Boston University
Institutional Biosafety Committee (IBC)
October 20, 2020 Meeting Minutes
Location: Zoom and/or by phone
Start time: 12:00 PM End time: 3:24 PM

Members Present: C. Abraham, I. Afasizheva, B. Slack, R. Davey, E. Loechler (Joined 12:25 PM, left 2:05 PM), R. Morales, T. Winters, R. Varada, S. Kurnick (joined 12:08 PM), J. Keeney, R. Timmerman, V. Britton, J. Barton, E. Muhlberger (left 12:35 PM)
Guests Present: T. Killen, F. Ennever, A. Ahmad, J. Davis, K. Tuohey, N. Yun, S. Benjamin, C. Thurman, G. Madico, P. Richmond
Staff Present: S. Ghosh, C. McGoff

I. Review of September 15, 2020 IBC Meeting Minutes

No comments or questions were voiced.
Motion: Approve
For: 12; Against: 0; Abstain: 0; Absent: 2

II. Lab Inspection Report

Members were informed that a new SOP has been developed based on a recent incident and related inspection by the BPHC. The Director of Research Safety informed the committee that a cluster of positive cases of COVID-19 were reported in a lab in the K-building. The researchers in this lab were using inactivated samples of the virus provided by researchers in the NEIDL. This information prompted an inspection of this lab and the NEIDL by the BPHC. The BPHC followed up the inspection with a report to the University citing issues with the lab's adherence to COVID-19 social distancing policies and requested that a new SOP be drafted to address lab procedures when working with inactivated samples of COVID-19 with a requested deadline of two weeks from the date of the letter. EHS staff from the NEIDL and Research Safety worked with IBC staff on developing a new SOP which was shared with all researchers working with this material. Based on feedback from the research community, the SOP is currently being revised.
Members noted that it was unclear whether the handling of inactivated material was directly related to the positive cases, however the SOP was developed in direct response to the BPHC request to proactively ensure that these types of incidents do not recur.
It was noted that NEIDL investigators have recommended that procedures be developed related to testing that may be able to determine whether the inactivate virus triggered the positive results or whether the testing was a result of COVID-19 being acquired outside of the lab. Members recommended that a secondary test be taken following their BU required testing, by any lab members who test positive for the virus, as the PCR test can be easily contaminated by someone who is working with small amounts of DNA. The Medical Director of ROHP clarified that earlier testing of these lab members found that there didn't seem to be an increase in positive results in those working with the inactivated virus, however some lab members that initially tested positive subsequently tested negative and were able to return to work. It was noted that there is discussion about improving accuracy in testing for those who work with this type of genetic material.

III. New Business

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

ROHP Report:
Members were informed that BU has had several researchers test positive to the SARS-CoV-2 virus through the BU screening program but there have been no reports of any known breaches or incidents.

ROHP has submitted ten (10) reports to BPHC of researchers who tested positive to SARS CoV2 and either work with active or inactive SARS CoV2 or work in shared space with others who do. There has been one researcher who reported that they were symptomatic and that person handles blood samples for COVID 19. All other cases of positive SARS CoV2 testing has been with asymptomatic researchers. It was noted that this is required by BPHC, and that follow up is done with EHS to assess the work environment when these incidents are reported.

EHS staff added that Healthway has been managing all researchers who test positive for SARS CoV2 and Heathway also communicates to EHS, Facilities and BPHC any positive cases.

EHS Report:
Members were informed that on 10/8/20, a researcher was preparing an ABSL-1 mouse to perform an IP injection of antibodies when the mouse bit the researcher. The mouse was not infected or administered any material at the time of the incident. The mouse is a K18 strain and the researcher was wearing the following PPE at the time of this incident: coveralls, shoe-covers, facemask, hairnet, double gloves. The researcher secured the mouse back into its cage and proceeded to wash the site of the bite with soap and water for 15 minutes. The researcher then reported the incident to their PI, the NEIDL Animal Research Core Director and ROHP. No medical treatment was required for this incident. The root cause was found to be: Training- No procedure/inadequate procedure. It was noted by the ASC veterinarian that this researcher was following the SOP correctly for ABSL-1 infected animals and this event is not reportable to NIH.

