Boston University
Institutional Biosafety Committee (IBC)
October 19, 2021 Meeting Minutes
Location: Zoom and/or by phone
Start time: 12:04 PM End time: 2:16 PM

Members Present:	C. Abraham, B. Slack, R. Ingalls (Joined 12:07 PM, Left 12:54 PM), Inna Afasizheva, R. Davey, E. Loechler (Joined 12:32 PM), R. Morales, T. Winters, C. Thurman, J. Keeney, J. Barton (Joined 12:07 PM), S. Ghosh,
Guests Present:	S. Benjamin, P. Richmond, A. Ahmad, J. Davis, T. Killeen, M. Fitzgerald, J. Wood, J. Penner-Hahn
Staff Present:	S. Ghosh, L. Campbell, C. McGoff

I. Review of September 21, 2021 IBC Meeting Minutes

No comments or questions were voiced.
Motion: Approve
For: 11; Abstain: 0; Absent: 1

II. New Business

A. Safety & Quality Assurance Program (SQAP) Report

The Safety Committees Assistant Director provided updates on the following:

- Biosafety manual revision should be completed by early 2022
- Revision of the IBC charter will include a section on noncompliance processes
- Introduced the new Quality Assurance Officer at the NEIDL, Julianna Penner-Hahn

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

ROHP Report:

9/21/21: An asymptomatic NEIDL laboratory technician, fully vaccinated, tested positive for SARS-CoV-2. Further testing on 9-23-21 and 9-24-21 were negative. He performs amplification of the N1 target outside of the hood and any inactivation of active virus is done inside the hood. He worked closely with BU Healthway and was deemed to have tested positive due to amplicon exposure. ROHP provided the researcher with reminders on how to prevent future contamination and returned back to work on 9-25-21. A report was submitted to BPHC.

9/21/2021: An asymptomatic, fully vaccinated, post-graduate student on the Charles River Campus tested positive for SARS CoV2. Further testing on 9-23-21 and 9-24-21 was negative. He reports he went for routine screening after he had been in the lab. This researcher works in a BSL2 lab with inactivated SARS-CoV-2 virus and N1, N2 and N3 targets. He worked closely with BU Healthway and was deemed to have tested positive due to amplicon exposure. ROHP provided the researcher with reminders on how to prevent future contamination. Researcher returned to work on 9-25-21. A report was submitted to BPHC.

9/27/2021: A fully vaccinated asymptomatic post doc associate at the NEIDL tested positive for SARS-CoV-2 on routine screening 9/27/21 with repeat testing x2 negative. This researcher confirmed that he did work in his lab on 9-27-21 prior to getting his routine SARS CoV2 testing. He works with parts of a different virus and denied work with SARS CoV2. He has however worked in shared space with others that do work with SARS-CoV-2. Biosafety and EHS are following up on cleaning. ROHP provided the researcher with reminders on how to prevent future contamination and returned to work 9-25-21. This researcher was cleared by BU Healthway to return to work on 10/1/21. A report was submitted to BPHC.

The IBC Program Manager reported that this incident does not involve recombinantly-modified virus. Therefore, it is not under the purview of the NIH and will not be reported to the NIH.

EHS reported that cleanup was done in each lab after the amplicon exposure incidents. Samples were collected and sent out for testing. Results are pending.

Discussion about how to prevent the occurrence of positive SARS CoV2 tests after amplicon exposure revealed that a guidance document has been supplied to labs outlining how to work with these potentially infectious amplicons. EHS and ROHP reiterated the recommendation that researchers should get tested before reporting for work in the laboratories.

10/8/2021: A senior research scientist in the NEIDL BSL 3 had punctured the tip of her left ring finger with the tip of a scissors with blood on it from infected SARS CoV2 mice (Washington 1 strain) and it punctured through two pair of gloves. ROHP was consulted and after further assessment, determined that the exposure was a very low risk; there was evidence of a superficial, nonbleeding pink spot on the skin. Researcher was advised to contact ROHP if any signs and symptoms of SARS-CoV-2 appear. This researcher received the COVID-19 vaccine. Researcher tested for SARS-CoV-2 the day of the incident and had more frequent testing over the next week. A report was submitted to BPHC.

