Boston University
Institutional Biosafety Committee (IBC)
December 12, 2023 Meeting Agenda
Location: Zoom and/or by phone
Start time: 12:00 PM End time: 1:19 PM

Members Present:	R. Ingalls, B. Slack, E. Muhlberger, I. Afasizheva, R. Davey, W. Lu, V. Gouon-Evans (left 1:01 PM), T. Winters, R. Morales (joined 12:52 PM), C. Thurman, S. Niemi, J. Keeney, R. Timmerman, V. Britton (joined 12:25 PM), N. Dey, S. Ghosh
Guests Present:	A. Lerner, C. Fernald, J. Presedo, A. Ahmad, A. Broos-Caldwell, A. Ellis, P. Richmond, M. Fitzgerald
Staff Present:	C. McGoff, L. Campbell

I. Review of November 14, 2023 IBC Meeting Minutes (R. Ingalls)
No concerns were voiced.
Motion: Approved
For: 13; Against: 0; Abstain 1; Absent: 2

II. Chair's Report: Nothing to report.

III. New Business:
A. IBC Office Updates: Nothing to report.
B. Incident Report: Members were presented with the corrective actions taken on last month's incidents and one pending incident.
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 – New Project

BUA	(PI)	Title	BSL	ABSL	Campus
2624	[redacted]	MAGNITUDE: A Phase 3 Multinational, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of NTLA-2001 in Participants with Transthyretin Amyloidosis with Cardiomyopathy (ATTR-CM)	1	N/A	BUMC
Primary Reviewer: Adam Lerner			Secondary Reviewer: Robin Ingalls		
Applicable NIH Guidelines: Section III-C-1					
Meeting Comments: This new protocol involves introduction of Cas9 mRNA and transthyretin-specific small guide RNA in human subjects via lipid nanoparticles as a method of reducing expression of mutant version of transthyretin with the hope of reducing burden of Transthyretin Amyloidosis (ATTR) in human patients. As per NIH guidelines section III-C-1, this belongs to Human Gene Transfer study. In Boston University these protocols are reviewed in a two-step process where it is first reviewed by the Human Gene Therapy (HGT) subcommittee which includes members with expertise in clinical trials as well as advanced molecular biological techniques. Recommendations of this committee is then discussed in the IBC full committee meeting where the final approval decisions are then made. The HGT subcommittee reviewed this protocol on 12/7/23 and its decision was discussed in today's IBC meeting. Lipid nanoparticles containing the Cas9 mRNA and guide RNA are provided by the xxx directly to the Pharmacy Department where registered nurses with extensive expertise on drug infusion in patient prepare the infusion cocktail and infuse them in experimental and control patients in a blinded manner. The Cas9 mRNA and the guide RNA are nucleic acids that cannot replicate by themselves and are not considered biohazardous materials. Administration, patient monitoring and collection and processing of blood and urine samples before and after					

infusion are done by the clinical trial unit and are not part of this IBC application. The following will be communicated to the PI:

- PI must complete LST, BSL1/2, Blood Borne Pathogen and rDNA/IBC policy training in BioRAFT (bu.Bioraft.com), and fill out ROHP clearance form (www.bu.edu/research/ethics-compliance/safety/rohp/rohp-requirements-for-medical-clearance-process/).
- In the Laboratory procedure section (Section VII.3) please add a few sentences to address the following: management of any known off-target effects of the drug (study protocol mentioned a few), and its clearance from blood (study protocol mentioned primate data). Also state that the study drug is stored in [redacted] at BMC and infusion will occur in [redacted] This is mentioned elsewhere but should be mentioned here very briefly, with reference to the study protocol that you already have attached with the application.
- Please state in the lab procedure section that all the PPE checked (lab coat, gloves, goggles, safety glasses, face shield, surgical mask, shoe cover, and head cover) is worn when the study drug is handled either in the pharmacy or the clinic. It seems excessive but may be appropriate for the protocol.

BUA Site Assessment: PI does not have a typical wet research lab. The company (Intellia Inc.) will send their drug formulation to the BMC Inpatient Pharmacy Services (IPS) in [redacted] When needed, the IPS will prepare the formulation in their clean room and transport it to [redacted] to transfuse to the study participants. The IPS location is [redacted] and the clinical unit is in [redacted] Blood and urine will be collected in GCRU and then they will be shipped to a core lab outside of BU. However, those protocols are not part of this application.

Motion: Conditional Approval (Administrative Review)	For: 14	Recuse: 0	Against: 0	Abstain: 0	Absent: 2

2. Bhz – Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1484	[redacted]	Innate and Adaptive Immunity to Viruses	2+	N/A	BUMC

Primary Reviewer: Robin Ingalls	Secondary Reviewer: Valerie Gouon-Evans

Applicable NIH Guidelines: N/A

Meeting Comments: This is a 3-year renewal of a NEIDL protocol that was under previous Director as the PI with BSL-2+ containment, now changed to the new NEIDL Director at a BSL-2 containment. This protocol describes the immunology core of instrumentation for the NEIDL which supports the research of a variety of NEIDL investigators, providing access to core instruments for their research. The assays are conducted by core personnel who are trained in the instruments and handling biohazardous materials. This core protocol functions at BSL-2 to conduct assays such as flow cytometry, Luminex assays, and ELISA. Biohazards include human cells/serum/blood (cell lines and primary cells), primate cells/serum/blood, bat blood, BSL-2 viruses (VSV). Some blood samples are from COVID patients but purified SARS-CoV-2 virus is not handled. Equipment used is either in a closed system (flow cytometer, Bio-Plex) or samples are handled in a BSC (ELISA). Liquid waste from assays is disinfected with bleach to a final concentration of 10%. PPE is described in details and varies appropriately with the biohazards. No concerns were noted.

