Boston University
Institutional Biosafety Committee (IBC) Public Meeting
September 17, 2024 Meeting Minutes
Location: Zoom and/or by phone
Start time: 12:00 PM End time: 1:34 PM

Members Present:	R. Ingalls, R. Davey, E. Muhlberger, I. Afasizheva, V. Gouon-Evans, W. Lu, T. Winters, R. Morales, N. Dey, C. Thurman, J. Keeney, V. Britton, S. Ghosh
Guests Present:	N. Sullivan, P. Richmond, K. Tuohey, G. Madico, A. Ahmad, A. Broos-Caldwell, A. Ellis, J. Wood, N. Yun, J. Moliva, A. Carter, M. Puim, M. Nilsen (Harvard), R. Polak (Harvard), A. Reid (Harvard), M. Neli (Harvard), S. Estime (Harvard), S. Jao (Harvard), P. Shoemaker (BPHC), M. Bailey, F. Fortin, M. St. Jean,
Staff Present:	C. McGoff, L. Campbell

I. Introduction to the Public Meeting

The Chair informed IBC members and guests that the IBC Annual Public Meeting is requirement set forth by the Boston Public Health Commission's Biological Laboratory Regulations Implementation and Enforcement Guidelines section 7.5. The Chair also stated that IBC is a NIH-mandated institutional regulatory body and provided a brief synopsis of the role of the IBC and how it oversees the compliance requirement set by federal, state and city and local authorities. All attending IBC members, invited guests and public introduced themselves.

II. Review of August 20, 2024 IBC Meeting Minutes

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

III. Chair's Report:

The Chair thanked all IBC members for their valuable time throughout the year in reviewing protocols, and the IBC office staff for their hard work. EHS and Research Occupational Health Program staff was thanked for their support for the Biosafety Program. The Chair updated the committee on changes to BU's Dual Use Research of Concern (DURC) and Potentially Pandemic Pathogen Policy, which was reviewed by the DURC Committee at a recent meeting.

IV. Presentations:

A. Presentation: BSL4 and BSL3 Research at Boston University

Dr. Nancy Sullivan, Director of the NEIDL, informed members and guests on the mission of the NEIDL and current and upcoming research.

B. Presentation: EHS Annual Biosafety Report

EHS Program Manager and Biosafety Officer, Dr. N. Dey provided the EHS annual report.

V. Protocol Review

1. rDNA/Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2663	[redacted]	Whole genome sequencing of BSL3 select agents within the containment environment	3	N/A	BUMC
Primary Reviewer: Elke Muhlberger			Secondary Reviewer: Robin Ingalls		
Applicable NIH Guidelines: These experiments will create recombinant DNA through PCR amplification. The products will not be inserted into plasmids of other means of preserving the amplified DNA. Once the products of DNA amplification are sequenced the DNA will be disposed of.					
Meeting Comments: This new protocol is to receive possible Eastern Equine Encephalitis (EEE) virus infected clinical samples from the Massachusetts Department of Public Health into the [redacted] suite, and conduct viral genome sequencing. RNA will be extracted from samples, converted to cDNA, and then amplified using PCR to create a library					

for sequencing. EEE virus is RG3 pathogen due to risk of aerosols that could infect exposed individuals; it is also a select agent. In this protocol, the virus will not be propagated in the lab and clinical samples would likely contain a very low titer of virus. The committee noted that the PI has significant experience in nucleic acid sequencing from high impact clinical samples. The Scientific Safety Officer also indicated that CDC clarified that Microchem is not a tested disinfectant against EEE viral RNA, although it can efficiently kill the virus itself. They suggested that PI must perform validation of its disinfectibility against EEE genomic RNA or should use other established disinfectants. It was also noted that the positive stranded viral RNA, like that of the EEE virus, can be infectious only if it is transfected in a cell. The following will be communicated to the PI:

- Provide prior experience of the listed members with a focus on handling viruses and BSL3 experience.
- Layman description – explain abbreviations (Mass DPH).
- Since EEE is a positive-sense RNA virus, the viral RNA is also classified as a select agent. CDC has recommended that MicroChem can only be use as a disinfectant for EEE RNA after performing proper validation steps. In the absence of such validation report, committee advises to use other agents that are known to be effective (based on published report). EHS suggested Vikron could be one such agent.
- Please clarify the samples that will be received from MA DPH. The biohazardous materials table lists: "equine encephalitis virus RNA containing samples". Is it possible to be more specific? Will the lab receive aliquots of the clinical samples that are sent to DPH for testing? In that case this would most likely be serum and CSF, which should be listed as they potentially could contain other biohazards. And will the lab only receive human samples or will there be samples from animals (e.g., horses) or mosquitos? Is there an IRB required if the samples are obtained from patients?
- Please clarify if shipment of these samples must be performed according to the NEIDL transportation plan developed for the shipment of select agents. It would be beneficial to classify these samples as "diagnostic samples" to avoid complicated shipping procedures.
- The safety procedures described in SOP SCI-SOP-7010 should be briefly described in this protocol. The IBC does not review SOPs.
- Transport of samples – Is the storage area in the same room as the lab area or will the samples be transported between rooms? If the latter, a leak-proof, shatter-proof container should be used for sample transport.
- It appears that the protocol only generate cDNA fragments for sequencing and library preparation but nothing that could be replicated in prokaryotic or eukaryotic cells. Please uncheck "recombinant DNA" because the generated DNA fragments are exempt from the NIH cDNA guidelines.