III. Protocol Review

1. Bhz – Annual Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2446		SARS-CoV-2 research. Diagnostic development and evaluation, antiviral testing, and host response evaluation.	BSL3	N/A	BUMC

Primary Reviewer: Rob Davey	Secondary Reviewer: Shannon Benjamin

Applicable NIH Guidelines: N/A

Meeting Comments: The purpose of this protocol is to study SARS-COV-2 diagnostics and prevalence, as well as treatment and host responses. This protocol has been reviewed multiple times over the last year for several amendments. In this annual renewal PI is adding one additional human cell line, a new disinfecting agent and a new personnel. Training are all complete and changes does not affect risk assessment. PI is also adding clinical samples obtained from the BU testing center provided by a BU collaborator through an established IRB protocolviruses from the clinical samples will be cultivated on cells in the BSL3. Samples are transported following DOT requirements. No major concerns were noted. The following will be communicated to the PI:

- In the NEIDL BSL3 lab 5% Microchem Plus is used a disinfectant instead of Microchem. Although both are adequate to inactivate SARS-CoV-2, clarify which particular one is used.
- In the RESEARCH LABORATORY FACILITY INFORMATION 1. Laboratory locations and corresponding Biological Safety Levels, remove “Rachel Fearns” from the Shared PI column for the suite.
- VII. RESEARCH PROJECT DESCRIPTION, #3, Please correct all instances of this reference “Biosafety Guidance for Inactivated SARS‐CoV‐2” to “Biosafety Guidance for Inactivated SARS-CoV-2”.

Motion: Conditional Approval (Administrative Review)	For: 11	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

2. rDNA/Bhz – Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
2439		Storage, Propagation and Distribution of BSL-3 Emerging Pathogens	BSL3	N/A	BUMC

Primary Reviewer: Rob Davey	Secondary Reviewers: Shannon Benjamin

Applicable NIH Guidelines: Sections III-D-1-b; Appendix B-III

Meeting Comments: The original protocol was for obtaining, developing stocks and storing viruses that can cause human disease and providing these to researchers. Work is also done (previously approved) with mosquitoes to study

infection cycle and isolate viruses from these insects. The new amendment seeks to add recombinant work to the protocol and suggests infection of mosquitoes with recombinant viruses as well as isolating and working with mosquito genes in insect and mammalian cells. However, reviewers expressed concerns about a procedure which suggests use of glass capillary tube for infecting mosquitos. Recombinant viruses that express green fluorescent protein will be made and used to monitor infection in cells. A new Co-PI with extensive molecular virology experience has been added to the protocol.

It was suggested that the proposed recombinant DNA work be put into a new protocol as the work is clearly departing from the initial intention of the protocol. The following will be communicated to the PI:

- IV.1, Laboratory locations and corresponding Biological Safety Levels, add "John Connor" to the Shared PI column for the suite.
- VII.3, It is unclear what specific mosquito genes are being introduced into mammalian cells and a better explanation of the goals of the project is needed for a proper risk assessment.
- VII.3, In the section where new mosquito work is described, please remove "The practices in the insectary are the same irrespective of the virus employed" and describe the actual practices to be used.
- VII.3, Please expound upon recombinant viruses that will be used in mosquito work.
- VIII.6, Under sharps, it is indicated that mosquitoes will be injected. It is unclear what they are being injected with. This could be virus or genetic material. If it is genetic material to make recombinant viruses, an assessment of the insectary will be needed to assess containment of such mosquitoes. If it is being used to inject viruses, then please state this. The work is already approved for infection of mosquitoes with normal viruses.
- Has EHS been contacted regarding the use of glass capillary for mosquito injection? Also it is not clear if this glass capillary will be used to inject mosquitos with recombinant risk group 3 viruses. Please provide clarification.

Overall recommendation of the committee is to extract the recombinant DNA and molecular analysis part of the existing protocol into a new protocol with better description of project goals and manipulations to be performed.

Motion: Defer	For: 11	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

3. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2350		Viruses pseudotyped with hemorrhagic fever virus glycoproteins and virus-like particles for study of infection mechanism	BSL2	N/A	BUMC

Primary Reviewer: Robin Ingalls	Secondary Reviewer: Jim Keeney

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

Meeting Comments: The goal of the project is to study viral entry mechanisms using replication defective pseudoviruses composed of murine leukemia viruses, lentiviruses, or vesicular stomatitis viruses engineered to express the glycoprotein of a donor virus of interest as well as a reporter gene to document viral uptake. Various factors that might affect infection are then studied. In terms of biohazards, the work involves BSL-2 level virus work including replication incompetent commercially available lentiviruses. Recombinant DNA work includes both virus and eukaryotic cells. Pseudotyped viruses are assembled in the eukaryotic cells (293) following transfection of a plasmid containing the glycoprotein of interest under a promoter and then infection of the cells with the packaging viruses (e.g., rVSV). Gene disruption in the host cells is accomplished using CRISPR/Cas9 system as well as siRNA. Additional biohazards include commercially available human cell lines (Hela, HEK293, 293FT, SW13, Huh7, U2OS, A549, THP-1, HepG2); non-human primate cell line (vero); primary monocytes, liver cells, and fibroblasts purchased commercially; and human skin explants from the University of Iowa tissue bank (prescreened). Cells and tissues are handled after fixation with formalin, paraformaldehyde or glutaraldehyde. DNA and RNA extraction is performed using Trizol. Liquid and solid wastes are appropriately handled. The rDNA section has been filled out correctly. No concerns were noted.

