Boston University
Institutional Biosafety Committee (IBC)
November 17, 2020 Meeting Minutes
Location: Zoom and/or by phone
Start time: 12:00 PM End time: 2:51 PM

Members Present: C. Abraham, B. Slack, R. Davey, E. Muhlberger, E. Loechler (Joined 12:30 PM), R. Morales, T. Winters, R. Varada, S. Kurnick, J. Keeney, R. Timmerman, V. Britton, J. Barton
Guest Present: T. Killen, F. Ennever, A. Ahmad, J. Davis, K. Tuohey, S. Benjamin, C. Thurman, P. Richmond, C. Bennett
Staff Present: S. Ghosh, C. McGoff

I. Review of October 20, 2020 IBC Meeting Minutes

Additional comments added by the AVPRC and Executive Director to the minutes draft in the lab inspection report section was presented for member's review before voting. No concerns were noted for those additions. No comments or questions were voiced for the rest of the minutes.

Motion: Approve

For: 12; Against: 0; Abstain: 0; Absent: 1

II. New Business

A. Safety & Quality Assurance Program (SQAP) Report: Issues on lab procedures of IBC protocol

The committee discussed a laboratory safety issue with regard to the performance of some animal inoculation procedures in the wet lab of a PI in the R-building. The IACUC and the EHS recently noted that infection of mice with several risk group 2 pathogens (RG2 agents known to cause respiratory tract infection) are being done on open bench in this research lab. In an email response the PI clarified that the infectious dose they are using in the inoculation studies are much lower than that can cause experimental infection in humans. They further clarified that most of these pathogens are commonly found in the nose of toddlers and adults and a symptomatic infection only takes place when other risk factors (such as weak immunity or other vulnerability) are also associated. Additionally, mouse-adapted strains (weakly pathogenic in humans) are used wherever possible and lab members are vaccinated for respiratory tract infections. They cited references to suggest that the animal infection procedures in their protocol is also followed by peer investigators everywhere and there has been no incident in their lab during their two decades of research involving these procedures. However, it was noted that the doses being used as stated in the IBC application is sometimes larger than what is indicated in the PI's clarification letter. The committee recommended that PI should provide reference information supporting their explanation that there is no risk of infections to the lab members from the indicated concentration of agents used during animal inoculation in the event of an accidental exposure (via spill, injection or aerosol). In addition, the committee asked the PI to align the information in the IBC protocol with the explanation they provided.

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

ROHP Report: On 10/25/20, an MD PhD student sustained a percutaneous exposure while working in a teaching lab with a cadaver embalmed with ethanol and formalin. Risk assessment revealed no blood borne pathogen risk factors and counseling was provided. ***EHS follow-up:*** A student was dissecting a cadaver on a metal cadaver table, which has two large 30 pound doors to close over the cadaver. When the doors are open (for dissection) the table is designed so that the doors can be pushed underneath the table and held back/in place by a metal clip. The metal clip is not reliable and can sometimes come undone. The student was examining the posterial abdominal area which required him to lean over the cadaver. The door on the side of the table that the student was standing in front of came unclipped while he was leaning over the cadaver. The door hit the student in the shin which caused him to jab his left finger with the scalpel he was holding in his right hand. Since there were no blood borne pathogen risk factors, there was no post-

exposure prophylaxis. The root cause was defective equipment. It is recommended that the cadaver table be replaced with a table that has a better design.

On 11/6/20, a PhD student turned the knob of the glass tube when the anaerobic depressurized glass tube in her left hand broke resulting in an approximately 1cm laceration and a trip to the emergency room for two stitches. The glass tube contained an ancient bacteria which is considered an environmental bacteria and not pathogenic to humans. ***EHS follow-up:*** EHS staff noted that the student did not report any noticeable damage to the tube prior to using it. The root cause was found to be not being conscientious. To prevent recurrence, the student will use cut-resistant gloves in addition to nitrile gloves when working with this material.

Members were informed that there have been several reports of employees and researchers testing positive for SARS CoV-2, both symptomatic and asymptomatic. ROHP has found no breaches in their follow-up reports. These are all reported to BPHC; so far there is no indication that positive tests are related to research working with the virus.

