Boston University
Institutional Biosafety Committee (IBC)
December 14, 2021 Meeting Agenda
Location: Zoom and/or by phone
Start time: 12:00 PM End time: 2:00 PM

Members Present:	C. Abraham, R. Ingalls, B. Slack, E. Muhlberger, I. Afasizheva, R. Davey, E. Loechler (Joined 12:09 PM, left 1:54 PM), X. Brown, R. Morales, T. Winters, C. Thurman, S. Niemi (Joined 12:03 PM), J. Keeney, R. Timmerman (Joined 12:02 PM), V. Britton (Joined 12:04 PM), J. Barton (Joined 12:14 PM), S. Ghosh
Guests Present:	J. Connor, T. Killeen, A. Ahmad, J. Davis, S. Benjamin, P. Richmond, J. Wood
Staff Present:	C. McGoff, L. Campbell

I. Review of November 16, 2021 IBC Meeting Minutes (C. Abraham)

No comments or questions were voiced.
Motion: Approve
For: 12; Abstain: 2; Absent: 3

II. New Business:

A. Update on SARS-CoV-2 variants: Biology and Biosafety of Omicron
Members were provided with a presentation by Dr. John Connor who provided information on the biology of the Omicron variant and the current status of the virus globally.

Discussion followed on whether or not current monoclonal antibodies utilized in the US will protect against Omicron. It was noted that in South Africa, where Omicron seems to have originated in mid-November 2021, 70% of the population already have some immunity as likely having recovered from SARS CoV2. Dr. Connor indicated he will be available to address any further questions on Omicron if needed.

B. BPHC inspection report for the NEIDL (S. Benjamin)
The Biosafety Officer provided a brief overview of the BPHC inspection reports for BSL3 and BSL4 involving document reviews, facility walkthroughs and tours, personnel interviews. The BSO reported minimal findings related to autoclave documentation and maintenance records during the BSL3 inspection occurring on 7/14/2021. The BSO also reported minimal findings related to autoclave training records and APR door maintenance records and alarms during the inspections occurring between 10/6/21-10/8/21. The BSO will respond to BPHC by addressing both the BSL3 and BSL4 findings.

C. Safety & Quality Assurance Program (SQAP) Report
Nothing to report

D. Research Occupational Health Program (ROHP) & Environmental Health and Safety (EHS) Report
ROHP Report:

- **11/18/2021:** A vaccinated and asymptomatic NEIDL researcher tested positive for SARS-CoV-2 11-18-21. Repeat SARS CoV2 PCR testing 11-20-21 was negative. Cepheid was unable to be run on the 11-20-21 sample.
  The researcher reported remaining asymptomatic, reported no amplification work was performed the day he tested but reported testing at the end of his work shift. ROHP determined this to be an amplicon exposure. Education was provided to prevent further incidents. A report was submitted to the BPHC. *EHS Report:* EHS working with the lab on decontamination and Cepheid handling according to the SOP.

- **11/26/21:** A Fifth-year graduate student reported being bitten by a transgenic mouse on the distal IP joint of her left thumb. The student was wearing three pairs of gloves, disposable sleeve covers, disposable gown, head and shoe covers and facemask while working in a biosafety cabinet at the time of the incident, and the skin was broken. The graduate student was advised to wash the area with soap and water for 10-15 minutes; watch for signs and symptoms of infection and follow-up with any concerns. A report will be submitted to the BPHC. *EHS Report:* It was noted that mouse bite was from a commercially-sourced mouse; root cause was determined as other. The researcher was retrained in animal-handling techniques. All other online trainings were up to date.

- **12/7/2021**: A BSL4 researcher in the NEIDL noticed a suit tear measuring about 3" long after having worked in containment with Filoviruses and while the researcher was in the chemical shower and it was reported to the BSO. The BSO reported to ROHP that the researcher confirmed he had no cuts, there were no spills in the BSC, air pressure in the rooms was okay; the researcher was wearing a positive pressure suit the whole time. This incident was not considered an exposure and will be reported to BPHC. Risk assessment deemed no exposure. BSO reassessing about getting new suits from a different vendor. No EHS report was provided.

