Boston University
Institutional Biosafety Committee (IBC)
April 28, 2020 Meeting Minutes
Location: Zoom and/or by phone
Start time: 12:03 PM End time: 3:05 PM

Members Present: I. Afasizheva, R. Ingalls (left 1:00 PM), B. Slack, E. Muhlberger (left 2:57 PM), R. Davey, C. Abraham (left 2:59 PM), E. Loechler (left 1:44 PM), R. Morales (left 3:02 PM), T. Winters, R. Varada (left 1.56 PM), S. Kurnick, J. Keeney, R. Timmerman (joined 12:26 PM), X. Brown (left 1:44 PM), V. Britton, J. Barton (Left 2:01 PM)
Guests Present: P. Urick, N. Yun, S. Benjamin, K. Tuohey, A. Ahmad, J. Davis, M. Auerbach
Staff Present: J. Hutchinson, S. Ghosh, C. McGoff

I. Review of April 14, 2020 IBC Meeting Minutes

No comments or questions were voiced.
Motion: Approve
For: 14; Against: 0; Abstain: 1; Absent: 1

II. New Business

A. Safety & Quality Assurance Program (SQAP) Report

Expedited Review: Members were asked if they had any objections/concerns to SQAP staff developing an SOP that would allow for low hazard research to be reviewed via an expedited review process. Specifically, work involving only risk group one (1) biological agents and exempt experiments (Section III-F of the NIH Guidelines) with recombinant or synthetic nucleic acid molecules. These protocols would be reviewed on a rolling basis via "Designated Member Review (DMR)" when the IBC Chair determines that the protocol meets these criteria. The Chair would then designate a single member to review the protocol. SQAP staff would send a polling email to the IBC so any member could call for Full Committee Review (FCR). If no member calls for FCR, the reviewing member would review; if at any time the reviewer determines that a more thorough discussion is necessary, the protocol would be sent to the next IBC meeting for FCR. No objections or concerns were voiced. A member suggested adding cell culture work to the SOP and another member indicated that DMR should not apply to work with animals.

2439 (Corley): It was reported that there were no findings from the Site Assessment done for a new BSL-3 protocol reviewed at the last meeting. Members were informed that a revised pathogen list was provided to the BPHC (as an attachment to the protocol) for review with Western Equine Encephalitis removed as this virus was not listed in the application.

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

2-27-20 **ROHP Report:** A senior research associate was seen by ROHP shortly after sustaining a needle stick injury with a needle contaminated with concentrated MRSA and mouse fluids. The needle went through the single glove on her left hand and through the skin in the lateral side of her palm. She did not believe any fluid was injected into her hand and informed her supervisor and washed the wound. She is up to date with her tetanus booster. At ROHP, the research associate scrubbed the wound for another ten minutes (with a surgical hand scrub sponge infused with 3% chlorozylenol (PCMX)) and was placed on a five day course of prophylactic antibiotics (with subsequent follow-up by ROHP). A report of a biological exposure was sent to the BPHC. **EHS Report:** It was verified that the needle was not contaminated with mouse fluid at the time of the injury. The researcher was wearing appropriate PPE, was up to date on required training, and is experienced in animal handling. It was noted that this incident is not reportable to NIH OSP as she was not using genetically modified materials or organisms.

3-3-20 **ROHP Report:** An assistant professor was seen by ROHP a few minutes after sustaining a shallow 3 mm laceration to his left middle finger through a glove. While in a coworker's lab area, he was mincing mouse tissue with a razor blade with no handle in a 3.5 cm petri dish instead of a 10 cm petri dish. He immediately removed the glove and sprayed with ethanol, then washed the wound with soap and water for

a few minutes before coming to ROHP; he is up to date with his tetanus vaccinations. The mouse had not been exposed to any infectious agents and was a transgenic mouse bred at BU (a knock-in mouse, GFP reporter in the locus). The laceration was barely visible when seen at ROHP and was not rewashed, and he returned to work with no restrictions. A report of biological exposure was sent to the BPHC. **EHS Report:** The root cause was determined to be missing equipment and not being conscientious. To prevent recurrence, he will take the Sharps Safety Training in BioRAFT and will only mince mouse tissue in the standard 10 cm petri dish per the standard operating procedure. It was noted that this incident was reported to NIH OSP and BPHC; NIH OSP indicated that the actions taken in response appeared appropriate and that no additional information is needed.