IV. 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			Secondary Reviewer: Shannon Benjamin		
Applicable NIH Guidelines: N/A					
Meeting Comments: Current approved protocol from the PI includes cultivation of SARS-CoV-2 and molecular analysis. In this proposed amendment they are adding procedures to cultivate the virus from de-identified positive patient samples on Vero cells. Samples will be fixed using TRIzol or formaldehyde and then analyzed outside of the BSL3 facility to investigate how the virus is replicating. The validity of these inactivation methods is well described and appear appropriate. They will also evaluate the ability of special solutions and surface treatment procedures to destroy viable viruses. Virus is either mixed with the solution or placed on the test surface and after a certain time residual virus is collected and assayed for growth on Vero cells. The host response to virus infection will be evaluated by sequencing cell mRNA using high throughput sequencing methods. Although the PI himself is currently being trained by the BSL3 staff, one member of the PI's lab has appropriate training received at U. Colorado and also has been oriented to the NEIDL procedures. The amendment submission was pre-reviewed by the BSL3 BSO. The PI addressed all concerns in the revised submission before the committee meeting. Few additional minor issues were identified in the meeting however. Committee discussed that even though established human cell lines obtained from commercial sources do not cause human disease due to histo-incompatiblity, it is not always known if they are tested for the absence of infectious agents. Both reviewers expressed concerns that what will be the response from the PI regarding the new SOP that has been generated by EHS (sometime after the amendment has been submitted for review) for working with inactivated SARS-COV-2 material. This SOP asks for details about using dedicated equipment outside of the BSL3 (Next Generation Sequencer, centrifuges, microscope for imaging fixed samples, plate reader for measuring CPE, etc.) and lab space. Members critically discussed whether the sequencing core can have a dedicated Next Generation Sequencer available for this and other projects using only SARS-COV-2 material or a dedicated microscope available in the NEIDL. Members discussed if such restriction is indeed required and expressed concerns that to have dedicated costly equipment for SARS-CoV-2 work may not be feasible. Implementation of this SOP would require most labs				

working with inactivated SARS-CoV-2 to stop their work immediately. EHS and the committee concluded that there is need to revise the SOP urgently. It was suggested by the EHS that BSL3 BSO will examine again the work environment and equipment use procedures in the PI's lab and if they are found being done properly and safely, the amendment may then be approved. However, more than half of the members present at the meeting did not go along with such a motion. They abstained from voting as they felt that if an SOP is present, it needs to be followed leading to a deferral decision for the amendment.

- VII.3, Clinical Isolate recovery section, please define "VTM".
  VII.3, Clinical Isolate recovery section, for consistency, please reference the actual name of the formaldehyde SOP in this sentence "...inactivated with formaldehyde according to the approved BSL3 SOP
- VII.3, for diagnostic experiments section, in the sentence "In BSL3, virus stocks will be inactivated using Trizol" please reference the applicable SOP by title or policy tech document number.
- VII.3, for diagnostic experiments section, has the inactivation of pathogenic material on silicone chips been tested/validated?
- VII.3, Virus Inactivation testing section, please include your justification for the use of VSV in the body of the protocol "inactivation approaches are intended to be broad spectrum and attack enveloped viruses generally. VSV is an enveloped virus for which we have robust assays. The RG2 coronaviruses do not have the same tools available and would add time and effort to the testing. They also might leave us having developed virus inactivating coatings that work on coronaviruses but nothing else. A coronavirus-specific inactivating compound is not consistent with the overall experimental goals of the project."
- VII.3, for host response testing section, please ensure that all descriptions of handling of SARS-CoV-2 inactivated samples align with the SOP posted on the Research Support website.
- VII.3, for work performed out of the BSL3 laboratory on inactivated samples section, please elaborate on this statement "For experiments that will involve the use of formaldehyde inactivated samples or detergent-inactivated samples, these will be treated as fully inactivated." Describe how these samples will be handled outside of the BSL-3. Please ensure that all descriptions of handling of SARS-CoV-2 inactivated samples align with the SOP posted on the Research Support website.

Motion: Deferred	For: 4	Recuse: 0	Against: 2	Abstain: 7	Absent: 1

2. rDNA/Bhz – Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
2375		Evaluation of treatments for high containment viruses using rodents.	4	4	BUMC

Primary Reviewer: Carmela Abraham Additional Reviewer: Nadya Yun	Secondary Reviewers: Robin Ingalls & Rao Varada