EHS Report: *O*n 9/22/20, ROHP received an email from a BU medical student reporting he sustained a splash to his left eye on 9/21/20 at 2:30 pm. The student was in touch with both ROHP and BU Student Health on 9/22/20 for further examination and counseling. The student was trying to open a microcentrifuge tube with some force and when it opened a few droplets of a reaction mixture (cDNA from RNA isolated from a human cell line) splashed into his left eye. The work did not involve cloning or any plasmid which could have replicated in a living system. The root cause was lack of PPE. EHS advised the student to wear safety eye protection and reviewed procedures for reporting incidents.

III. Protocol Review

1. Bhz – Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
2446		SARS-CoV-2 research. Diagnostic development and evaluation, antiviral testing, and host response evaluation.	3	N/A	BUMC

Primary Reviewer: Rob Davey Additional Reviewer: Shannon Benjamin	Secondary Reviewer: Carmela Abraham
Applicable NIH Guidelines: N/A	
Meeting Comments: This protocol was deferred in the October 2020 IBC meeting because the reviewers of the protocol felt at the time that PI's protocol does not provide satisfactory explanation on safety measures to be practiced while working with SARS-CoV-2 as stipulated in a newly developed SOP. However, they said the SOP was prepared after the original submission of the amendment. The SOP has since then been modified to a guidance and posted on the IBC website. In this new submission of the amendment PI provided clarification of the lab procedures and aligned them to the new guidelines. The purpose of the amendment remain the same as the one reviewed in the last IBC meeting. They will isolate SARS-CoV-2 from patient samples (swabs). Samples from de-identified positive patient samples will be cultivated on Vero cells. Fixed samples will be stained for virus antigen. Nucleic acids will be isolated using TRIzol. The validity of these inactivation methods is well described and appear appropriate indicating that the material will be inactivated. They will also evaluate the ability of surfaces and solutions to destroy viable virus. Virus is either mixed with the solution or placed on the test surface and after a time residual virus is collected and assayed for growth on Vero cells. Overall, the work appears to be appropriately performed by staff using approved handling and inactivation procedures that are compliant with the SOPs regarding pathogen inactivation and handling of inactivated SARS-CoV-2 material.	

Motion: Approve	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

2. rDNA/Bhz – Annual Renewal

BUA	(PI)	Title	BSL	ABSL	Campus

1157		A systems biology approach to tuberculosis - BSL3 Part.	3	N/A	BUMC

Primary Reviewer: Elke Muhlberger Additional Reviewer: Shannon Benjamin	Secondary Reviewers: Carmela Abraham

Applicable NIH Guidelines: Sections III-D-1-b, III-D-2-a; Appendix B-III-A

Meeting Comments: The protocol investigates transcriptional network in *Mycobacterium tuberculosis*. They grow these bacterial stocks in BSL3 suite and perform transformation in them with different plasmids and then extract DNA and RNA from them to do variety of biochemical analyses including transcriptome analysis and Chip-Seq.
It was not clear if there is an approved SOP that describes removal of *M. tuberculosis* material inactivated by incubation with 1% formalin for 30 min. It was not clear to the committee if an SOP has been developed that describes the precise conditions of heat inactivation, including volume, bacterial load, heat block, measurement of temperature and time. If this is not the case, it should be indicated that an SOP will be developed and approved by NEIDL EHS before heat inactivated samples will be removed from the BSL-3 lab. It was noted that the application states BSL3 suite W934 is being used for storing bacterial stocks in cryovials, but this BSL3 suite was decommissioned many years ago. It was not clear where in the NEIDL the biohazardous materials for this protocol are stored. It was also noted that PI does not have proper access to BSL3 facilities in the NEIDL and therefore clarification is needed if any work is being done currently or the protocol is just being maintained to keep it active for future work.