BUA Site Assessment: PI does not have sufficient information regarding the BSCs he intends to use to make a complete a full BUA. All training records for the staff listed are up to date. The listed lab was inspected in July 2024 and all BSCs are duly certified.

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

2. rDNA/Bhz – Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
2642	[redacted]	Propagation and Characterization of Risk Group 4 viruses	4	N/A	BUMC
Primary Reviewer: Rob Davey		Secondary Reviewer: Valerie Gouon-Evans			
Applicable NIH Guidelines: Section III-D-1 and Section III-D-1-c					
Meeting Comments: The goal of this protocol is to test vaccines and therapeutics using non-human primate (NHP) models including cynomolgus or rhesus macaques, or African green monkeys. Vaccine efficacy will be assessed by first vaccinating animals followed by exposing them to the RG4 pathogens in the [redacted] laboratory. Vaccine platforms may include vectored viruses carrying immunogens to stimulate protective responses, along with protein					

subunit vaccines, nucleic acid vaccines (DNA or RNA), and live attenuated vaccines. On the other hand, therapeutic testing (antibodies, antivirals, and small molecule drugs) involves treating animals shortly before or after pathogen exposure without the need for countermeasure development during model refinement. Efficacy will be evaluated by monitoring viral loads and immune responses in collected samples, followed by necropsy and tissue analysis for further insights. This amendment is to specifically add monkeypox (MPOX) Clade 1 virus, de-identified patient samples from area where MPOX is endemic, and Ebola virus expressing green fluorescent protein EBOV-GFP. Similar approach for testing vaccines and therapeutics against this MPOX will be made. The MPOX work will be performed in BSL4. However, MPOX is classified as a BSL3 agent and no justification was given that would cause it to be elevated to BSL4. IBC noted that working with agents at higher containment level may reduce risk to personnel but actually creates greater risk for personnel who would not normally be exposed to more dangerous agents such as Ebola virus or Nipah Virus, which are often worked with in the BSL4. it was noted that the personnel on the protocol routinely work with other BSL4 pathogens and so, no additional unnecessary exposure would likely occur. It is requested that some level of justification should be added to the protocol. Committee also discussed whether commonly used disinfectant for RNA viruses such as Microchem, will work for a DNA virus like Monkeypox. However, information about other published reports was provided that confirms that Microchem effectively inactivate and disinfect Monkeypox. Additionally recombinant ebolavirus expressing green fluorescent protein has been added to measure the rate of infection. This virus is routinely used in the BSL4 by others and is of the same risk category as Ebola virus. The following will be communicated to the PI:

- The committee recommends that to avoid any confusion on Monkey pox virus naming, only the WHO recommended nomenclature for the monkey pox should be used (which is 'MPOX').
- Raising agents to higher levels of biocontainment than necessary is an administrative concern for how resources are used and should be deferred to the NEIDL administration for input.
- The committee recommended that elevating agents should not occur unless there are justified biological safety concerns about the agent or specific needs or circumstances where workers are already handling other higher level pathogens. Please provide brief justification for why Monkey pox virus work can be or should be done in BS4 containment.
- If use of the BSL4 space is approved for MPOX work, please check that all SOPs are updated to include DNA pox viruses, like Monkey pox, as current SOPS may only refer to RNA viruses.

3. rDNA/Bhz – Annual Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2446	[redacted]	SARS-CoV-2 and MPOX research. Diagnostic development and evaluation, antiviral testing, host response evaluation, and in vitro model development.	3	N/A	BUMC
Primary Reviewer: Robin Ingalls		Secondary Reviewer: Tom Winters			
Applicable NIH Guidelines: Section III-D-1-a					
Meeting Comments: The project studies inactivated SARS-CoV-2 and West African clade MPOX virus in order to develop and improve diagnostic testing options and new therapeutics. They plan to test small molecules against both agents and test host response of cells against the two agents. Laboratory manipulations include virus culture including recovery of virus from clinical samples (NP swabs from SARS-CoV-2 diagnostics). Viruses will be propagated in cell culture including cell lines that express human receptors for SARS-CoV-2. De-identified nasal samples obtained from the BU Central Teaching Lab (though appropriate IRB approval) will be inactivated and RT-PCR and Next Generation sequencing (NGS) will be done in the PI's lab. Inactivation of cultured SARS-CoV-2 will also be done by approved inactivation protocol using detergent, formaldehyde, or TRIzol. The protocol also include development of diagnostic silicon chips using inactivated samples and study of viral growth in self-contained "organ-on-a-chip" devices. Further, the protocol includes testing of antiviral compounds both on surfaces and in droplets, and in host cells. Recombinant viral work will also include creation of double stranded synthetic DNA for creating MPOX					