BUA Site Assessment: All safety plans are in place. All ROHP clearances and trainings are current. PPE use is appropriate. Fume hood and biosafety cabinets are all duly certified. *PI recused himself from voting.*					
Motion: Approve	For: 11	Recuse: 1	Against: 0	Abstain: 0	Absent: 0

4. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2063		Lung injury and sepsis	BSL2	ABSL2	BUMC

Primary Reviewer: Inna Afasizheva	Secondary Reviewer: Colleen Thurman
Applicable NIH Guidelines: Section III-D-1-a, III-D-2-a, III-D-4-a.	

Meeting Comments: This protocol investigates molecular mechanism of lung injury from higher oxygen level in the lung (hyperoxia) or bacterial infection with a goal to apply the gained knowledge in treating patients with lung injury. They also investigates the mechanism of sepsis in mouse model. The protocol has three major goals; 1) to determine the role of hyperoxia on micro-RNA expression in cultured cells; 2) to determine the inflammatory response on microbes during bacterial pneumonia and 3) to understand the mechanisms of sepsis development in the colon after bowel perforation as a result of severe infection. For the second and third goals, animal models consisting of various transgenic mouse will be used. Protocol provides detailed description of all experimental procedures including culturing cells, *in vitro* studies, rDNA work, bacterial culture, and mouse work. It was also noted that the protocol includes two recent amendments that included experiments with human cell lines. However, the protocol for work with human fluids and specimens was not provided and proper risk assessment could not be done. The following will be communicated to the PI:

- Please update BBP training for Ausra and Jin; Chem Safety for Ausra and Kwok.
- Update ROHP clearance for Ausra.
- Please use correct item # and sub-item numbers with different number set styles. It is confusing as presented currently.
- Please elaborate the description of how human cells and fluids are transported to the laboratory.
- How are they received and stored.
- Describe the laboratory procedure for the use of human cell and fluids, what safety measures are used in their handling (such as biosafety cabinet use, PPE use) and how the wastes are disposed of.
- VII. 3. 2. 4. Mouse study for inflammation (CLP) PPE should include sterile gloves for surgical procedure. This is covered in the statement “under aseptic conditions” but is not described specifically in the PPE description below.
- VIII. 1. Check animal handling/cage changing.
- VIII. 5. Provide correct BSC certification date. The protocol was submitted on 9/1/21. The recent certification dated cannot be 11/30/2021 (may be it is the expiration date).
- IX. Live animal use should be checked
- Section A.4. IACUC 15546 is now PROTO201800356 approved through 9/26/2024. The IACUC 15545 is now PROTO201800354 approved through 1/1/2022 (TR201800007 is for this protocol, most recent TR202100000034).
- Section H. Animal Experiments: Add new IACUC numbers above.

BUA Site Assessment: The lab needs to establish blood borne pathogen exposure control plan, which they are currently working on. Update on ROHP clearances have been submitted for or a few lab members. The BBP and Chemical Safety training are also due for few lab members and their delinquency has been communicated to individual members. Their biosafety cabinet and fume hoods are duly certified.

Motion: Conditional Approval (Re-review by primary and secondary reviewer)	For: 11	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

5. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1530		A Systems Biology Approach to Tuberculosis Biosensors for Physiological Monitoring Identifying Molecular Signatures of Drug Susceptibility A Diagnostic for Viral DNA	BSL2	N/A	CRC