Applicable NIH Guidelines: Sections III-D-4-a

Meeting Comments: This protocol analyzes small molecule drugs and antibodies in animal models to determine if they can alleviate disease caused by high consequence pathogens including SARS-CoV-2. In this amendment PI is trying to use a recombinant mRNA that will express chimeric coronavirus protein that also contain a nuclease and will test if expression of such mRNA will contain the SARS-CoV-2 infection. Animals will receive the mRNA via nebulizer. PI added new rDNA section for this amendment but clarified that he is getting prepared RNA from his collaborator and as such there will be no plasmid preparation steps. The BSL4 BSO clarified that they are preparing a SOP for this work to define how any residual RNA on the animal skin can be inactivated. It was also noted that RNA molecules are so easily degraded by the skin RNases that it is unlikely that any residual RNA on the animal fur will be of any concern. Any material taken out from BSL4 containment will be inactivated using standard methods, which will be described in the SOP, reviewed and approved by EHS and the IBC chair before sending to BPHC. Committee noted that PI's IACUC approval for this work will be available only after IBC approval of this amendment. It was clarified that while SARS is a designated select agent, MERS and SARS-CoV-2 are not.
PI recused himself from voting.

Motion: Approve	For: 12	Recuse: 1	Against: 0	Abstain: 0	Absent: 1

3. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1917		Metabolic cooperation in natural and synthetic microbial consortia	2	N/A	CRC

Primary Reviewer: Ed Loechler	Secondary Reviewer: Bob Timmerman

Applicable NIH Guidelines: Section III-F-8 (Exempt)

Meeting Comments: This protocol investigates the effect of symbiosis of microbial communities in the health of plants, animals and humans. The scientific portion of PI's 3-year renewal is unchanged from the previously reviewed version of this protocol back in 2019. Personnel list has not changed, though training has been updated. This is a well written protocol where no major concerns were noted.

- Please update PI's lab safety and BSL1/2 training.
- Disposal of liquid biohazard wastes need to be changed from 10% bleach to bleach with a final concentration of 10%.

BUA Site Assessment: Biosafety cabinet is duly certified. No other issues were noted.

Motion: Conditional Approval (Administrative Review)	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

4. rDNA– New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2481		Ingestible micro-bio-electronic device (IMBED) to diagnose and monitor Crohns disease	1	N/A	CRC

Primary Reviewer: Ed Loechler	Secondary Reviewer: Jim Keeney

Applicable NIH Guidelines: Section III-F-8; Appendix C-II

Meeting Comments: The goal of this project is to build a device that can be ingested by patients that can sense biomarkers associated with Crohns disease (CD) and transfer the signals to an external recording device. The ingestible micro-bio-electronic device (IMBED) aims to enable physicians to read the state of their patients gastrointestinal (GI) tract and will support the diagnosis, monitoring, and management of CD. The recombinant probiotic *E. coli*, provided by a collaborator at MIT, will be engineered to detect inflammation biomarkers and produce luciferase as a reporter output. Personnel will wear appropriate protective equipment. Cultures will be treated with freshly prepared 10% bleach before disposal. No strains have any known virulence, though they can be resistant to common laboratory antibiotics (e.g., kanamycin, ampicillin or erythromycin). Although members of the protocol are not particularly experienced in microbiology, they will be trained by a member of their collaborator's laboratory. The committee discussed that there is no special restriction required for the transportation of probiotic *E. coli* from MIT to BU. The agreement policy part of the application needs to be filled out and signed.

- Please provide more information about how the bacteria will be handled and stored.
- The agreement policy part of the application needs to be filled out and signed.

BUA Site Assessment: The exposure control plan (ECP) is in place. All lab members are working to get ROHP clearance. All necessary facilities and emergency controls are in place. Trainings are all complete.

Motion: Conditional Approval (Administrative Review)	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

5. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1248		The pVHL/Jade-1/beta-catenin axis in renal cancer; Polycystin, Jade-1 and beta-catenin in cystic kidney disease;	2	2	BUMC

		Transcription factors in renal disease and renal development			
Primary Reviewer: Barbara Slack			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-II-D					

Meeting Comments: The PI investigates the role of Jade-1 protein in kidney disease and cancer. The protocol involves overexpression and knock down/out of expression of Jade-1 and Jade-1 pathway components in cell culture, transgenic mice, and knockout mice. It also includes injection of nude mice with cultured cells to examine cell growth in a xenograft model as well as treating Jade-1 knockout mice with chemical carcinogens such as N-ethyl-N-nitrosourea (ENU) or streptozotocin, to determine if these mice are at increased risk for cancer. Protein-protein interaction screens using yeast 2-hybrid system, tissue sections for histology, RNA, DNA, protein assays, high-throughput screens using the imaging core, and the proteomics core will be the major techniques to be used in the protocol. Adenoviral and lentiviral vectors will be used to modify expression of specific proteins in human cultured cell lines and to be used for inducing xenografts. Human tissue from tissue banks and BUSM Biospecimen Archive Research Core (BARC) will also be used. These are considered non-human subject research (NHSR) by the IRB.