3-5-20 **ROHP Report:** A research technician in the NEIDL was not wearing a mask while doing a mini-prep (adding buffers to a set of tubes in a BSL-2 area) when a bubble formed in one tube and she felt a small sensation on her left nostril at the juncture of the outer cartilage and the mucus membrane. She was unclear whether this was an exposure or whether it was a coincidental sensation. The tubes contained E. coli K12 and a (yellow fever 17D) plasmid, she had added a lysis buffer to the tube and was adding a third buffer when the incident occurred. After the incident, she washed and scrubbed the outer nostril and nearby mucus membrane with soap and water and came to ROHP an hour later. No IBC protocol number was provided for the work. Signs of potential exposure were discussed, and she was advised to contact ROHP if any concerns developed; she returned to work with no restrictions. A report of a potential lab exposure was sent to the BPHC. **EHS Report:** The root cause was determined to be not being conscientious and poor contamination control. It is possible that the miniprep kit's buffers #2(<1% sodium hydroxide) or #3(<25% guanidinium chloride) made contact with her face either by splash or glove contact. To prevent recurrence, the PI and the research technician will review the miniprep procedure with a focus on PPE use and contamination control. Members discussed that the PI provided clarification to ROHP regarding the vaccine strain and that this was BSL-1 work with E. coli (not infectious). SQAP staff will follow-up with the PI regarding IBC approval.

3-11-20 **ROHP Report:** A veterinary research support specialist, while working at ABSL-2, accidentally sustained a needle stick to his right index finger from a 20-gauge needle used to deliver Meloxicam to a macaque that had not been given any hazardous agents. He immediately washed and decontaminated the pinpoint wound with Chloroxylenol scrub and was further evaluated by ROHP. He reports he was wearing two pairs of gloves, hair cover, goggles over his own glasses, face mask, scrubs with Tyvek, and sleeve covers when he was stuck while disposing the needle into the sharps container at the same time another technician was disposing a sharp. He was unsure whether the medication was delivered to the macaque. The macaque was last screened and negative for Herpes B in December of 2019. Samples from the macaque were sent for Herpes B screening that day. The specialist's last Tdap was 11/9/15. The pinpoint wound was treated with first aid. He was provided education regarding Herpes B and provided counseling along with a prescription for antiviral prophylaxis. ROHP verified that he received the medications. A blood sample was collected and sent to the National B Virus Resource Center. A report will be sent to the BPHC. Follow-up was scheduled for three different dates, and the last one was on 4/22/2020. It was noted that results have not been received yet. **EHS Report:** The root cause was determined to be lack of awareness/understanding of procedure and no procedure or inadequate procedure. To prevent recurrence, Animal Research Core SOP's should be amended to specify that only one person should be utilizing a sharp at any given moment and the Animal Research Core staff should then be retrained on the SOP changes. A member asked if the shingles vaccine would be helpful; it was noted that the shingles vaccine is not effective for Herpes B. It was noted that the specialist is an experienced researcher.

EHS reported on two (2) incidents reported by ROHP at the January 2020 meeting (the EHS investigation was not complete at the time):

1-8-20: A PhD scientist called ROHP to report a possible exposure to 100ml of Wescodyne plus cell culture waste. All necessary precautions were taken, and the root cause was identified as "none identified" given that there is uncertainty regarding whether the waste even contacted his pinpoint wound. This incident was considered extremely low risk for any blood borne pathogen exposure. In the future, gloves can be saved for evaluation and EHS can conduct a glove leak test to examine the integrity and identify potential holes and/or tears. Appropriate decontamination procedures were reviewed for washing the affected area and immediately following up with ROHP. It was noted that ROHP does not do serum testing.

1-27-29**:** A PhD student accidentally sustained a pinpoint cut from a scalpel she used on frozen (unfixed) human brain material. EHS reached out to the student and was informed that test results of the tissue donor showed that the donor was HIV positive. The student was tested for HIV and results were negative and the matter has since been closed. The root cause was determined to be not conscientious. To prevent recurrence, EHS advised the student to complete the Sharps Safety Training in BioRAFT and to be conscious of posture and weight distribution when handling sharp instruments.