Primary Reviewer: Barbara Slack	Secondary Reviewer: Sajal Ghosh

Applicable NIH Guidelines: Section III-D-1-a, Appendix B-II-A, Appendix G-II-B-1

Meeting Comments: The goal of the project is to decipher gene regulation and metabolism in multiple bacteria including *E. coli* and non-pathogenic mycobacteria and related non-pathogenic actinomycetes. Chromatin Immunoprecipitation (CHIP) will be used to determine which bacterial genes are bound by various transcription factors. Transcription factors and other genes of interest will be overexpressed or deleted. Gene will be measured by qPCR microarrays, RNA-Seq and/or fluorescent measurements. Strains of *E. faecium, S. aureus*, and *P. aeruginosa* will be exposed to different compounds, toxins and stress conditions and analyzed by RNA-seq. Results will be used to develop diagnostics and biosensors. Bacterial will be cultured in filter-capped flasks and will be handled in biosafety cabinets. Transformation work will be done in *E. coli* and characterized using microfluidic device. For cleaning and disinfection of the device, 10% fresh bleach treatment followed by wash with 70% ethanol and water will be done. In another part of the protocol they will examine the how exposure of different antibiotics or chemical compounds such as toxins, lipids or steroids, different media formulations, affect gene expressions in pathogenic bacteria. Separately, they also will work with plasmids that express part of the SARS-CoV-2 genome that will be used for developing diagnostics (no work will be done with live SARS-CoV-2) and to validate application of a biosensor for identification of metabolites in bodily secretions such as sweat, interstitial fluid, saliva and urine samples. It was noted that this was a nicely written protocol and only minor issues were noted. The following will be communicated to the PI:

- Section III:
  - PI needs to complete the rDNA/Infectious Agents/Select Agents/Experienced question. PI's LST, BSL1/2, BBP and Chem Safety trainings also have expired.
  - BBP training for Martinez and Tierrafria also need to be updated.
  - Except for Kuzmanovic and Lally, medical clearance for all have expired.
- Section VII.3. State which toxins will be used.
- Section VIII.3. Add surgical mask.
- Section VIII.5. Update Biosafety Cabinet Certification date.
- Section A. *Mycobacterium gilvum* and M. avium are listed in the hazardous biological agent list but the lab procedure only indicates use of *Mycobacterium smegmatis*. Please clarify or consolidate.

BUA Site Assessment: All safety plans are in place. Few members need update of their ROHP clearances and some trainings. They have been informed of those deficiencies. Their biosafety cabinet is duly certified.

Motion: Conditional Approval (Administrative Review)	For: 11	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

6. Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2349		Rapid antibiotic susceptibility testing in fluid shear environments	BSL2	N/A	CRC

Primary Reviewer: Carmela Abraham	Secondary Reviewer: Jim Keeney

Applicable NIH Guidelines: N/A

Meeting Comments: The protocol investigates better and faster ways to determine if bacteria are resistant to antibiotics. Their work will potentially benefit treatment of antibiotic resistant bacterial infections. The investigators are developing new technique for rapid detection of antibiotic susceptibility using *Staphylococcus aureus* as the model system. Human blood spiked with bacteria is used in their experiments. Transportation of blood samples from

Brigham Women's Hospital and experimental procedures are described in great detail in the protocol. ROHP medical director clarified that the lab has been vaccinated for *Streptococcus pneumoniae*, but they will clarify with the PI if any new personnel is working in the lab and vaccine will be provided to new members when needed. The following will be communicated to the PI:

- Section VIII.1. Please check 'Plating, colony counting.'
- Section VIII.7A. Please modify the bleach treatment section to state that liquid waste will be inactivated (not sterilized) with bleach at a FINAL concentration of 10% for 30 minutes prior to the disposal down the drain.

BUA Site Assessment: The ROHP clearance and trainings, including the shipping training, are current for the lab. They have bloodborne exposure control plan. Their biosafety cabinet and fume hoods are duly certified.

Motion: Conditional Approval (Administrative Review)	For: 11	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

7. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2348		In vivo imaging of structure and function in the vertebrate brain	BSL1	ABSL1	CRC

Primary Reviewer: Ed Loechler	Secondary Reviewer: Colleen Thurman

Applicable NIH Guidelines: Section III-D-4-a, III-E-1, III-E-3-a; Appendix C-VIII.

