biosafety cabinet will be sterilized with UV safety light and wiping with 70% ethanol prior to use. The following will be communicated to the PI:

- Chemical safety training date for [redacted] needs update.
- Please include 1-2 sentences in the laboratory procedures section describing the cloning work and propagating plasmids. This information is already provided in the recombinant DNA section and could be easily copy-pasted.

BUA Site Assessment: PI has not been available yet for scheduling the lab visit.

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

7. Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
837	[redacted]	Iodine, Perchlorate, and Thiocyanate: Effects on Thyroid Function in Pregnant Women	2	N/A	BUMC
Primary Reviewer: Tom Winters		Secondary Reviewers: Jim Keeney			
Applicable NIH Guidelines: N/A					

Meeting Comments: The goal of this protocol is to study the role of environmental chemicals such as perchlorate and thiocyanate in the production of thyroid hormone in the body. Iodine is essential for thyroid, hormone production and normal neurologic development. Environmental exposure to perchlorate and thiocyanate may inhibit uptake of iodine into the thyroid gland. Nitrates in foods may also do the same. In this clinical study maternal and child levels of perchlorate, iodine, creatinine, thyroid hormone and thyroid stimulating hormone are measured in the urine and blood of study participants. A new project added in this three-year renewal will examine the same components in the mother /infants, cows, and water collected in Ireland. The measurement techniques and essays are well described. No biosafety cabinet is used. Liquid and solid waste are disposed of properly. Disinfection with bleach at 10% concentration and alcohol at 70% concentration are listed. Personal protective equipment is appropriate. The specimens are stored in a freezer in PI's own lab. Transport is provided in leak proof and shatter proof containers.

The following will be communicated to the PI:

- [redacted] needs to update the BSL1/2, BBP, and Chem Safety BioRAFT trainings.
- ROHP clearance needs to be updated for both [redacted] and [redacted].
- Since the lab has moved from the [redacted] Building to [redacted] building ([redacted] and [redacted]), this information must be updated in the application.

BUA Site Assessment: The lab. location has changed from [redacted] to [redacted] building room # [redacted]. Room # [redacted] should also be added to the protocol.

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

8. rDNA/Bhz – Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
896	[redacted]	Environmental PPAR Agonists: Disruption of Adipose, Liver and Bone Function	2	2	BUMC

Primary Reviewer: Inna Afasizheva | Secondary Reviewer: Colleen Thurman

Applicable NIH Guidelines: Sections III-D-1-a, III-D-2-a, III-D-4-a, III-E-1; Appendix B-I, B-II, G-II-B.

Meeting Comments: This protocol investigates how environmental pollutants, such as polychlorinated biphenyls, organotins, or perfluoroalkyl substances affect obesity and osteoporosis. Their research is particularly focused on the analysis of interaction of two nuclear receptors with the pollutants and how translational and transcriptional activities affected by these interactions correlate with metabolic diseases. No major changes have been made to the protocol since the last approval although the committee noted that lentivirus work has been removed. The biohazard materials used in the protocol include human and non-human primate cell lines, human serum and use of AAV-9 viral vectors. The protocol uses multiple high hazard chemicals in cell culture work as well as in animal models; their storage, stock solution preparation and waste disposal are clearly described. Low dust bedding is used by the lab for HHC work. Liquid waste will be disinfected in 10% bleach (final) and red biohazard boxes. The following will be communicated to the PI:

- Protocol lists PI as the only personnel working in the protocol. Please confirm if this is correct. If additional personnel are involved, list them on the table.
- Please indicate where the mouse work will take place in Section IV and in lab procedure section (Section VII.3).
- Provide description, source and transduction procedures (as you had in your previous submission) for the AAV-9 vectors.
- Check Animal handling and cage changing.
- N95 respirator is not needed for the work proposed as the lab will be working in a BSC for dumping cage waste. Please uncheck.
- Since the R-8 animal facility does not have cage washing system, how is Tributyltin/Triphenyltin used cages are handled in there?
- Although the lentivirus work is no longer being carried out and has been taken out from the Hazardous Biological agent list (Section A), they are still mentioned in Section VIII.7B, VIII.10 (storage), Section H (Prokaryotic and Eukaryotic experiments – pLKO.1 vector, vector packaging section, etc. Please remove them.
- Update IACUC approval dates (three protocols listed in Hazardous agent list (Section A)
- Please revise the applicable NIH guidelines sections to “Sections III-D-1-a, III-D-2-a, III-D-4-a, III-E-1; Appendix B-I, B-II, G-II-B.”