- Please mark yes if the project continues to be a NON-DURC.
- The laboratory procedure section (Section VII #3) mentions the use of "Boston University EHS approved SOP" when referencing inactivation procedures. Please provide appropriate NEIDL SOPs for formalin and TRIzol inactivation methods.
- In the "Extraction of DNA" section, there is a non-functional link to a publication that describes heat inactivation. Please provide an updated link. Also, provide an SOP for the procedures described therein. Committee recommended that if such SOPs do not exist, it should not be indicated in this protocol that the treated material will be removed from the BSL3 lab unless documentation is provided that shows the described methods work.
- It is stated that liquid waste will be treated with 1% Vesphene or 10% Clorox bleach. When will bleach be used?
- Section VIII #3- Update PPE use to include the use of PAPRs. Due to the global PPE shortage, PAPRs are now exclusively used in BU BSL3 labs. Remove the sentence in the "other" section.
- BSC certification date must be updated.
- Section VIII #7A- Liquid waste disposal section should indicate that Vesphene will be added to a final concentration of 1% for at least 30 minutes.
- Section VIII #10 - Clarify the storage location of samples, "W934F" in the W building. This facility was decommissioned several years ago. Are samples still stored there or in the NEIDL BSL3?
- It is noted that no work is being done on this protocol in the NEIDL. Please clarify the current status of the protocol and purpose of this renewal.

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

3. rDNA/Bhz – Annual Renewal

BUA	**(PI)**	**Title**	**BSL**	**ABSL**	**Campus**
2442		Investigating the role of viral proteases in disease pathogenesis	3	N/A	BUMC

Primary Reviewer: Elke Muhlberger Additional Reviewer: Shannon Benjamin	Secondary Reviewers: Carmela Abraham

Applicable NIH Guidelines: Sections III-D-1-b, III-D-2-a, III-D-3-b; Appendix B-III-D and G-II-C

Meeting Comments: In this amendment the PI is proposing to add an experimental procedure where SARS-CoV-2 virus will be inactivated by the application of UV-C light. Committee noted concerns from both reviewers and BSL3 biosafety officer that UV irradiation is not considered a reliable method for the inactivation of liquid viral material.

The PI provided few published reports that suggest UV-C as a useful inactivation tool for SARS-CoV-2 and also provided a preliminary draft of an SOP about how the UV-C-mediated inactivation process will be carried out. However, it was not clear under which conditions the PI will perform the mentioned inactivation testing (volume, viral load, closed tubes or plates, distance to UV source etc.) and whether the testing result was reviewed and approved by NEIDL EHS. Following discussion with the BSL3 BSO, PI sent an email to the IBC just the day before the IBC meeting, where they requested removal of the appended SOP draft on UV-C inactivation protocol as well as removal of corresponding cited publications. The last minute changes were requested as the testing parameters described in these publications do not align with the UV-C applications proposed in the amendment. Some occupational safety concerns for the use of UV-C source were also noted. PI has been connected to the radiation safety department, who are currently helping the PI in designing and execution of the experiments involving UV-C exposure. The committee determined that because of incomplete nature of the experimental design and absence of sufficient safety validation data, a proper risk assessment for this amendment could not be done. It was recommended that they implement and validate the inactivation procedure first before developing an SOP. The inactivation data will have to be approved by EHS and IBC Chair before the inactivation method is adapted for regular use.

Motion: Withhold Approval	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

4. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1424		Molecular determinants of RAS dependency in human cancers	2	2	BUMC

Primary Reviewer: Barbara Slack	Secondary Reviewer: Susanna Kurnick

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

Meeting Comments: The goal of this protocol is to define the KRas dependency in a number of cancers including lung, pancreatic and colorectal cancers and to study signaling networks. These include identification of non-coding RNA expression signatures, establishment of an epithelial-mesenchymal transition (EMT)-cancer stem cell signaling network in *KRAS* mutant cancers, and to identify key molecular determinants that link EMT to KRas dependency. Models to be used in the protocol include human cancer cell lines in culture and mouse xenografts of human cancer cells. They will isolate RNA from *KRAS* mutant cancer cell lines and perform gene expression analysis, protein expression and cell growth of KRas-dependent and independent cell lines. Lentiviral shRNA vectors will be used to knock down *KRAS* or other cancer-related genes in different lines. Small molecule inhibitors will also be used. They will study EMT in these cells by western blot, by Induction with growth factors, and by blocking with anti-cancer agents currently in use (kinase inhibitors). PI clarified that these anticancer agents have all been tested in animal models to be non-toxic. Protocol also include use of Xenograft model which involves injection of human cancer cells into nude mice.