- Please update all safety training including the rDNA/IBC Policy training.
- Lab Procedures: please update links to protocols relating to chemical handling protocols. The links provided appear to be out-of-date.
- Section VIII.1. Please check 'animal handling.'
- Section VIII.3. Please check respirator (N95)- Lab Procedures section says these will be used with streptozotocin (CCL3- carcinogen).
- Section VIII.5. Please update biosafety cabinet certification date.
- Section VIII.7. States that ENU will be inactivated in 0.1 M potassium hydroxide and disposed of in sink. Because of its high pH, this waste must not be discarded in the sink. It must be collected and disposed of separately. Please modify the text in the application accordingly.
- Section A. Please list human cell lines that will be used in this table. (There is a list already in the rDNA table-it can be copied to the table in Section A).
- Table IX. Please uncheck synthetic nucleic acid.

BUA Site Assessment: The ECP is being revised. ROHP and safety training for the PI needs update. Fume hood is duly certified. BSC certification expired but new certification has been scheduled.

Motion: Conditional Approval (Administrative Review)	For: 11	Recuse: 0	Against: 0	Abstain: 0	Absent: 3

6. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1505		G protein signaling circuits in health and disease	2	2	BUMC
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; Appendix: B-II-D, G-II-B-1					

Meeting Comments: This protocol studies the role of various G protein associated factors in cellular functions. G-proteins (guanine nucleotide binding protein) are known for transferring external stimuli to the inside of the cell via G-protein coupled receptors. Function of G-proteins (particularly the trimeric G-proteins) inside the cell are acutely regulated by numerous cellular proteins. Abnormalities in these highly regulated cellular mechanisms lead to different disease phenotypes including developmental defects, cancers, neurological diseases and others. Retrovirus and lentivirus based packaging systems will be used to overexpress or downregulate these regulatory proteins. For a limited set of experiments, cultured breast cancer cells will be injected subcutaneously into immunocompromised mice, tumor growth and metastases will be imaged using an *in vivo* imaging system (IVIS bioluminescent detection system). Manipulations of viral particles will be done while wearing standard BSL2 PPE (lab coat, gloves, safety glasses), minimizing the aerosolization. In response to a question from one member, it was clarified that the lentivirus vectors used in this protocol are 3rd generation vectors. Members also discussed that retroviral and

lentiviral vectors, although are replication deficient, they can still cause insertional mutagenesis and thus can be potentially harmful.

- BSL1/2 training for the PI and ROHP clearance for Alex and Zhiming need to be updated.
- In the PPE Section VIII.1 – Check animal handling.
- VIII.3 – Some sort of respiratory protection should be worn (such as surgical mask).
- VIII.7A - Liquid waste treatment with bleach, final concentration needs to reach 10%.
- In Section A. Hazardous Biological Agents, Table 4 – please update IACUC approval number.

BUA Site Assessment: ROHP clearance for several members need update. Safety training of the PI has expired. Biosafety cabinet is certified but the fume hood needs recertification. EHS is assisting the lab for recertification.

Motion: Conditional Approval (Administrative Review)	For: 12	Recuse: 0	Against: 0	Abstain: 0	Absent: 2

7. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2247		Mechanisms of Extinction Memory Enhancement for Cocaine Addiction Treatment	2	2	BUMC

Primary Reviewer: Inna Afasizheva	Secondary Reviewer: Colleen Thurman

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

Meeting Comments: The goal of the study is to develop and validate of new treatment strategy for preventing relapse to cocaine abuse. The research investigates combinational approach involving pharmacological and behavioral interventions. Female and male rats will be used as a model to examine combined effects of environmental enrichment (EE) and glycine transporter-1 (Gly-1) inhibition with cocaine-cue extinction training. The investigation will particularly focus on the functions of brain receptors for NMDA glutamate, neurotrophic factor derived by brain and two other novel targets that influence memory. Experimental approach includes lentivirus-mediated knockdown and overexpression in rats treated with EE and GlyT-1 inhibitors combined with extinction training.