III. Protocol Review

1. Bhz – Three-year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2445		Characterization of *Escherichia coli* infection and Shiga toxin type-2 *in vitro* and *in vivo* models	2	2	BUMC

Primary Reviewer: Robin Ingalls	Secondary Reviewer: Rao Varada

Applicable NIH Guidelines: N/A

Meeting comments: This is a 3-year renewal to study the mouse model for shiga toxin producing E. coli. It was noted that the PI has IACUC approval for the animal work.

- S. Kurosawa is missing from the personnel table.
- D. Stearns-Kurosawa should be listed as Associate PI on the personnel page (her email is there but not her name).
- Building and room # is missing from the Research Laboratory Facility table.
- Provide details re: growth of bacteria in the laboratory for studies (e.g., plate or broth cultures, low titer/high titer, etc.).
- What toxin will be injected ip? LPS? Shiga toxin? Is it made or purchased?
- Human cell lines and vero cells are listed in the biohazard table but there is no work with cell lines described in the methods.
- Work with Citrobacter rodentium is not described in methods.
- Update the BSC certification date.

Site Assessment: The lab has an ECP; the PI needs to add himself to the protocol; D. Stearns-Kurosawa needs chemical safety training; and research spaces need to be added.

Motion: Conditional Approval (Administrative Review)	For: 16	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

2. Bhz – New Protocol

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

Primary Reviewer: Robin Ingalls	Secondary Reviewer: Rao Varada

Applicable NIH Guidelines: N/A

Meeting comments: This is a new protocol that is related to work being done under an existing BSL-4 protocol. This protocol specifically covers the vaccination of mice with glycoproteins derived from filoviruses (Ebola, Sudan). Some of the proteins have modifications of aa sequences. There is no use of live BSL-4 viruses in this protocol. It was noted that the PI has IACUC approval for the animal work.

- How is vaccine administered? (e.g., SQ, IM, etc? w/ or w/o adjuvant?)

• Are purification of the proteins covered in the BSL-4 protocol? Site Assessment: N. Macgregor needs to be removed from the protocol.					
Motion: Conditional Approval (Administrative Review)	For: 16	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

3. rDNA/Bhz – Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
2342		Identification of inhibitors of high containment virus infection	4	N/A	BUMC

Primary Reviewer: Elke Muhlberger	Secondary Reviewer: Nadya Yun				
Applicable NIH Guidelines: Section III-D-1-c					
Meeting comments: The PI is proposing to add work with primary lung epithelial cultures derived from pluripotent stem cells. No comments or concerns were voiced; it was noted the PI has prior approval for use of human material.					
Motion: Approve	For: 15	Recuse: 1	Against: 0	Abstain: 0	Absent: 0

4. Bhz – New Protocol

BUA	(PI)	Title	BSL	ABSL	Campus
2446		SARS-C0V-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: The proposed work addresses the need for more diagnostic testing options, the identification of therapeutics, and research into understanding how infection leads to a response that is fatal. Personnel will receive training as part of the NEIDL training program and BSL-3 experience is listed for Dr. Seitz. Live virus work will be done at BSL-3 with appropriate PPE. It was noted that NEIDL SOPs indicate that bleach is prepared "fresh" daily and EHS staff noted that it is stable for 24 hours; surfaces are sprayed with a contact time of thirty (30) minutes, and overnight use is for inactivation. Members discussed concerns about the use of ionic and non-ionic detergents for inactivation and emphasized the importance of demonstrating that proposed methods have been validated and are consistent with EHS approved SOPs. It was noted where attachments can be found in the application.