- Section III.- Please update training for Gulthein and ROHP clearance for several lab members
- Section VIII.1- Please check animal handling and animal inoculations (a mouse xenograft model is described).
- Section VIII.3- PPE used in lab seems excessive (are N95 respirators, shoe covers, head covers necessary for lab work; assuming live animal work is being all done in animal containment facility?)
- Section VIII.4- N95 may not be necessary if all these activities occur inside of a BSC.
- Section VIII.5- BSC certification date expired on 10/29/2020
- Section VIII.6. Please specify that sharps containers, once full, will be discarded in double red bag-lined biohazardous waste containers.
- Section A. Human cancer cell lines can conceivably cause human disease if introduced via a needle stick (Gugel, EA, NEJM 315:1487, 1986); this should be indicated on the table. Provide current IACUC approval number in the table.
- Section H. rDNA vector packaging system. Lab Procedures text identifies system to be used as a third generation system, rDNA table says it is 2nd generation. Please clarify which is correct.
- Last item on Agreement Policy not checked (ROHP clearance).

BUA Site Assessment: Exposure Control Plan (ECP) is in place. Some members need ROHP clearance and some also need updated training. Biosafety cabinet certification date expired, but the lab already contacted service provider for re-certification.					
Motion: Conditional Approval (Administrative Review)	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

5. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2259		Metabolism and regeneration in primary neurons	1	1	CRC
Primary Reviewer: Barbara Slack		Secondary Reviewer: Colleen Thurman			
Applicable NIH Guidelines: Sections III-D-1-a, III-D-2-a, III-E-1					

Meeting Comments: The goal of this protocol is to study epilepsy in neuronal primary cultures. They are testing novel neuronal modulation methods including the effect of fiber-based ultrasound stimulation and of nanoparticle assisted ultrasound stimulation in primary rat neurons. They are using calcium imaging and electrophysiology as assessment tools. They describe how embryonic primary spinal cord tissues are obtained and how they perform cell culture work with those tissue slices. AAV-associated viral particles (Addgene) will be used to induce GCaMP expression in primary neurons. Committee noted that the protocol does qualify to stay as a BSL1 protocol as only AAV vectors are being used in rat cells. It was also noted that eye protection is not mandatory for ABSL1 work.

- Section I. Summary statement box should be left blank as it is required only for amendments.
- Section III. PI's rDNA training is out of date. Protocol indicates PI has no experience with rDNA work – is this correct?
- Section VII.3.
  - Please describe how AAV particles and nanoparticles will be handled, utilized in experiments, and disposed of. Define LFP (local field potentials?).
  - What is the IACUC approval number?
  - If mice primary neurons will also be used along with rat neurons, please add mouse work to the Project Description and Lab Procedures section.
- Section VIII.1-Please check 'animal handling'.
- Section VIII.4- Shoe covers required in vivarium. Back fastening gowns are not required in ABSL1 lab, regular lab coat is sufficient.
- Sections IX. Live animal use box should not be checked unless biohazardous materials are being administered into live animals. It appears that viruses will be used *in vitro* only. If not, please elaborate in Lab Procedures.
- Section H. rDNA table: Rat and mouse primary neurons both should be listed under Eukaryotic Experiments (not under Prokaryotic experiments section).

BUA Site Assessment: Biosafety manual is available in the lab and ECP is in place. All members have ROHP clearance but PI needs to complete rDNA/IBC Policy training. Biosafety cabinet is duly certified.