Meeting Comments: The goal of this project is to identify the neural circuits involved in the generation of cognitive behaviors, notably flexible decision-making, based on reasoning, planning and observational learning. Animal models (e.g., rats, mice and zebra finches) are trained to exhibit these behaviors. Genetic tools used include: viral vectors, recombinant DNA and gene editing, which alter neural circuits. Behavioral analysis involving *in vivo* imaging of neural circuits in awake behaving animals is employed. Genetically encoded fluorescence proteins and calcium sensors are used to label neurons and provide visible markers for structure and function in the intact nervous system. The probes are achieved by: (1) Intracranial (targeted) or retro-orbital (systemic) injections of adeno-associated viral vectors (AAVs), and (2) Breeding of animals from existing transgenic lines. All viral transfers (portioning virus stock into aliquots, loading virus into injection needles) occur in CILSE rooms. Appropriate PPE (labcoats, goggles, gloves and surgical mask) are worn. Laboratory staff abide by stated safety precautions. Materials in contact with virus are decontaminated in 10% bleach and disposed of in dedicated biohazard containers. All surfaces are washed with a 10% bleach and rinsed with 70% ethanol. Surgical tools are rinsed with betadyne and washed with soap and water before being sanitized. Surgical methods were described and are IACUC approved. The lab will import a transgenic rat from Janelia Farm Research Campus and Zebra Finches from Rockefeller University which will be breed and housed in CRC vivarium. It was noted that this is a generally well written proposal, with potential hazards generally well accounted for. The following will be communicated to the PI:

- Please update rDNA/IBC Policy training for Dr. Scott and Hongiie Xia. Update rDNA/IBC Policy training, and BBP training where applicable.
- ROHP clearance for Kane, Scott and Xia need update.
- Check animal handling/cage changing.
- Check pipetting infectious liquid for AAVs.
- Check surgical mask due to COVID requirement.
- The PPE section question 2 Indicates work that could produce aerosols will be done in a BSC, but use of BSC is not checked. Please complete this section or clarify.
- Section A. 4. Indicates that AAV being injected into rat (IACUC pending), but Section H Animal experiments suggests mice might also be inoculated (clarify if one or both species are being used).
- Add approved IACUC protocol information.
- PROTO201800577 Chronic recording and manipulation of neural activity in behaving songbirds through 10/12/2023 zebra finches in the Laboratory Procedure section.
- Add the following IACUC protocol information in the Hazardous Biological Agent List as appropriate:
    - PROTO201900690 Neural mechanisms of cognition through 2/7/2022 rats

- PROTO201900084 Imaging Cortico-hippocampal Dynamics in Mice through 1/23/2023 mice
- PROTO201800674 (Transgenic GCaMP Rats) and PROTO201800578 (Songbird breeding and egg production) are closed.

- Update applicable NIH Guidelines question to Section III-D-4-a, III-E-1, III-E-3-a; Appendix C-VIII.

BUA Site Assessment: Some lab members need to update ROHP clearances. Trainings are current for all members. PPE usage is appropriate.

Motion: Conditional Approval (Administrative Review)	For: 11	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

8. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1528		Microchip to Detect Influenza Infection and Type in Nasopharyngeal Swabs Integrated Microfluidic Platform for Detection and Diagnosis of Avian Influenza Portable Low Power Nucleic Acid Extraction Module	BSL2+	N/A	CRC

Primary Reviewer: Barbara Slack	Secondary Reviewer: Ron Morales

Applicable NIH Guidelines: III-D-2-a, Appendix C-II, Appendix B-II

Meeting Comments: The goal of the project is to develop plastic microfluidic diagnostic chips and a paper-based lateral flow device to detect and identify influenza A, B, respiratory syncytial virus (RSV), or SARS-CoV-2 in microliter-scale human nasopharyngeal samples. Nasopharyngeal swabs will be collected from human subjects; waste water will be collected and processed for PCR analysis. DNA segments from viruses will be used as positive controls. Cultured MDCK or Hep-2 cells will be infected with commercially purchased Influenza A, B or RSV. Medium from infected cells, used as positive controls, will be added to the lateral flow device, which is impregnated with colloidal gold, and virus will be measured by PCR. All samples are treated with guanidine thiocyanate extraction buffer, either commercial or lab-made, which inactivates virus. Microchips will be bleached after use. Chips and paper-based lateral flow strips will be discarded as biohazardous waste after use. Cell lines will also be used for viral plaque assays; after infection cells will be fixed with formaldehyde and stained with crystal violet. Work with virus and virus-infected material will be carried out using BSL2+ precautions. Medical Director confirmed that they provide vaccination for Influenza A and B to the lab members and will make sure that all are vaccinated for the SARS-CoV-2. Only few minor concerns were noted. The following will be communicated to the PI:

- Please use same last name for Lena throughout the protocol to avoid confusion that they may be two different individuals.
- Section VII.3- Lab Procedures: Please state how formaldehyde-treated human cells stained with crystal violet, and also virus infected human cells (if not to be treated with formaldehyde) will be disposed of.
- Section VIII.7A- Remove the statement that describes collecting liquid waste in 70% ethanol as a method of disinfection and replace with the use of bleach to a final concentration of 10% for liquid waste treatment.
- Section VIII.7B- please add a line to this section stating how cultured human cells will be disposed of (see the first comment above).
- Section IX. Please check N/A under ABSL (at the bottom of the table).