- For referenced SOPs, include some procedural details or attach the SOP.
- Provide evidence that the proposed inactivation methods have been validated (i.e., referencing a summary of the literature for other viruses such as SARS-CoV or MERS-CoV and/or indicating if the methods have been validated at BU).
- Clearly indicate if SOPs exist for the proposed inactivation methods and if so, specifically reference the SOPs; clarify if these SOPs have been approved by EHS, including the proposed use of ionic and non-ionic detergents.
- Ensure that all inactivation SOPs have been provided (attached to the application).
- Clearly delineate in the application which procedures will be done at BSL-2 and which will be done at BSL-3.
- Clarify if the listing of ABSL1 in the Inactivated Biological Samples Use section is an error.
- II. Investigator Contact Information: 617-638-0339, this should be updated with the correct number.
- VII. Research Project Description:
    - #3, when referring to inactivation via Trizol, reference the applicable SOP. Rephrase this sentence to reference the applicable SOP "Infected samples will by placed into trizol according to manufacturers instructions in order to assure inactivation."
    - #3, add appropriate contact time in all places where use of disinfectants, for surface decontamination, are referenced.
- VIII. PPE and Safety Equipment:
    - #1, inactivation SOPs require vortexing, select vortexting
    - #3, remove "face shield" and "N95". Select "disposable scrubs" and "other" then enter "Sleeves, coveralls, and dedicated shoes".

Site Assessment: All BSCs were recently certified; SOPs and biosafety plans are in place; and BSL-3 training will begin when the current group completes training.

Motion: Conditional Approval (Secondary Reviewer Review)	For: 16	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

5. rDNA/Bhz – Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
2443		Investigating host-pathogen interactions regulating the pathogenesis and immunogenicity of BSL-3 viral agents.	3	3	BUMC

Primary Reviewer: Rob Davey Additional Reviewer: Shannon Benjamin	Secondary Reviewer: Susanna Kurnick

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

Meeting comments: The PI is proposing to add rodent models of disease and two (2) personnel. It was noted that the PI needs to demonstrate a knowledge of the literature for all viruses that will be inactivated, including an understanding of associated risks. Members discussed that the description of animal work needs to be clarified per established ASC SOPs/practices and the BSL-3 BSO indicated that many of her comments are to ensure consistency with ASC SOPs. It was noted that the PI has been in contact with animal core staff regarding the proposed work.

- The DURC questions need to be answered.
- Indicate if the methods for inactivation of SARS-CoV-2, Yellow Fever and West Nile virus have been documented in the literature or been validated at BU for inactivation of the agent itself or an appropriate surrogate.
- Provide a summary of the literature where proposed inactivation methods are shown to be effective. If literature cannot be provided or the literature is inconsistent, then validation of inactivation is needed before material can be removed from the BSL-3 environment.
- It is indicated that “lysis buffer used for cell lysis and virus inactivation will be similar to those described in the SOPs listed above”. The term “similar” should not be used – make clear what the methods/procedures that will be used are.
- A third or fourth generation lentivirus system should be used, or justification provided if lower version is to be used.
- Recombinant virus work with +ve stranded RNA virus genomes: State that this work will be physically separated from mammalian tissue culture work so that accidental introduction into cells will be avoided.
- For the animal work, animals are placed individually in Ziplock bags and organs in bleach in tubes. Clarify if this is necessary as it appears to increase interaction with infectious animal tissues – clarify if carcasses and organs could be placed in autoclave bags and autoclaved instead.
- Consider autoclaving sharps rather than treating with bleach.
- Include Dr. Crossland as personnel if he will be performing necropsies.
- 5B states 5% microchem will be used to wipe cages whereas other sections state 10% bleach; be consistent or state that either may be used.
- Needles should be handled using needle blocks whenever possible.
- Animal procedures: intranasal injection should be referred to as intranasal inoculation.
- Anesthesia/Euthanasia procedures: Clarify when you are discussing anesthesia versus euthanasia in this section. The response test is called the "toe pinch" or "pedal reflex." Animals should be taped to boards for necropsy rather than pinned with needles. It is not clear whether/when CO2 euthanasia versus IP overdose will be used.
- Blood and tissue extraction: A 28g needle must be used (rather than 18g).

VIII- Check animal handling.