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

6. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2256		Imaging cancer cell metabolism	2	2	CRC
Primary Reviewer: Rob Davey		Secondary Reviewer: Colleen Thurman			
Applicable NIH Guidelines: Sections III-D-1-a, III-D-2-a, III-E-1					

Meeting Comments: This protocol investigates cancer cell metabolism through spectroscopy/imaging techniques with a goal to be able to get quantitative variations in individual cells in a tumor. They will image cells and tissues from animals and human biopsies to evaluate imaging systems to detect cell metabolic state. The biohazard concerns are from the human cell lines, animal work, recombinant DNA and human tissue samples. Cell samples are prepared

in one lab space and then carried to the microscope in sealed containers. Xenograft tumors will be generated in mice and the effect of anti-tumor drug treatments on them will be assessed through approved IACUC protocol. Replication incompetent 3rd generation lentiviruses will be used to suppress expression of tumor genes such as PTEN and ACAT-1. Samples of human brain have been pre-screened to exclude prion and Alzheimer's Disease (AD). The work will involve culture of common and specialized human cell lines using standard culture techniques. Glass slides and needles will be used with appropriate precautions and transfer of materials will be done in sealed containers. It was noted that appropriate IACUC approval is in place and IRB approval is not required for samples obtained from tissue banks.

- PI's rDNA training is out of date. Protocol indicates PI has no experience with rDNA work – is this correct?
- It is stated in the laboratory procedure section that tissues have been pre-screened for prion and AD, but in the Section B it is stated that the tissue, organ and brain will not be used. This should be corrected and prescreening information should be added.
- In the hazardous biological agent list add lentivirus. Also indicate which cell lines will be used for xenograft studies and provide IACUC approval number and approval date (PROTO20180053 approved 8/19/2020).

Personal Protective Equipment and Safety Equipment

- Question 1: Check off animal handling
- Question 4: Respirator and goggles not required for ABSL-2 if working in Class II BSC, most spaces require double gloves, shoe covers. Check appropriate boxes.

Recombinant DNA

- Question 2: Animal experiment: Use proper nomenclature for nude mouse (e.g. NU/J).
    - Define acronyms for "Donor" answers (ACAT and PTEN).
    - Correct IACUC approval date and protocol number: PROTO20180053 approved 8/19/2020.
    - Name the specific "viral vector" in animal experiment.
- Question 17: nude mice are knockouts, just spontaneous *Foxn1* null.

BUA Site Assessment: ECP is in place. All have ROHP clearance but few members need to update their BBP training. BSC is certified. All engineering controls are in working condition.

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

7. Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2198		Inner-City Asthma Consortium	2	N/A	BUMC

Primary Reviewer: Tom Winters	Secondary Reviewer: Valeda Britton

Applicable NIH Guidelines: N/A

Meeting Comments: This protocol tests the hypothesis that urban children with difficult to control exacerbation, who are prone to asthma, will benefit from the use of anti-IL-5 monoclonal antibody drug mepolizumab. The goal is to prevent multiple exacerbations of asthma. They identify these refractory asthmatics with elevated peripheral eosinophil counts. In this clinical study they will draw blood for several analyses, obtain nasal mucus samples by nasal lavage, obtain nasal epithelium samples by swabs and sputum specimens induced by inhalation of saline solution. Analyses of these specimens will be performed in the research lab at the Medical School Building at BU. These specimens will be obtained in the Yawkey Building at the Pulmonary Clinic. Nasal epithelial samples are collected, stored, and shipped to a central lab for analyses. Transportation appears appropriate. Waste appear to be handled properly. Sharps are used and the bloodborne pathogen program is invoked.

- Update personnel list to include all current personnel involved in the project.
- Clarify how Nicole Gonzalez will train Emily Bull if Lisa Gagalis who is training Nicole, has already left. Has Nicole been trained already so now she can train Emily?
- rDNA/IBC policy training must be completed for the PI (Dr. O'Connor).
- ROHP update for Manuelian and O'Connor needed.

- An N95 must be used during the collection of samples as they are performing aerosol-generating procedures, as well as eye protection and other PPE for AGP's.
- PPE in the laboratory is appropriate except a surgical mask should be added.