III. Protocol Review

1. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2295		Role of Fibroblasts in Disease	2	NA	BUMC
Primary Reviewer: Carmela Abraham		Secondary Reviewer: Rob Davey			
Applicable NIH Guidelines: Section III-D-1-a, Section III-D-2-a, III-E-1; Appendix G-II-B and Appendix B-II					
Meeting Comments: The goal of this study is to understand the contribution of individual cell types in the development and outcome of autoimmune diseases scleroderma and lupus. Scleroderma and lupus are serious diseases characterized by an attack by the person's own immune system on their tissues resulting in hardening of the skin and scar tissue formation and inflammation in the internal organs. The protocol uses cultured human cells and lentiviral vectors to express genes being studied. Cells are grown in tissue culture at BSL2 and RNA or proteins extracted for analysis. Human dermal fibroblasts are obtained from fresh skin biopsies through collaborator. Cells are also prepared for FACS analysis by formalin fixation. In some cases, plasmids or small interfering nucleic acid oligomers are transfected into the cells using lipofectamine based methods. PI is the only personnel in the protocol at this time. BSL2 work will be performed in a BSC with eye protection, disposable gloves, and lab coat, which is appropriate PPE for this work. The following will be communicated to the PI: ● The protocol states "Note our lab is not involved in the transport of the tissues from the procurement site". Please clarify who is bringing the tissues to the lab? Is it mentioned in Dr. IBC? ● Liquid tissue culture waste should be inactivated with 10% bleach, final concentration. ● Section H1: Will rDNA gene be expressed? Should be marked YES. BUA Site Assessment: The lab has bloodborne pathogen exposure control plan. PI's training record and ROHP clearances are all current. PI has access to certified biosafety cabinet and fume hood.					

Motion: Conditional Approval (Administrative Review)	For: 17	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

2. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1697		Translational control in virus-infected cells	2	NA	BUMC

Primary Reviewer: Robin Ingalls	Secondary Reviewers: Barbara Slack

Applicable NIH Guidelines: Section III-D-1-a, Section III-D-2-a; Section III-D-3-a, Section III-E-1; Appendix B-II-D and Appendix G-II-B

Meeting Comments: The lab is interested in understanding how viruses force the host cells to alter the protein synthesis program. Although in most cases viruses force host cells to make only virus proteins, host cells also launch antiviral programs to counter virus-mediated usurpation of cellular processes. They manipulate viral genes to modify virus replication and translation and analyze the effect by various virological and molecular biological techniques. The work involve use of model RG2 ssRNA and dsDNA viruses as well as vaccinia virus. Additional biohazard work involves testing imaging to differentiate between viruses. This involves BSL-2 strains of influenza virus – both live and fixed virus, and clinical samples from patients (internal and outside collaborators). The protocol also include dengue, RSV, enterovirus EV-D68, polio virus and several other uncommon negative strand RG2 RNA viruses. Their work involves significant recombinant DNA work including use of 3rd generation lentivirus vectors. Project also involves use of nanoparticles in collaboration with Boston University PIs to determine if nanoparticles can kill viruses if activated with a laser. PI indicated that they are not growing D68 and polio but only receiving samples for cellular imaging. Personnel working with vaccinia virus are immunized with vaccinia and flu virus. Committee also discussed that there is no need to add surgical mask as a PPE unless it is required for the proposed work. It is expected that laboratory members will use surgical mask until the current pandemic is over. The following will be communicated to the PI:

- Section III.1- Training for to be done by The latter is not listed under personnel. Under training: will be trained by , and then will train ? Is this correct? needs to update LST (9/2/20 is last date listed;
- Section VII.3- For project with and , at what point will the nanoparticles be added (if it is in the Reinhold lab, it is not stated so);
- What are nanoparticles composed of, and how will nanoparticle-containing viruses be disposed of? (Is a separated stream required for inactivated virus with nanoparticles?). What happens to the quartz cuvettes?
- Section VIII.5- update certification date of BSC;
- Section VIII.11- is material transported to CRC by lab personnel?
- Section IX. Please check N/A under ABSL level.

BUA Site Assessment: The lab has exposure control plan. The biosafety cabinets are certified. Update safety training needed on some lab members who have been notified.

Motion: Conditional Approval (Administrative Review)	For: 17	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

3. Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2347		Culturing human cells for three-dimensional bioprinting	2	NA	CRC

Primary Reviewer: Xin Brown	Secondary Reviewer: Jim Keeney

Applicable NIH Guidelines: N/A

The objective of the project is to build tissue constructs using cells and hydrogels through bioprinting. Resulting tissue constructs will be studies through fluorescent microscopy, biochemical assays and PCR to analyze behavior of these artificial tissues in a controlled manner. In addition to cell lines, unfixed primary cells isolated from animal and human tissues, obtained from commercial company Bioreclamation IVT or from Lonza (certified to be free of any known pathogens) are also used. The compounds used in the protocol are mostly biodegradable polymers used as scaffold for generating tissue-like structures. This is nicely described straightforward protocol. It was noted that the departmental administrator is not a BU employee, but rather an employee of the Fraunhofer Institute. The following will be communicated to the PI:

- Although this is not the case in the medical campus, on CRC, pipets and pipet tips should be disposed in the sharps container, not in the biohazard box. Please make appropriate changes in the Solid Waste disposal method section.