- Please update rDNA and BSL1/2 training for Dr. Man.
- Please verify that CAS Biological Science Center Rm 205 for animal work only supports ABSL-1 work. If other investigators engage in ABSL-2 work in that space, change it to ABSL-2.
- The use of BSC is missing from description of work with lentivirus production. Pipetting, centrifugation, sonication of lysates and application of viral particles to neuron culture should be performed in BSC. Please update the Laboratory Procedure section of the protocol with this information.
- Please include double gloves use for virus injection to rats.
- Contaminated infusion cannula is disposed of in solid waste without prior decontamination. Please decontaminate all instruments used in lentivirus injection before placing in red bags. Correct the same issue on the PPE and Safety Equipment question 7B.
- Please include leak-proof containers for lentivirus transportation in question VIII.11.
- Please add HEK293 cells in the hazardous biological agent list and in the rDNA eukaryotic experiments.

BUA Site Assessment: All safety training and ROHP clearances are current. Biosafety cabinet is duly certified.

Motion: Conditional Approval (Administrative Review)	For: 12	Recuse: 0	Against: 0	Abstain: 0	Absent: 2

8. Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1965		HIV Aging of Immune Function	2	N/A	BUMC

Primary Reviewer: Tom Winters	Secondary Reviewer: Valeda Britton

Applicable NIH Guidelines: N/A

Meeting Comments: This protocol is investigating the effects of aging and other factors (such as smoking, alcohol, IVDU, co-infections) on HIV disease and immune dysfunction. They will look at young subjects (<35 year old) and older subjects (>50 year old) with chronic HIV infection who are treated with anti-retroviral therapy (ART) and look at how host factors and viral factors (such as viral load) influence HIV-induced immune dysfunction and systemic inflammation. Whole blood drawn from the research cohort and appropriate control subjects will be used to evaluate the function of peripheral blood mononuclear cells (PBMCs). Extra tubes of blood will also be drawn, if needed, to measure complete blood count and HIV-1 RNA viral load, as well as for screening co-infection with HBV, HCV, and CMV. Urine samples will also be collected for alcohol and drug screening. T-cells from the PBMC will then be characterized by flow cytometry, examining at their expression of CD4 or CD8, CD38 and HLA-DR surface antigens, among others. Soluble inflammatory markers will also be measured. HIV cell-associated DNA or circulating RNA will be determined by qPCR. Appropriate PPE and storage procedures were included. Waste disposal procedure is appropriate which include liquid waste disposal using bleach at a final concentration of 10%. It was noted that the protocol does not involve culturing any HIV from the clinical samples. EHS performed a safety assessment for receiving samples from BMC clinical space and no concerns were noted.

- Please expand acronyms at their first use.
- Indicate the location of the ID clinic where blood and urine samples are being collected.
- Sharps will be used (to draw blood) but was listed as not being used in PPE question VIII.6. Safety precautions for sharps need to be explained.
- The IRB approved protocol (H-33095) is listed in Section B with an expiration date of 11/24/2017. Please update the expiration date.
- HIV-infected blood should be listed in the Hazardous Biological Agent list as it causes human disease.

BUA Site Assessment: The lab is developing their exposure control plan. ROHP clearance and safety training are not current for few members. They have been notified to update them.

Motion: Conditional Approval (Administrative Review)	For: 12	Recuse: 0	Against: 0	Abstain: 0	Absent: 2

9. rDNA/Bhz – Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
2332		Investigations of negative-strand virus and alphaherpesvirus biology	2	N/A	BUMC

Primary Reviewer: Inna Afasizheva	Secondary Reviewer: Rao Varada

Applicable NIH Guidelines: III-D-1-a, III-D-2-a, III-D-4-a, III-E-1, III-F-1, Appendix B-II-D and G-II-B

Meeting Comments: The overall objective of this protocol is to understand the interplay of molecular players in virus infected cells and to utilize the gained knowledge towards development of therapeutics and vaccines. This amendment is to add multiple human and mouse cell lines and a recombinant vesicular stomatitis virus that will be used to express surface glycoproteins of filoviruses and coronaviruses. Description of all the new agents added in this amendment are described clearly. It was noted that there is no animal work in this protocol.