BUA Site Assessment: Just few lab members need to update their ROHP clearance. All trainings are current. Biosafety cabinets and fume hoods are all duly certified.

Motion: Conditional Approval (Administrative Review)	For: 11	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

9. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
805		Study of Prion Diseases in Animals	BSL2	ABSL2	BUMC

Primary Reviewer: Sajal Ghosh	Secondary Reviewer: Colleen Thurman

Applicable NIH Guidelines: Section III-D-1-a, III-D-2-a, III-D-4-a, III-E-1; Appendix B-III-D, G-II-B
Meeting Comments: The goal of this protocol is to investigate the manifestations of prion diseases of both genetic and infectious origin. The work involves expression of cellular prion protein and variety of mutant prion proteins in *in vitro* tissue culture and injection of infected cell lysates or brain extract from infected laboratory animals into commercially purchased transgenic mice. The protocol also involve significant amount of rDNA work involving 3rd generation lentiviral vectors to make mutant versions of prion protein and CRISPR-Cas9 technology to eliminate expression of some specific cellular genes to assess their role in this disease. Various prion extracts are injected directly into the brain of anesthetized animals and are monitored in the animal science center ABSL2 rooms for disease development. The animals are euthanized as per IACUC protocol before any samples are taken out for histology or molecular biological analysis. They also collaborate with another BU PI on testing the effects of various mutant prion proteins on primary neuronal cells. For this purpose, iPS cells are generated from the blood of CJD patients and then differentiated into neuronal cells. The protocol provides detail description of precautions taken by the researchers in the lab and during the work. They strictly use disinfection or sterilization protocols applicable for prion protein. Liquid wastes will be treated with 40% bleach for 1 hour, or 1N NaOH for 1hr or overnight as needed; solid wastes including disposable sharps will be autoclaved at 132°C for 4.5 hrs and stowed away for incineration. All of their wet lab work is being done in USDA inspected prion-designated room . Minor concerns were noted. The following will be communicated to the PI: ● I.2. Since this is a 3-year renewal, there is no need to check 'personnel'. ● III.1 Add titles to table for Gatdula and Vultaggio (Grad student and lab manager). ● III.3. Training Update needed: Amin –rDNA/IBC policy, Harris – BSL1/2, BBP, Chem Safety. ● ROHP clearance updated needed: Vultaggio, Yedlapudi. ● VII.3. Please state which prion proteins are being used in this protocol. Is this prion protein infectious to humans? ● VII.3. Update old IACUC Approval Number AN-14997 to new number PROTO201800135 in the laboratory procedure and all other applicable places. ● VII.3. Change the statement 'sterilized with Ethanol' to 'disinfected with ethanol' in laboratory procedure section. ● VII.3. USDA permit 127692 is mentioned in Laboratory Procedure section, but that may be outdated, permit number says "pending" in Section A. USDA inspection for Permit 130140 has happened on Oct 5 2021. Please refer this permit in both Section VII.3 and in IX. Section A. ● VIII. 1. Check Animal Handling/Cage changing. ● VIII. 4. Double gloves and surgical mask should be checked off for ABSL2 work in . ● VIII. 5. Update BSC certification date. ● IX. Section A. 4. AN14997 is now PROTO201800135 approved through 5/6/2024. ● IX. Section H. Animal Experiments. Please update IACUC to PROTO201800135 approved through 5/6/2024. BUA Site Assessment: They have blood borne exposure control plan and other safety plans are in place. Their biosafety cabinet and fume hoods are certified. ROHP clearance for few members are being updated. Dr. Harris needs to update some of his trainings. USDA inspection is complete.

Motion: Conditional Approval (Administrative Review)	For: 11	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

10. Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1689		Placental immunology and preterm birth	BSL2	N/A	BUMC

Primary Reviewer: Tom Winters	Secondary Reviewer: Valeda Britton

Applicable NIH Guidelines: III-D, Appendix C-II, Appendix B-II
Meeting Comments: The project focuses on cytokines and interferon production in cells within the placenta and in response to inflammatory stimuli to investigate the hypothesis that pre-term labor may be caused by inflammation secondary to infections or Immunologic factors. However, they are not enrolling new subjects or collecting new

placenta samples. In this protocol placenta tissue DNA is extracted which are used as templates for PCR amplification for targets of interest. Immunohistochemistry staining of fixed slides is also done. The proposed use of PPEs for this protocol is appropriate. No sharps are used as slides that already contain fixed tissue as well as cells are being used. The blood-borne pathogen program is invoked as they are working with non-fixed placenta tissue that has been frozen. The wastes appear to be handled properly. Also the transportation precautions appear appropriate when materials are transferred between labs. No concerns were noted.