BUA Site Assessment: The lab has current bloodborne pathogen exposure control plan. Safety training and ROHP clearances are current for all members. Their biosafety cabinet is duly certified.

Motion: Conditional Approval (Administrative Review)	For: 17	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

4. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1733		Pathogenesis of muscular dystrophies	2	NA	BUMC

Primary Reviewer: Barbara Slack	Secondary Reviewer: Bob Timmerman
Applicable NIH Guidelines: Sections III-D-1-a, III-D-2-a, III-E-1; Appendix E	

Meeting Comments: The goals of this protocol is to identify pathogenetic mechanisms and potential new therapeutic strategies for a group of severe childhood muscular dystrophies and an additional adult-onset dystrophy (FSHD). They will investigate the effect of loss of epigenetic silencing and aberrant expression of DUX4 transcription factor. The work in the protocol include growth of human cell lines, deidentified primary human myogenic cells in BSL2 lab, their differentiation and further analysis by standard methods like SDS-PAGE, RT-PCR, IC, IP, and DNA seq. Mouse myogenic cell lines are also used. Third generation lentiviral vectors encoding cDNAs, shRNA packaged in HEK293 cells; BacMam and Adenovirus vectors obtained from collaborators to express proteins in human skeletal muscle cultures are also used. All human samples are handled with universal precautions in BSL2 using gloves and eye protection, cryostat decontaminated after every use, tissue fragments collected, disinfected, discarded as biohazardous waste; stainless steel gloves are used to change microtome blade, dedicated blades for human tissue that are decontaminated after every use; and staining solutions are disinfected with bleach after each use. De-identified human samples are collected under an exempt IRB protocol. EHS clarified that hard body containers are used for transportation of glass slides. The following will be communicated to the PI:

- Section VII.3- If viruses are no longer being packaged in the lab but are being obtained from commercial sources, please state that in part 3 of the lab procedures section.
- Section VIII.1- check 'plating, colony counting' if propagating plasmids in bacteria.
- Section VIII.5- Updated certification date of the biosafety cabinet.
- Section H.19 – Please update applicable NIH Guidelines to “Sections III-D-1-a, III-D-2-a, III-E-1; Appendix E”

BUA Site Assessment: Biosafety Cabinet is certified. Updated their safety training on some members; lab has been informed of this requirement. Lab uses hard body containers for the transport of slides from one room to another.

Motion: Conditional Approval (Administrative Review)	For: 17	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

5. rDNA/Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
527		Investigation of rare dental diseases in human and mouse	2	NA	BUMC

Primary Reviewer: Inna Afasizheva	Secondary Reviewer: Ron Morales
Applicable NIH Guidelines: Section III-D-1-a, Section III-D-2-a; Appendix G-II-B and Appendix B-II	

Meeting Comments: This protocol aims to study rare dental diseases in human and mouse model. The PI previously analyzed pathophysiological mechanisms of Ellis-van Creveld (EVC) syndrome in a mouse model using molecular biology, cellular biology and mouse genetics approach. However, the work on this part of the protocol is currently on hold although PI still possess all rDNA materials associated with that work as he may need to revive the work if needed. The new proposed work in the protocol involves analysis of teeth from affected and unaffected family members with rare dental diseases. The collected teeth will be prepared and processed for histological analysis and microscopic imaging. The committee expressed concerns that the protocol did not provide sufficient information on the collection and work with teeth in the laboratory. The following will be communicated to the PI:

- PI's ROHP clearance need to be updated to BSL2 work. Update needed on ROHP clearance for .
- Please provide more detail on teeth collection from human participants and their processing in the lab;
- Where the teeth samples are being collected?
- How are they being safely transported to the lab?
- What safety protocols (PPE, disinfection and waste disposals are managed?
- Provide more detail on what type experiments or manipulations are done on those teeth samples.
- State if biosafety cabinet is used for processing teeth samples. If not, explain why not?
- Change 70% isopropanol to "70% ethanol" as disinfectant.