BUA Site Assessment: Lab has access to the biosafety manual and chemical hygiene plan. Personnel list needs to be updated as few members are leaving. PI's rDNA/IBC Policy training needs update. BSC certification expired but re-certification process is underway.

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

8. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2255		Proteomic analysis of protein interaction networks in models of human health and disease	2	N/A	BUMC/CRC

Primary Reviewer: Carmela Abraham	Secondary Reviewer: Ron Morales

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

Meeting Comments: This protocol focuses on mapping protein networks in cultured cancer cells and biochemically fractionated neuronal (synapse) samples, generated and processed in collaboration with several research groups. Their objective is to identify novel macromolecular associations and mechanistic relationships. This protocol was reviewed thoroughly just three weeks ago when an amendment to add inactivated biological samples were added to the protocol. No further changes were made in this 3-year renewal and no concerns were voiced.

BUA Site Assessment: Bloodborne pathogen exposure control plan has just been updated. Couple of members need to update ROHP clearance.

Motion: Approve	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

9. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
936		Mechanisms, diagnostics and therapeutics for Neurodegenerative diseases	2	1	BUMC

Primary Reviewer: Barbara Slack	Secondary Reviewer: Rao Varada

Applicable NIH Guidelines: Sections III-D-1-a, III-D-2-a, III-E-1; Appendices B-II, B-V, G-II-B.

Meeting Comments: The goal of this protocol is to study protein aggregates in Alzheimer's and Parkinson's disease and develop therapies. They are using a number of different approaches using cell lines mostly human neuronal lines, some NHP lines and PC-12 cells. They are using rat or mouse brain slices or primary neurons and *C. elegans.* They will treat mice and rats as well as transgenic mice with cerium oxide after amyloid and related proteins are overexpressed via the use of third generation lentivirus vectors. Since some of these proteins are potentially oncogenic, appropriate care will be taken for their handling. The protocol will also use postmortem human eyes and brain tissues from donors with confirmed AD or Parkinson's disease and age-matched control received from tissue banks and hospitals. They have described in detail their sectioning procedures. They will use disposable blades and homogenize the lens manually and will use 70% ethanol for equipment disinfection. All the sharps will be for one-time use only. They have appropriate IRB (exempt) and IACUC protocol approval for their work. It was noted that IRB protocols from the CRC do not post an expiration dates on exempt protocols, but the BUMC do have expiration dates. However, IBC do not ask for an expiration date for these protocols.

- Section III.2- rDNA training for Goldstein is overdue.
- Section VII-3-procedures- Harvesting of rodent tissues post-mortem is mentioned; describe if any live animal manipulations are performed including method of euthanasia.
- Section VIII.1- Please check 'animal handling' and 'animal inoculation' (injecting cerium oxide into rat and mouse brain).
- Section VIII-4: shoe covers required; wear other PPE as posted at the entry door.

- Section VIII.5. Update certification date of BSC (11/01/2019).
- Section VIII-6: Sterilize surgical instruments by autoclaving after a thorough clean with soap water to remove any organic materials. Exposing delicate instruments or materials to bleach is not recommended. Consider alternatives including the use of cold sterilants like Spor-Klenz or Sporicin.
- Section VIII.7. Liquid waste: Please specify bleach at a final concentration of 10%
- Table IX. Not sure that 'live animal use' needs to be checked, unless cerium oxide qualifies as a biohazard.
- Section A. PC-12 cells are derived from rat, and do not need to be in this table (are BSL1). Human neuroblastoma cells could conceivably cause disease/tumor if accidentally injected.

BUA Site Assessment: Lab is updating the bloodborne pathogen exposure control plan. All members have ROHP clearance. PI's rDNA/IBC policy training needs update. BSC certification has expired but the lab already made arrangement for recertification.