Motion: Approve	For: 12	Recuse: 0	Against: 0	Abstain: 0	Absent: 2

10. Bhz – Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
2438		BSL-2 phase of medical countermeasure testing in rodents	2	2	BUMC

Primary Reviewer: Inna Afasizheva	Secondary Reviewer: Rao Varada

Applicable NIH Guidelines: N/A

Meeting Comments: This protocol determines the efficiency of vaccines against high consequence pathogens in animal models. In this amendment a new vaccination protocol has been proposed where a vesicular stomatitis virus (VSV)-based vector that express viral glycoprotein has been added to the protocol. This vector will be used in animal models that include mice, guinea pigs and hamsters. NEIDL veterinarian clarified that the existing animal handling

protocol has not changed in this protocol for hamsters (the additional animal species in this amendment). It was also noted that recombinant DNA information for this vector has been added in PI's other IBC protocol 2232.					
Motion: Approve	For: 12	Recuse: 0	Against: 0	Abstain: 0	Absent: 2

11. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
892		Molecular mechanisms of pulmonary inflammation	2	2	BUMC

Primary Reviewer: Carmela Abraham	Secondary Reviewer: Robin Ingalls & Susanna Kurnick

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

Meeting Comments: The proposed research investigates how the immune system in the lungs respond to the pathogens that cause infections in the lung. The goal is to use their discoveries to improve the body's ability to fight off these agents and decrease the suffering. Experiments involve bacterial or viral infections *in vivo* and *in vitro*. The *in vivo* infections are with mice. The *in vitro* infections are in murine primary cells, murine cell lines, or human cells or cell lines. All experiments are performed with BSL2 precautions. PI has extensive experience in handling these pathogens and conducting these mouse infection models. It was noted that the coronavirus stains used in the protocol are endemic common cold virus and not the pandemic SARS-CoV-2 strain. ROHP director clarified that all new members in this protocol should be vaccinated for Pneumonia. Further, Dr. Ennever informed that the IRB protocol mentioned in the application has an exempt status (NHSR).

- Since members are using *Streptococcus pneumonia*, it is advised that all new personnel be vaccinated with PV 13 or similar and get Tdap shots every 5 year.
- In the PPE and Safety Equipment Section
  - #1- Check off animal handling
  - #4- As use of N95s are not mandatory anymore in LASC, please clarify if they are still being used in this protocol.
  - #5- Update BSC recertification date
  - #6- No need to dispose the sharp container into the biohazard box
  - #8-Please describe in the laboratory procedure when MB-10 disinfectant is used (in VII #3)

- In section B, please clarify whether the IRB protocol was approved? If so, please provide IRB expiration date.
- If receiving inactivated SARS-CoV-2-infected NHP tissues from Dr. Griffiths, please check off inactivated biological samples in section IX (Materials used in Research), provide description of the work in laboratory procedure section and complete Section I.

BUA Site Assessment: It was mentioned that LASC and EHS has discussed that if the work with infectious material is to be done in biosafety cabinets, use of N95 masks can be replaced with surgical masks.

Motion: Conditional Approval (Administrative Review)	For: 12	Recuse: 0	Against: 0	Abstain: 0	Absent: 2

12. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2264		R01 project (R01AA025080): Brain microRNA-mRNA regulatory networks and alcohol use disorders.	2	N/A	BUMC

Primary Reviewer: Carmela Abraham	Secondary Reviewer: Jim Keeney

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

Meeting Comments: This study aims to identify small RNAs which do not code for proteins but can regulate the expression of messenger RNA (mRNAs) that are involved in brain reward pathways. The goal of the research is to understand the molecular basis of alcohol use disorder (AUD) and ultimately develop novel therapeutic approaches for AUD. DNA and RNA samples are extracted from human saliva, blood, postmortem brain tissues, and embryonic stem cells. It was unclear whether the PI is working with previously stored cells and tissues or is still receiving them

from outside sources. There is no data included about receiving these samples that he is analyzing in this protocol. The BMC Research Compliance Officer clarified that use of embryonic stem cells does not require IRB approval.

- PI's rDNA/IBC training is expired and needs to be updated.
- It appears that lentivirus particles are being prepared in the lab by transfecting appropriate sets of plasmids. Please complete the prokaryotic experiment part in the Recombinant DNA section of the application.
- Section VIII. 7B. Please state what is solid waste in this protocol and how are they disposed of in the lab. Also provide more detail on "Off-site treatment by biowaste vendor OR steam sterilize in an autoclave with quality control checks".
- Section 10. Remove "lab personnel" since no personnel other than Dr. Zhang is there on the application.

BUA Site Assessment: The lab has ECP. Safety trainings are updated. Biosafety cabinet needs recertification but they are not doing any work at this time. He is not using the autoclave.