BUA Site Assessment: Lab has bloodborne pathogen exposure control plan. PI stated that they work with fixed teeth sample and they do not perform any procedure that generate aerosol. A biosafety cabinet is therefore, not required for their work.

Motion: Conditional Approval (Administrative Review)	For: 17	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

6. Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2529		Neurovascular dynamics of sleep across the lifespan	1	NA	CRC

Primary Reviewer: Tom Winters	Secondary Reviewer: Valeda Britton

Applicable NIH Guidelines: N/A

Meeting Comments: This project investigates how disrupted sleep is a risk factor for Alzheimer's disease by studying brain activity during sleep across the lifespan an individual. The study is designed such that one group receives an MRI and enter a development cohort. The other group will participate in upto three study visits where performance of physiological tasks will be tested, an EEG, a functional MRI will be done and a saliva sample for gene typing will be collected. Biosafety risks for the protocol include collection of saliva specimen by spitting into a tube, sealing tube and it is stored on site in a locked cabinet. They are then shipped for analysis and shipping training has been provided to the researchers. The only personal protective needed are gloves. Seventy percent alcohol is use as a disinfectant. No bloodborne pathogen program is invoked as specimens are saliva only. BSL-2 practices are followed. EHS informed the committee that the protocol also involves collection of blood samples by GCRU staff and storage in PI's research lab. The following will be communicated to the PI:

- The application does not show any record of shipping tranining. Please update and/or clarify.
- Note that ROHP clearance for all members must be secured before starting lab work.
- Add and rooms for collection and storage, respectively, of biological samples.
- EHS informed that blood samples are stored in 919, please add this work in the laboratory procedure section, as storage of clinical samples in research lab needs to be mentioned in the IBC protocol.
- Check the 'other' box in PPE question 2.
- Check lab coat and at least one form of eye protection.

BUA Site Assessment: Site assessment was done. No safety concerns were noted.It was noted that PI also stores blood sample in CILSE 919 room. This needs to be added to the protocol.

Motion: Conditional Approval (Administrative Review)	For: 17	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

7. Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2428		Predicting and Optimizing Language Outcomes in Minimally Verbal Children with Autism Spectrum Disorder	1	NA	CRC

Primary Reviewer: Ed Loechler	Secondary Reviewer: Tom Winters

Applicable NIH Guidelines: N/A
Meeting Comments: The overall goal of this study is to investigate minimally verbal children with Autism Spectrum Disorder (ASD) to understand interventions that may promote language development. The study has 4 components that will look at underlying motor and neural mechanisms, optimizing language outcomes, and investigate genetic risk factors. The final aim will investigate common and rare variants associated with minimally verbal ASD and the component associated with this biosafety review. Saliva samples will be collected by the study participants themselves using Oragene Discover kits, which will be sent to ASD participants and immediate family members. Families will bring the saliva kit back on a visit to Boston University. Researcher receiving samples will wear gloves during labeling, wrapping (e.g. in bubble wrap, then absorbent material/paper towels) and placing of the sample into a leak-proof secondary container (e.g. a biological shipper bag). Samples will be stored in a locked cabinet in the office of one of the protocol members. Sample saliva from subjects is self-collected at home. Researcher receiving will take the sample receptacle and further wrap for shipping. Anticipating 1-2 months of storage, the samples accumulated will then be shipped to the collaborating lab in Los Angeles, CA according to specific instructions for processing. There is no expected infectious agent in the samples beyond what would be in the community. The samples will not be further processed or handled in this facility. The Research Safety Director and the ROHP Medical Director clarified that according to OSHA regulations, saliva or urine samples from healthy individuals are not considered biohazardous unless they are visibly contaminated with blood. However, as these body fluids in some cases may contain infectious pathogens even in the absence of blood, BU currently categorizes these samples as BSL2 material. The committee recommended that the biosafety manual contain clear guidance as to when to consider these group of biological samples as biohazardous material and whether IBC approval is necessary for their use. It was noted that revisions of BU Biosafety Manual are currently being worked on. The committee unanimously agreed that because none of the researchers are being exposed to any saliva sample in this particular case, this research should be considered as BSL1 and IBC approval for the continuation of the proposed work is not necessary. PI will be informed separately about this committee decision. BUA Site Assessment: This is a clear BSL1 level work. The biosafety training and ROHP clearances of all members are current. All necessary safeguards are in place.