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

10. Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1975		Exploring the use of adult neural crest stem cells derived from non-ocular sources to treat corneal endothelial disease	2	N/A	BUMC

Primary Reviewer: Tom Winters	Secondary Reviewer: Bob Timmerman

Applicable NIH Guidelines: N/A

Meeting Comments: This protocol is attempting to regenerate corneal endothelial cells, as they do not regenerate naturally. They are using multipotent stem cells and differentiating them into corneal endothelial cells. These will be derived from neural crest, stem cells from adult hair follicles or will be obtained from human cadaver corneas. The hair follicles and human cadaver corneas are obtained from surgeons at Boston Medical Center. Human cadaver corneas come from an eye bank and are tested for hepatitis B, hepatitis C, and HIV. Mouse cornea can serve as an alternate source of corneal endothelial cells. The bloodborne pathogen program is invoked as hair follicles with tissue attached is being used. The PPE used in the protocol is appropriate and wastes are handled appropriately. Wescodyne, 10% bleach and 70% alcohol are used as disinfectants. The IRB approval is listed with no date. It was clarified that the use human clinical materials in this protocol had been deemed to be non-human subjects research back in 2014. There is no expiration date for this determination. BUA site assessment for this protocol has not been completed yet.

- Please state if the department administrator is a BU employee. The check box is left blank.
- Update biosafety cabinet certification date.
- BUA Site Assessment must be completed for the approval of this protocol.

BUA Site Assessment: Site assessment is not complete yet.

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

11. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
844		Gene regulation in muscle development	2	1	CRC

Primary Reviewer: Xin Brown	Secondary Reviewer: Susanna Kurnick

Applicable NIH Guidelines: Sections III-D-1-a, III-D-2-a, III-D-4-a, III-E-1; App B-II-D, G-II-B, M

Meeting Comments: This protocol investigates the role of MEF2 transcription factor and its target genes in muscle cells *in vitro* and *in vivo*. The protocol lists many molecular biology approaches to alter these genes in cells and in animals, including transfection, transduction with replication defective adenoviruses and AAVs, and generation of transgenic mouse through oocyte microinjection. Molecular and morphological effects of these alterations will be

studied. This protocol was very detailed and well written. Most administrative issues noted in the administrative pre-review comments have been addressed.

- It is stated in Solid Waste disposal section that Wescodyne is being used to disinfect surgical instruments. This needs to be added to the list of disinfectant.
- Check off animal handling/cage changing.
- Please indicate the use of respiratory protection in the laboratory if these are considered BSL-2 procedures.
- BSC certification is out of date.

BUA Site Assessment: Biosafety cabinet is duly certified. All members have ROHP clearance and all safety trainings are current.

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

12. Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2487		Exosomes in IBD	2	N/A	BUMC

Primary Reviewer: Rob Davey	Secondary Reviewer: Jim Keeney

Applicable NIH Guidelines: N/A

Meeting Comments: The goal of this protocol is to identify better markers of inflammatory Bowel Disease (IBD) for improved patient diagnosis and recovery progress, where the primary focus will be on the isolation and analysis of exosomes. The work will involve collection of samples from patients and healthy people and look at proteins present as well as RNA for detection of genetic factors that contribute to the disease. Some cell culture work will also be done with the samples. The PI and all staff have experience working with recombinant DNA and the post-doc has additional experience with infectious agents. It is unclear whether the human samples are screened for common transmissible diseases and whether the research personnel are experienced in handling human samples. Committee discussed if it is always possible to get the clinical samples screened for pathogens and if possible, how many pathogens can be tested in reality. It was noted that whereas some providers, such as tissue banks, do test for common pathogens such as HIV, Hep-B or Hep-C, it is not always the case for samples obtained from the clinic. Investigators need to rely on information provided by the clinicians and are required to follow universal precautions. Committee noted that these biosafety issues are not clearly discussed in the application which raised concerns on the understanding of researchers. The committee further discussed that the laboratory procedure section needs to be expanded to provide a better understanding of actual bench work and proper risk assessment.