Motion: Conditional Approval (Administrative Review)	For: 12	Recuse: 0	Against: 0	Abstain: 0	Absent: 2

13. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1367		B cell and its antibody in health and disease	2	2	BUMC

Primary Reviewer: Carmela Abraham	Secondary Reviewer: Susanna Kurnick

Applicable NIH Guidelines: Sections III-D-1-a, III-D-2-a, III-D-4-c, III-D-4-c-(1), III-D-4-c-(2), III-F-8; App B-1, C-VI, E-III, G-II-A

Meeting Comments: This protocol studies the anti-inflammatory function of subpopulations of B-lymphocytes and their antibodies in various diseases. These include but not limited to obesity, diabetes, cancer, cardiovascular and autoimmune diseases. The protocol involves specific depletion of this subset of cells by diphtheria toxin in custom transgenic animal models and comparing the molecular changes against unmodified cells.

- Please make sure all safety trainings are current for Mao, Pareek, Rubio and Zhong. The rDNA/IBC policy training has expired for Landesman and Pareek.
- Please state which animal house rooms are being used in this protocol.
- Please clarify the statement "All sharps will be closed before dispose into approved sharp containers". Capping of sharps are not recommended.
- Bleach should be added to the liquid waste to a final concentration of 10%.
- It is stated in section VIII.7B that "All solid biological wastes will be disinfected by spraying with 70% alcohol and disposed in red biohazard box for incineration." Note that this process is not required and may be removed.
- Are rooms and locked since they contain biohazard materials?
- Section A. Hazardous Biological Agents – Mouse or Homosapien are not strain names. Please remove them.
- MC38 cannot be of both mouse and NHP origin. It is a mouse line and therefore does not need to be included in the table.
- Section B. Please clarify what primary human samples are being used in this protocol and if IRB approval is required, provide IRB approval number and expiration date.
- In section F - After aliquoting the diphtheria toxin, it should be stored at -20°C not 20°C.
- Provide IACUC approval number and approval date in the rDNA/animal experiments section if any rDNA material is introduced in animal.

BUA Site Assessment: They have updated ECP. ROHP clearance for some members needs updating and they have been notified. Safety trainings are current. Biosafety cabinet and fume hoods are duly certified.

Motion: Conditional Approval (Administrative Review)	For: 12	Recuse: 0	Against: 0	Abstain: 0	Absent: 2

14. rDNA/Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2465		Elucidating mechanistic connections between guidance signaling, microtubule regulation, and growth cone steering; Exploring the mechanism by which TACC proteins promote cell motility	2	1	BUMC

Primary Reviewer: Rob Davey	Secondary Reviewer: Colleen Thurman

Applicable NIH Guidelines: Section III-F-8; Appendix C-II (exempt)

Meeting Comments: This protocol will study cell movement involving cytoskeleton regulators. This is important for embryonic development and cancer invasiveness. The work is all recombinant nucleic acids related. Plasmids encoding altered proteins are used to produce messenger RNAs (mRNAs). African clawed toad embryos are injected with the transcribed mRNAs. The eggs then translate the mRNAs into proteins. The PI has gained experience since 2000 working with plasmids and the Xenopus system. However, she is the only staff member listed on the protocol. The biohazard concerns are the use of *E. coli,* which is handled appropriately, disinfecting with final 10% bleach and disposal of material in biohazard boxes. Glass needles are used to inject oocytes but these are contained in a microinjection system and are unlikely to cause any injury. The protocol provides only a very general list of genes (such as cytoskeletal markers fused to fluorescent proteins). A better description of them is needed, particularly relating to their oncogenesis potential to the research personnel.

- In the Overview and Grants Funding Information section, there is no need to fill in the table (this is only for renewals, amendments).
- Xenopus embryos are not considered animals until 3 days post-spawn when they hatch). Until then they are just reagents. Therefore, ABSL level is not required (should be N/A) unless hatched larvae or adults are to be used.
- Research Project Description Q3: Please specify that recombinant plasmids are being propagated in the *E. coli* K12.
- Clarify if any of the cytoskeletal marker protein used in this study are of human origin or have any oncogenic potential.

BUA Site Assessment: ROHP questionnaire has been completed. All required trainings are completed. The PI will share biosafety cabinet of the neighboring lab.