expressing fluorescent proteins (such as Venus, mCherry, or Cerulean). In this renewal the request is made to add avian influenza H5N1. In June of this year the CDC and USDA granted H5 avian influenza viruses an exemption to the select agents restriction for 3 years to encourage research and simplify clinical laboratory diagnostics. Thus, this addition does not change the safety level of the existing protocol to cover RG3, non-select agents. The work is performed under BL-3 precautions in certified biosafety cabinets. Liquid and solid wastes are handled appropriately. Disinfection with 10% bleach followed by 70% ethanol is also appropriate for the proposed work. Storage and transportation is clearly defined. PPE including eye protection and a PAPR are described as appropriate for the BSL-3 lab. ROHP consultation is recommended to discuss vaccine availability and will be provided to all researchers including COVID vaccine and JYNNEOS vaccine. The following will be communicated to the PI:

- Please change "monkeypox" to "MPOX".
- Please clarify in the protocol that the West Africa Clade of MPOX is clade II. This is relevant as the virus spreads worldwide and will make an easier distinction to any work that might be done with clade 1 (which is not on this protocol) and also to make it clear that this disease is not restricted to Africa only.
- Please note that 10% bleach will be made fresh.

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

4. rDNA/Bhz – Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
2633	[redacted]	Investigations of viral and host immune interactions	2	2	BUMC

Primary Reviewer: Elke Muhlberger	Secondary Reviewer: Colleen Thurman

Applicable NIH Guidelines: III-D-1-a, III-D-2-a, III-E-1, III-D-4-a

Project Summary: We will study how viruses enter and infect cells, investigate how the immune systems of animals and humans respond to viral infections and how the interactions between viruses and the immune system lead to human disease. Understanding these processes are important to the development of treatments and vaccines against viruses.

Meeting Comments: This protocol investigates mechanisms of virus-host interaction and its effect on immune response. Specific focus is being made on humoral immune responses, including how antibodies develop, what epitopes they target, the quality of the antibody response, and the mechanisms by which they act on the target. They will use BSL2 level experiments to investigate responses for members of the Filoviridae family, Old World and New World Arenaviridae family, Paramyxoviridae, Coronaviradae, (including Middle East Respiratory Syndrome coronavirus/MERS, Severe acute respiratory syndrome associated coronavirus-type 2/SARS-CoV-2), Alphaviridae and influenza viruses. These will all be done by treating human cell lines with pseudotyped viruses expressing envelope proteins from those high consequence pathogens or with virus-like particles (VLPs) and then measuring immune response. In this amendment they are adding animal research component where animals will be infected with these agents and animal immune response will be measured. They also plan to create humanized animals and testing the effect of the infection by those pseudotyped viruses or VLPs. The following will be communicated to the PI:

- IV. Please use [redacted] or [redacted] for ABSL2 mouse experiments. [redacted] is not an animal space.
- IV. The BSL2 rooms for mouse work are [redacted] (housing) and [redacted] (procedure). Other rooms in [redacted] (such as [redacted] and [redacted] and [redacted]) are ABSL1 housing. [redacted] spaces are [redacted] and [redacted] with [redacted] and [redacted] generally used for mouse work. But, [redacted] is not an animal use space. Please make these corrections.
- VII.3 Please correct the room locations in Section 15 as elaborated above.
- Clarify if the creation of humanized mice is done in [redacted] lab or they are made in Dr. [redacted] lab. If it is the later, provide Dr. [redacted] IBC approval number where this work is being done or is being planned.

• The PI should clarify if human bone marrow is used for these studies. Human bone marrow cell transplant is mentioned in the Laboratory Procedure Section. If the PI plans to use this material, the source of the material must be indicated including required IRB permits. • Is recapping needles really necessary? It seems that the mice won't be injected with hazardous material. The PI should justify why they plan to recap needles. Is there an ABSL2 SOP in place that describes the safest procedure? If needles must be recapped after drawing up mouse injections, recommend a needle block. • 15.1 "breeding" not breading • Sharps containers should be closed when 75% full and autoclaved. • VIII. 5. Provide updated biosafety cabinet certification date (date should be less than one year old). • VIII. 6. Add IBC # of Dr. [redacted] submission under which pathology work will be performed • VIII. 8. For ABSL2 work with mice in the [redacted], 5% Microchem and Peroxigard are the standard surface disinfectants available. • IX Section H. Check Animal experiments and mention in H.2.C the humanized mice as host, pseudotyped virus and VLPs as vector and indicate the origin of the donor. Mention IACUC application as pending. • 17. Description of studies indicates use of humanized mice strains and genetic approaches to generating mice including CRISPR/Cas9, so this should be yes.					
Motion: Conditional Approval (Admin Review)	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

VI. Public Comments:

There was no comment from the public attending the meeting.

VII. 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.