- Please state if lab members have experience in working with primary human materials.
- The work description is a very brief set of bullet points. Please expand the laboratory procedure section to provide more detail on bench work associated with all major proposed experimental work. This is required to perform a better risk assessment.
- Include information on where and how the clinical samples will be collected and how will they arrive to your research laboratory and where will they be processed in the lab, emphasizing biosafety issues for each of these steps.
- Emphasize biohazard concerns on using human clinical samples and risk mitigation plan that the researchers practice in the lab for each of these steps.
- If any work is being done with established human cell lines (as suggested in the Hazardous biological agents section), provide more detail of the proposed work.
- Please clarify in the laboratory procedure section if you have IRB approval for collecting clinical samples.
- Protocol states that transfer of materials from the clinic will be in sealed tubes wrapped in absorbent paper, enclosed in sealable biohazard bags and put in an ice-box. Committee suggested that it would be better to say “tubes will be sealed in the bag” instead of saying the bag is “sealable”.
- Provide IRB approval and expiration dates for the two IRB protocol numbers cited in Section B.

BUA Site Assessment: Safety Training and ROHP clearances are all complete. Biosafety cabinet recertification is scheduled. Chemical fume hood is in working condition.					
Motion: Conditional Approval (Primary and Secondary Reviewer Review)	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

13. rDNA/Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2488		Patterning Microbial Populations Through Collective Dynamics	1	N/A	CRC

Primary Reviewer: Ed Loechler	Secondary Reviewer: Jim Keeney
Applicable NIH Guidelines: Section III-F-4	

Meeting Comments: The mechanisms that control biofilm gene expression in time and space are still unknown. Biofilms are communities of microbes living in an aggregated matrix that exhibit phenomena reminiscent of multicellular organisms, including patterns of development and cell-to-cell signaling. This protocol will investigate how electrical activity controls gene expression in *Bacillus subtilis* biofilms using a microfluidic electrode device. Biofilms grown on electrode arrays will be electrically perturbed and changes in gene expression dynamics will be assessed using fluorescent reporter constructs. Microbial strains will be grown on plates and in liquid tubes. Bacterial colony growth will be observed using microscopes. To probe mechanism bacteria will be altered genetically using traditional bacterial cloning techniques. Project members have appropriate experience and training is up-to-date. Liquid wastes will be treated with "bleach overnight" and discarded in the drain.

- The proposal provides no details about what genes will be altered, or how, and how altered genes will be employed to address the experimental goals of studying the effects of membrane potential and potassium ion gradients.
- Indicate the source of the bacteria to be used in the protocol.
- Vectors are listed, but not described. Reporter genes are mentioned, but not what genes they will be reporting on.
- Provide more detail of the concentration of bleach (such as 10% bleach final concentration and 30 min exposure time).
- Add 10% freshly made bleach to the list.

BUA Site Assessment: The ROHP clearance for one personnel is due. Biosafety cabinet is not required for the project. Liquid waste disinfection will be done by treating with freshly made bleach.

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

14. Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2493		Age-Associated Lipidomic Changes in Alzheimer's Disease	2	N/A	BUMC

Primary Reviewer: Carmela Abraham	Secondary Reviewer: Bob Timmerman
Applicable NIH Guidelines: N/A	

Meeting Comments: The PI proposes that abnormal metabolism of lipids is a risk factor in Alzheimer's disease (AD) and occurs before patients become symptomatic. They will use clinical data and analyses of specimens collected by the Boston University Alzheimer's Disease Research Center, Framingham Heart Study and other biorepositories. Postmortem brain and liver tissues and blood from AD patients and age-matched controls will be studied. Lipids will be extracted with methanol and analyzed. Expression of nucleic acids and proteins will be analyzed too, especially for phosphatidylethanolamine N methyltransferase (PEMT) enzyme. It was clarified that PCR assays will be used as a method for data analysis. In response to a question on how many sharps can be dumped in the sharp container, EHS clarified that it should be up to the fill-up level marked on the container. One member expressed concern if the samples obtained from other sources are screened for prion. It was clarified that they are postmortem samples from

AD patients but prion screening data on them is unknown. However, PI will use 40% bleach treatment for the tissue wastes, which is an approved disinfection method for prion contamination. Although there were no remaining concerns, protocol was not approved because BSA site assessment was not complete yet. The protocol will be approved administratively once the EHS clearance on site assessment is received.					
Motion: Conditional Approval (Administrative Review)	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 0