Motion: IBC approval not required	For: 17	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

8. rDNA/Bhz - Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
1166		HIV-1 infected men on highly active antiretroviral therapy (HAART) often have HIV in semen after virus disappears from their blood. The purpose of our study is to determine whether sexually-transmitted infections cause elevated levels of HIV-1 in the semen of men on HAART, and whether this HIV-1 carries drug-resistance mutations. If so, this could indicate that high risk sex behavior in HAART-treated HIV infected men promotes the transmission of drug resistant forms of HIV.	2+	NA	BUMC

Primary Reviewer: Elke Muhlberger	Secondary Reviewer: Robin Ingalls

Applicable NIH Guidelines: Sections III-D-1-a; Appendix B-II-D; Appendix G-II-B
Meeting Comments: The original goal of this study is to determine whether sexually-transmitted infections cause elevated levels of HIV-1 in the semen of men on highly active antiretroviral therapy (HAART), and whether this HIV-1 carries drug-resistance mutations. If so, this could indicate that high risk sex behavior in HAART-treated HIV infected men promotes the transmission of drug resistant forms of HIV. This amendment seeks to add the work outlined in a pilot project funded by the BUMC Sexual Medicine Research Fund on the "Use of monoclonal antibodies to prevent sexually transmitted infections and unplanned pregnancies: role complement in the female reproductive tract". The

lab has added the associated laboratory procedures, biological agents (cervical mucus samples), staff and human subjects protocol information. The following will be communicated to the PI:

- Please confirm that the cervical mucus samples are obtained from the already provided sources for other samples collected from women. If this is not the case, please indicate source for mucus samples
- Provide brief description of how the samples are transported from the study participants to the PI's Laboratory.
- The IRB information currently listed in the IBC application is actually an exempt protocol. Clarify if the samples for this amendment are obtained through a separate IRB application (as collecting cervical mucus samples may not be an exempt protocol).

Motion: Conditional Approval (Administrative Review)	For: 17	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

9. rDNA/Bhz - Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
487		Initiation and regulation of RSV mRNA transcription and genome replication (NIH) The B cell repertoire as a window into the nature and impact of the lung virome (NIH) Mechanisms of Marburg virus gene expression (NIH) Developing combination therapies against pneumo- and paramyxoviruses causing severe respiratory infection (NIH subcontract) Interplay between respiratory syncytial virus and nucleotide biosynthesis pathways (NIH) Studies to assess the mechanism of inhibition of L and N-P inhibitors Characterize the transcriptional and genome replication mechanism of paramyxoviruses for the discovery of broad spectrum antivirals	2	NA	BUMC

Primary Reviewer: Rob Davey | Secondary Reviewer: Sajal Ghosh

Applicable NIH Guidelines: Sections III-D-1a; III-D-2a; III-D-3a; Appendices B-II-D; B-V; G-I; G-II-B (April 2016)

Layman's Description: RNA viruses are a significant cause of human disease. The aim of these projects is to try to understand genes involved in critical stages in viral life-cycles as this might be helpful for designing drugs that target these viruses.

Meeting Comments: The original protocol is to study the role of viral polymerases in virus replication and gene expression of number of RNA viruses including RSV, human metapneumovirus (HMPV), measles virus (MV), parainfluenza virus (PIV) by studying properties of their RNA polymerases in cell lines or purified proteins in cell-free assays system, by studying them in minireplicons. Some of their work will also involve risk group 4 viruses such as Filoviruses. However, no live virus work will be done with Filoviruses. Instead, inactivated infected cell lysates obtained from NEIDL collaborators will be used to study their RNA polymerases. In this current amendment, PI has removed all previously approved experiments on the study of SARS-CoV-2 replication mechanism and added proposal to study function of few specific genes including the RNA polymerase gene of Nipah Virus (NiV) using very similar experimental approaches, as they have been doing for other viruses. Therefore the risk assessment for this amendment does not change. All safety protocols, disinfection procedures, PPE use plans are nicely described and are appropriate and remain the same.

In the current amendment, they are adding Nipah virus for similar studies. Although the NiV belongs to the RG4 category, PI will only be using inactivated cell lysates obtained from NEIDL collaborator. Reviewers recommended to modification of the project title to a shorter one. The following will be communicated to the PI:

- Your current protocol title include seven individual projects. Committee suggested if you could consolidate to make a shorter but broader and all-inclusive title.

Motion: Conditional Approval (Administrative Review)	For: 17	Recuse: 0	Against: 0	Abstain: 0	Absent: 0