BUA Site Assessment: N95 respirator is not needed for the work proposed as the lab will be working in a BSC for dumping cage waste. Low dust bedding is used by the lab for HHC work. Biosafety Cabinet is duly certified. PI needs training update. Lab location in Evans needs to be removed. Lab does not do lentivirus work any longer and does not

use human serum anymore. AAV-9s are made by vector biosystems for organ specific knockdown. Histological analysis of tissues will be performed in the pathology core or they will be sent to MD Anderson.					
Motion: Conditional Approval (Administrative Review)	For: 14	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

9. Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2438	[redacted]	BSL-2 phase of medical countermeasure testing in rodents	2	2	BUMC

Primary Reviewer: Rob Davey | Secondary Reviewer: Colleen Thurman

Applicable NIH Guidelines: N/A

Meeting Comments: The goal of this protocol is to determine the efficacy of vaccines against risk group agents in animal models including rodents. This particular protocol however, describes the procedures to handle rodents for vaccination. The animal challenge part of the work is described in a separated IBC protocol. Animals will be vaccinated with protein based or vectored (live attenuated virus systems) to express immunogenic proteins. Standard strains as well as recombinant mice that are knockout for interferon receptors or other factors that may alter disease outcomes are used. Work with hamsters is also indicated. IACUC protocols for this work are listed. The vectored vaccines will be based on recombinant vesicular stomatitis viruses. While the recombinant VSV is well described, the hazardous biologics section also indicates that adenoviruses will also be used. There is no recombinant nucleic acids section, yet the VSV and likely adenovirus being used are recombinant as it is indicated they encode glycoproteins and other viral proteins as immunogens. Personnel will work with lab coat, gloves, eye protection, surgical mask, shoe cover and head cover in the lab. Animal work uses the same protective gear, which would seem better suited to this type of work. Microchem (5%) is used for cleanup. This is good for inactivation adenoviruses and likely applies to VSV as it is an enveloped virus. 10% fresh bleach will also be used. The following will be communicated to the PI:

- It was noted that recombinant VSV and Adenovirus will be used in the protocol. However, the protocol lacks the Recombinant DNA section. While the recombinant VSV is well described, the rDNA work describing how the SARS-CoV-2 or filovirus glycoprotein sequences were put into the vector is not described. Your BSL2 protocol [redacted] does not have any additional information about construction of these recombinant viruses either.
- The hazardous biological agents section also indicates that adenoviruses will also be used. It is assumed that this will also be recombinant. A description of this system (is it replication self-limiting?) needs to be added to the general approach section. If it is replication limiting, then precautions are appropriate. If not, describe precautions to contain shedding of adenovirus in the animal space.
- There is no recombinant nucleic acids section, yet the VSV and likely adenovirus being used are recombinant as it is indicated that they encode glycoproteins and other viral proteins as immunogens. The rDNA section must be completed where recombinant VSV and adenovirus must be added. This should be added even if the materials are acquired from a third party.

BUA Site Assessment: O-rings and safety cups are available for use with centrifuges. All BSCs are up to date. Onsite service technician maintains NEIDL autoclaves. Autoclave tape and biological indicators confirm successful autoclave cycles. The lab has access to Biosafety Manual and Chemical Hygiene Plan.

Motion: Conditional Approval (Administrative Review)	For: 14	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.

Three-Year Renewals reviewed by DMR:

10. Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1164	[redacted]	Osteoarthritis Findings Before and After Bariatric Surgery (OABS)	2	N/A	BUMC
Primary Reviewer: Sajal Ghosh		Secondary Reviewer: Tom Winters			
Applicable NIH Guidelines: N/A					
Motion: Conditional Approval (Administrative Review)	For: 14	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

11. rDNA/Bhz – Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1340	[redacted]	Neuromodulation and Cortical Memory Function	2	2	CRC
Primary Reviewer: Ed Loechler		Secondary Reviewer: Steve Niemi			
Applicable NIH Guidelines: Section III-D1 and D4; Appendix G, Appendix Q					
Motion: Conditional Approval (Administrative Review)	For: 14	Recuse: 0	Against: 0	Abstain: 0	Absent: 1