BUA Site Assessment: No new patients are currently being enrolled in this protocol. Blood borne exposure control plan is in place. Biosafety cabinet is duly certified. ROHP clearance is being worked out.

Motion: Approve	For: 11	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

11. Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1701		Multi-Scale Integration of Extracellular Matrix Mechanics in Vascular Remodeling	BSL2	N/A	CRC

Primary Reviewer: Tom Winters	Secondary Reviewer: Pinghua Liu

Applicable NIH Guidelines: N/A

Meeting Comments The goal of this protocol is to study how the microstructure in the walls of human blood vessels affect its stiffness. They compare differences in structure and stiffness between healthy blood vessels and those from diabetic donors to establish disease models. The research group receives arterial tissue from NDRI (National Disease Research Interchange, NIH NeuroBioBank, and from the Brain Banks at the BU Alzheimer Center. They test biaxial tensile strength, elastin levels, and collagen levels of the vessels. They then ship sections of the fixed tissue to the Massachusetts Histology Lab for Movat staining and review of the slides. The proposed PPE use is appropriate for BSL2 work, but no biosafety cabinet is used. Committee recommended that biosafety cabinet should be used. Razor blades are used and discarded into a sharps container. Waste disposal appears proper and liquid waste is collected in acid waste and discarded as chemical wasted. Blood-borne pathogen program is invoked as they use sharps in initial cutting of blood vessels. Shipping of fixed tissues are done in double packaging with leak and shatter-proof secondary container. The following will be communicated to the PI:

- Please remove checks from the Annual renewal/amendment change box and remove statements from the the summary changes box. Those are only for amendment submissions.
- Provide title of the Halvorsen and describe his experience in the “state how many years experience, when and where” question.
- Pipetting infectious liquid is checked but it is not clear from the laboratory procedure section what infectious liquid is being used. Please clarify.
- Work described in the protocol require the use of biosafety cabinet. You have a certified BSC. Please the box and provide all requested information.

BUA Site Assessment: They have blood borne pathogen exposure control plan in file. Some members ROHP clearance need update and they are working on it. Training is current for all members. They have biosafety cabinet which is duly certified.

Motion: Conditional Approval (Administrative Review)	For: 11	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

12. Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2527		Molecular characterization and therapeutic targeting of Protein Kinase D2 in t(4;14) multiple myeloma	BSL2	N/A	BUMC

Primary Reviewer: Inna Afasizheva	Secondary Reviewer: Xin Brown

Applicable NIH Guidelines: N/A

Meeting Comments: This new application focuses on t(4;14) translocation that is observed in 15% of newly diagnosed patients with Multiple Myeloma (MM). Project seeks to investigate the role and function of the Serine/Threonine Protein Kinase in t(4;14) observed in high risk patients with MM and to identify drug targets in MM. The approaches include gain/loss function study, genetics, and high throughput screening, CRISPR-Cas9 mediated gene manipulation and analysis of their effect on the protein kinase metabolism. Brunello sgRNA viral library lentiGuide-pro (system developed in Broad Institute) will be transduced in MM cells, cultured with selection marker, and used for Mass Spectroscopy (MS) and genome-wide screening. Experimental procedures to determine role of PRKD2 in MM cells growth and survival involve CRISPER-Cas9 mediated model and cellular models co-cultured with primary stroma cells from MM patients. The phosphoproteomic analysis will be done in collaboration with a BU collaborator. Cells overexpressing MMSET (nuclear receptor binding domain) will be used for MS analysis. Selected protein kinase inhibitors will be tested *in vitro* using proliferation, viability, and apoptosis assays. Primary samples obtained from patients will also be subjected to gene expression profiling, western blotting and assess drug sensitivity. Following will be communicated to the PI:

Reviewers expressed concerns that while the laboratory procedures described scientific objectives in great detail in the protocol, there is very little description of what biologically hazardous materials will be used and what safe handling procedure will be used or how the wastes will be disposed of. Because of the absence of this information, a proper risk assessment was not possible. Committee recommended submission of a revision of the application where hazardous materials are identified in each experiment types and risk management in those experiments are described. IBC program manager will contact the PI and will provide guidance on how to address these issues. Additionally, following specific issues also need to be addressed:

- Please provide protocol for manipulations with CRISPR-Cas9 system.
- Provide protocol for use, storage, and source of Brunello sgRNA viral library lentiGuide-pro.
- Please replace the statement “Our proliferation, viability and apoptosis assays” with corresponding actual protocols. Animal work has been proposed but no animal work related PPE, animal biosafety level, or IACUC application information have been provided. Remove the reference to animal work now. The protocol may be amended later before the initiation of animal work.
- Provide source of primary human samples and how they are being shipped to your lab clarifying where will they be unpacked and by whom (to confirm proper management of primary human samples).
- Please update protocol with description of how primary bone marrow stroma cells collected from MM patients.
- Add Surgical mask in PPE question 3.
- The certification of the BSC is expired on 12/05/2019.
- In the PPE and Safety Equipment section, please mark yes for spill kit. It is mandatory to have spill kit in the lab.

BUA Site Assessment: The lab has exposure control plan in file. PI is current with training and ROHP clearances. Their biosafety cabinet and fume hood are duly certified.

Motion: Defer (Re-review by PR and Chair and viewed by all members. Will go back to FCR for the committee to review)	For: 11	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

13. Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2526		Nanoparticle-mediated photothermal therapy for treatment of infection.	BSL2	N/A	CRC

Primary Reviewer: Carmela Abraham	Secondary Reviewer: Ron Morales
Applicable NIH Guidelines: N/A	
Meeting Comments: The group will test the feasibility of a combinational approach of nanoparticles (designed in the PI’s Lab) and light for lysing wide range of bacteria without using chemical antibiotics. In doing so, they will test	

binding of nanoparticles to the bacteria and will test impact of light + nanoparticles (photothermal therapy) on bacterial growth profile. Biohazard aspect of the protocol are nanoparticles and growth and culture of number of risk group 2 bacteria. This is a simple and straightforward protocol. Only few minor issues were noted. The following will be communicated to the PI:

- Provide the source of the nanomaterials.
- It is the policy at BU that mixed waste containing nanomaterial shall be treated and inactivated and disposed of as nanomaterial hazardous waste. Please add this statement.
- Is the *Staphylococcus aureus* include MRSA?
- Liquid waste to be inactivated by 10% bleach FINAL concentration for 30 minutes. Elsewhere it is mentioned correctly.
- Provide information for the biological safety cabinet to be used.

BUA Site Assessment: ROHP clearance and training are all current. Biosafety cabinet and the fume hood are duly certified.

Motion: Conditional Approval (Administrative Review)	For: 11	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

14. Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2530		Investigating the ability of various types of human cells to uptake of vitamin D and its metabolites	BSL2	N/A	BUMC

Primary Reviewer: Ron Morales | Secondary Reviewer: Sajal Ghosh

Applicable NIH Guidelines: N/A

Meeting Comments: In this new protocol PI plans to investigate the ability to uptake vitamin D and its metabolites by various types of cultured human cells, including adipocytes, muscle cells, keratinocytes, vascular endothelium, immune cells and fibroblasts. The lab will conduct liquid chromatography and beta scintillation counter measurements of vitamin D uptake and its metabolites in the various cell lines. Each cell lines will be treated with varying concentrations of vitamin D and their lipid extract analyzed. The protocol maneuvers described are straight forward. The main biohazard concern in this proposal is their use of human materials. Procedures that could potentially produce aerosols identified in this protocol include homogenizing, vortexing, vigorous mixing, and sonication of sample materials. PI has been doing this line of metabolite analysis study for decades. They have radiation permit for their use of 3-H labelled Vitamin D3 metabolites. No concerns were noted with their use of PPE or waste management. However, because of malfunction of the pressure maintenance system, PI's lab cannot perform any tissue culture work. Those need to be fixed before the protocol can be approved. The following will be communicated to the PI:

- Please note that Fuller rooms and are currently not usuable as they are not maintaining negative pressure and will need to be fixed before they can reuse the spaces.
- The liquid nitrogen Dewar must be moved to another properly functioning lab room.
- There is currently no Biosafety Cabinet (BSC) in room . The BSC is presently located in room which he cannot use. The BSC will need to be relocated to and recertified before any work can begin.

BUA Site Assessment: ROHP clearance of some members need update. Few trainings also require update. The room 1021, where the BSC is currently located is not maintaining negative pressure correctly. This need to be fixed.

Motion: Conditional Approval (Administrative Review + only when BSC is moved to and approved by the EHS)	For: 11	Recuse: 0	Against: 0	Abstain: 0	Absent: 1