BUA Site Assessment: All BSC's have current certifications (95354 and 95395 certified on 8/1/2023, 95488 certified on 9/28/2023). O-rings/safety cups available for use with centrifuges. Eye washes/fire extinguishers are certified. AED/First aid kit available. Biohazard stickers are present. Door signs are posted. Lab has emergency spill kits. Biological and chemical indicators verify successful cycle runs and autoclaves regularly serviced by Steris.

Motion: Approve	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

3. Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus

1823	[redacted]	Storage, Propagation and Distribution of Fracisella tularensis Storage, Propagation and Distribution of Yersinia pestis Receipt and Storage of the 2019 novel Coronavirus and other coronaviruses	3	N/A	BUMC

Primary Reviewer: Rob Davey	Secondary Reviewer: Guillermo Madico Additional Reviewer: Jim Keeney

Applicable NIH Guidelines: N/A

Meeting Comments: The goal is this protocol is to collect, store and distribute high consequence risk group 3 pathogens that require BSL3 containment. Agents are bacterial pathogens such as *F. tularensis*, *Y. pestis* and coronaviruses which include SARS-CoV-2 and MERS-CoV. No manipulation of these agents are proposed in the protocol. The submission include change of the PI from [redacted] to [redacted] along with inclusion of two new member and removal of one member from the earlier Members listed in the protocol are well qualified with several years of experience each for handling these agents. Disposal of liquid wastes indicates that while liquid waste is not anticipated but "If there were, the appropriate procedures would be the use of 10% freshly prepared bleach (followed by a wipe down with 70% ethanol or isopropanol to remove bleach residue) to disinfect surfaces or equipment. A clear description of the procedure for the safe receipt and storage of these agents is presented. Use of appropriate PPEs is mandated and the external packaging of the specimens will be removed in a BSC that has recent certification. The following will be communicated to the PI:

- Since recruitment or funding are not part of IBC risk assessment, IBC recommends rephrasing the statement to say "Distribution will only be done to investigators who have approved IBC protocols for the receipt and working with the agents requested".
- Also, repeat this statement in the laboratory procedures section as well.

BUA Site Assessment: Lab has been duly inspected. PPE and waste management procedures are appropriate. Personnel training and biosafety cabinet certifications are duly updated. They were certified May 2023 ([redacted]) and July 2023 ([redacted]) and are due to be recertified May and July of 2024. The labs listed in the protocol ([redacted]) were last inspected September 2023.

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

4. Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2628	[redacted]	Investigating treatments and preventive measures for SARS-CoV-2	3	N/A	BUMC

Primary Reviewer: Elke Muhlberger	Secondary Reviewer: Guillermo Madico

Applicable NIH Guidelines: N/A

Meeting Comments: The objective of this project is to acquire, cultivate, preserve, and assess coronaviruses viruses that cause human disease. Samples for the study will be obtained from BEI, BMC clinic or other investigators with appropriate approval for the collection of clinical samples. The coronaviruses will be centrally stored and managed using the NEIDL's existing freezer management system. The availability of these coronaviruses will expedite research and allow their distribution to other investigators with approved IBC protocols. Additionally, the project is designed to use these coronaviruses in various research applications, including in vitro cell infections. The following will be communicated to the PI:

- Contrary to the title, the protocol only describes isolation and storage of coronaviruses in clinical samples. Please reconcile.