Motion: Conditional Approval (Administrative Review)	For: 12	Recuse: 0	Against: 0	Abstain: 0	Absent: 2

15. Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2477		Role of Senescence in Wound Healing, Tissue Repair, and Scarring	2	1	BUMC

Primary Reviewer: Barbara Slack	Secondary Reviewer: Colleen Thurman

Applicable NIH Guidelines: N/A

Meeting Comments: The goal of the proposal is to study the role of senescent cells in wound healing. This will be investigated in various young and old transgenic mice models including Dorsal skin wound model and Incisional hypertrophic scar model. The senescent cells in these models will be detected by using reporter constructs. Some experiments will also include human skin, wound, or scar tissue from the operating room clinic of the PI. Anesthetics and pain killers are used while collecting these samples. Laboratory procedures include tissue flash-freezing in liquid nitrogen, RNA extraction, fixation for histology using paraformaldehyde in fume hood and beta-galactosidase staining performed in chemical fume hood. Human and animal tissues used in the study are disposed of in biohazard bag-lined boxes. It was noted that because X-gal may be irritating to the mucous membranes and upper respiratory tract, lab coats, gloves and goggles are used while performing these experiments. No concerns were noted regarding use of transgenic animals. EHS conducted an assessment for BMC infection control issues and no concerns were noted.

- Lab Procedures section: Human specimens transported from surgery to 690 Albany in "leakproof styrofoam coolers with lids". Are the lids on these coolers secured in some way, such as leakproof and shatterproof if dropped? Are they comparable to the gasketed shatterproof leakproof plastic containers for transport described in section VIII.11? Consider amending Lab Procedures section to conform with the description in section VIII.11, if the latter is more accurate.
- Lab Procedures: Please confirm that biohazard waste boxes containing human and animal tissues will be marked for incineration.
- Section VIII.3. Are head covers and shoe covers necessary in lab (all live animal work being done in ASC)?
- In the Radiation and X-Ray section, Question 4: location of the irradiator is listed as Evans basement. Is this still accurate or will the newer Multi-Rad irradiator on W8 be used?

BUA Site Assessment: The lab has ECP. All members have ROHP clearance. Training is up-to-date for all members. Their biosafety cabinet and fume hood are certified.

Motion: Conditional Approval (Administrative Review)	For: 12	Recuse: 0	Against: 0	Abstain: 0	Absent: 2

16. Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2480		The role of chronic inflammation induced by periodontitis in the development and progression of Alzheimers disease.	2	2	BUMC

Primary Reviewer: Xin Brown	Secondary Reviewer: Rao Varada

Applicable NIH Guidelines: N/A

Meeting Comments: The objective of this new protocol is to find out whether chronic inflammation induced by gum infection affects the development of Alzheimer's disease (AD). An animal model will be developed in which a subcutaneously implanted mini pump will be used to deliver lipopolysaccharides (LPS) and to test how or if it helps in developing factors associated with the AD. Commercially purchased LPS from *P. gingivalis,* a common pathogen in chronic periodontitis will be used in these experiments and will be compared with the LPS of gastrointestinal tract pathogen such as *E. coli.* After 4 weeks of treatment, mice will be sacrificed. The level of proinflammatory cytokines will be determined by ELISA, presence of amyloid and phosphorylated tau will be analyzed by immunohistochemistry. The loss of both jaw bone and long bone associated with chronic inflammation will be assessed with micro CT. Committee discussed extensively what should be the containment level for this protocol. Although the protocol is not using any hazardous agent, or LPS is not on the BU high hazard chemicals list, inappropriate handling of LPS could become a serious health concern to the users. In fact, most peer institutions advocate for BSL2 containment for its handling. Committee did not ask to uncheck high hazard chemical box in the IBC application. However, Animal Science Center director clarified that if the LPS is already in solution and is used in small amounts, ABSL1 containment is sufficient. As the PI clarified that the LPS vials will be reconstituted in her own lab and the solution will be added to the circulation pump only once during the entire 4-week period of the experiment, there will be minimal LPS exposure to the ASC staff or researchers. Committee concluded that while BSL2 containment should remain in place for this protocol, the requirement is to be lowered to ABSL1 for the work in the ASC. Committee also noted that RPO license is not required for irradiating cells or tissues.

- Please check lab coat, shoe cover and scrubs for the animal work PPE.
- In the liquid waste disposal section, instead of adding 10% bleach to liquid waste, bleach should be added to liquid waste to achieve a final concentration of 10%.
- Change highest animal biosafety level in Section IX to ABSL-1.

BUA Site Assessment: The lab is in good standing and following all required safety practices.

Motion: Conditional Approval (Administrative Review)	For: 12	Recuse: 0	Against: 0	Abstain: 0	Absent: 2