- It is not clear if all personnel listed for BSL3 work are experienced in working specifically in the NEIDL BSL-3 space. Please clarify. Indicate who will be providing NEIDL-specific BSL-3 training.
- The protocol is a bit lengthy. It would be helpful to streamline the protocol and remove unnecessary sections (e.g., PCR and primer selection). It is indicated that the samples will be inactivated with TRIzol/TRIzol-LS. So they can be removed from BSL3 for downstream analysis. There is no need for PCR or sequencing inside BSL3. It is recommended to remove all work that will not be done in BSL3.
- If master stocks are inactivated for RNA analysis, TRIzol LS (not TRIzol) must be used because these are liquid samples. This must be corrected. Also, please state specific SOP numbers for each inactivation procedure mentioned in the protocol.
- Protocol states the use of MERS-CoV and SARS-CoV-2 only in hazardous agent list (Section A), but states Coronaviruses in the body of the application. Please be aware that if this work identifies coronaviruses that are not MERS-CoV or SARS-CoV-2, an IBC amendment must be submitted for the existence of new virus. State the purpose of use of MERS-CoV-2 and SARS-CoV-2 in this protocol.
- It is mentioned that clinical samples will be used as a source for coronaviruses, but it is not described what procedure will be used to isolate the virus and how a clean virus stock will be prepared. Please add these details. Please also state how it will be confirmed that no other pathogens (viruses, bacteria, fungi) are present in these samples.
- It is mentioned that PBMCs will be isolated from patient blood. Please describe what the PBMCs will be used for. Will PBMC isolation from patients be done in BSL3?
- "Homogenizing and tissue grinding" is checked in box VIII.1. It is not clear why this is required. Please describe respective experiments in research description section or uncheck this box.
- VIII.4 – uncheck PPE used for animal work as there is no animal work described in this protocol.
- VIII.11 – transport section must be rephrased because it does not provide description of procedure for hazardous samples, instead it only talks about non-infectious, virally-inactivated materials, like cell serum or plasma, which is not necessary.
- Does cell lines, 293T, A549, HEK 293, HeLa, THP-1 and U937 come from BEI, as mentioned in Section A? The purpose of these cell lines in this protocol has not been stated.
- Please remove all cell lines from table B, Other potentially Infectious material.
- NHP blood and material is listed in table B, Other potentially Infectious material, but it is not clear where this material will come from and what it will be used for. This information should be added in laboratory procedure. Remove if not applicable.
- Does the acquisition of clinical samples require IRB approval? Please clarify.

BUA Site Assessment: Training records for all members listed (except for [redacted] on the protocol are up to date. Personnel member ([redacted]) is currently not yet cleared by ROHP for BSL3. The Biosafety cabinets listed on protocol 2628 are up to date on certification. They were certified May and July of 2022 and are due to be recertified May and July 2023. The labs listed in the protocol ([redacted]) were last inspected September 2023.

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

5. Bhz – New Application (Previously Withhold Approval)

BUA	(PI)	Title	BSL	ABSL	Campus
2625	[redacted]	Enhancing Lymphatic Function with Transplanted Muscle Cells After Bacterial Infection	2	2	BUMC

Primary Reviewer: Weining Lu	Secondary Reviewer: Colleen Thurman Additional Reviewer: Bob Timmerman
Applicable NIH Guidelines: N/A	
Meeting Comments: This is a resubmission of a new protocol whose approval was withheld in last month's meeting. This project aims to study how methicillin-resistant *Staphylococcus aureus* (MRSA) affects lymphatic vessel contractility, lymphatic muscle cells (LMC) recovery, and LMC regeneration after MRSA infection. The project will	

perform lab experiments such as single-cell RNA sequencing, immunostaining of proliferation markers, and using calcium-reporter mice to measure the calcium flux of LMCs in mice infected with MRSA by injecting MRAS bacteria into the mouse hindlimb subcutaneously. PI's statement in the original submission that no MRSA work has been carried out in PI's lab raised significant concerns related to PI's ability to safely handle a serious biohazardous agent like MRSA. Several additional concerns around detail of the experimental procedures and disinfection of sharps were also brought up. Since that meeting, IBC office had separate meeting with the PI to provide guidance on how to address the meeting concerns. In the revised submission PI provided point-by-point response to each comments and the submission was sent to the reviewers before being discussed in today's meeting. In the revised submission, most importantly, PI clarified with proper citation (first-authorship paper) that he has extensive hands-on experience on culturing MRSA and using MRSA in animal experiments during his post-doctoral work at Harvard. It is just that no MRSA work has been started yet in his own lab here at BU. However, the revised protocol still needs few minor corrections. The following will be communicated to the PI:

- Please include all responses related to procedural details (that PI provided in the point-by-point response) into the body of the application in appropriate sections (some has been added but not all; such as assays to determine status of MRSA infection; infection clearance in animals; Ca2+ channel agonist experiment).
- In Section VII RESEARCH PROJECT DESCRIPTION, Part 3, laboratory procedures and manipulations, PI wrote, "Subsequently, the saline will be replaced with a DRUG to stimulate calcium channel activity, which will continue to be imaged for an additional 20 minutes." Please give the full name of the "DRUG' used in this experiment and if it is a hazardous chemical.
- Although the PI responded in the PI comments section that "no needles will be disinfected" before placed in designated sharps containers to avoid accidental needle sticking with contaminated MRSA, "needles" were still listed together with "surgical instruments" to be disinfected in Section VIII.6, PPE and Safety Equipment section.
- In Section VIII.7, please replace "suitable disinfectants" with "bleach at a final 10% concentration" so the liquid wastes can be decontaminated by bleach at a final 10% concentration for 30 min to render *S. aureus* non-viable before being poured down the drain.
- In Section IX, MATERIALS USED IN RESEARCH, Section A. Hazardous Biological Agents, please provide "Antibiotic Sensitivity Profile" for the three MRSA strains USA 300 LAC, USA 300 LAC agr deficient, and BAA-2422 (so that ROHP knows what antibiotic can be used to treat a lab incident).

Motion: Conditional Approval (Administrative Review)	For: 15	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.