VII. Research Project Description

- #3 – 1.3 experimental procedures: Provide clarification as it relates to this sentence “Virus stock will be made in 502S prior transfer to BSL3 suite”. Clarify which “viral stocks” are being made in 502S prior to transfer to the BSL-3 suite. If “viral stocks” refers to “viral vectors”, revise the sentence to clarify.
- #3 – 3.1 Generation of virus stock: Indicate the MOI or concentration of virus to be generated.
- #3 – 3.2 Generation of virus stock: Fix this sentence “Virus will be concentrated or not prior aliquoting, and stored as described above.” – it is unclear.

- #3 - III. Transport of viral agents to 606: In the sentence "The transport container is then inserted into the passthrough box, and the interior of the box will be heavily wiped down with freshly prepared bleach at a concentration of 10%". Change the highlighted phrase to "sprayed". When describing this procedure, reference the appropriate SOP that applies.
- #3 – B II Animal experiments and manipulation in biosafety cabinets: Remove all references to the use of 5% Microchem. Replace with the disinfectants that were included in the original protocol submission.
- #3 - V. Waste handling: When describing the disposal of animal carcasses, reference SCI-SOP-0147 Animal Carcass Handling and Removal from ABSL-2, -3, and -4 Laboratories.
- #3 - V. Waste handling: When referencing the disposal of sharps containers, indicate that the container will be closed or secured prior to disposal. Reference the appropriate waste handling SOP.
- #3 - V. Waste handling: When referencing cleaning of surgical and/or necropsy tools, reference appropriate ASC SOP which covers this procedure.
- #3 - VI. Safety and sample inactivation: Clarify what inactivation procedures will be used or if you will you be using the standard operating procedure describing the approved procedures to inactivate BSL-3 samples for single cell RNA sequencing (scRNA seq) drafted by Saeed? "For preparation of cDNA library from fresh unfixed cells, barcoding of RNA will be performed in room , and safely removed from the BSL3, as described in section A. II."
- #3 – VII. Experimental Procedures: Clarify if animal work with risk group 2 viruses (dengue virus and hepatitis C virus) will be performed using ABSL-3 facility and practices. When referencing the use of anesthetization with isoflurane, reference SCI-SOP-0305 Procedures for the Administration of Gaseous Anesthesia to laboratory animal species in the NEIDL ABSL-2, 3 and 4 Laboratories.
- #3 - 2. Monitoring of infected animals: When describing animal checks, reference appropriate ASC SOP.
- #3 - 4. Blood and tissue extraction: Reiterate that disposable lancets will be disposed of in a sharps container. Confirm material that multivettes are made of.
- #3 - II. A. Immunochemistry/Histology: "chemically inactivated via submersion fixation aldehyde-based fixatives prior removal of the BSL3" the methods described in SOP "Inactivating non-select agent BSL-3 materials using formalin or paraformaldehyde" are for cells. Has a method of inactivation for animal organs been validated? Provide a SOP for this procedure and validation information.
- Indicate if there is a SOP for solid tissue dissociation – if so, provide to EHS for review.

VIII. PPE & Safety Equipment

- # 3, how will a face shield be used if wearing a PAPR?
- #7B, reference SCI-SOP-0147 Animal Carcass Handling and Removal from ABSL-2, -3, and -4 Laboratories.
- Section A – Hazardous Biological Agents: Table 2, indicate "yes" in column #1 for SARS-CoV-2 Table 4, confirm that, in fact, there will be no animal work with SARS-CoV-2. If there will be work, change entries to reflect this.
- Section H – rDNA - #19: Add III-D-1-b [Experiments involving the introduction of recombinant or synthetic nucleic acid molecules into Risk Group 3 agents will usually be conducted at BL3 containment. Experiments with such agents will usually be conducted with whole animals at BL3 or BL3-N containment] and III-D-4-b [Experiments involving the introduction of recombinant or synthetic nucleic acid molecules into Risk Group 3 agents will usually be conducted at BL3 containment. Experiments with such agents will usually be conducted with whole animals at BL3 or BL3-N containment].

Motion: Conditional Approval (Reviewers to Review)	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

6. rDNA/Bhz – Three-year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2191		Signaling Dynamics for Tissue Homeostasis and Repair	2	N/A	CRC

Primary Reviewer: Ed Loechler	Secondary Reviewer: Tom Winters
Applicable NIH Guidelines: Section III-D-1-a, III-D-2-a, III-E-1	
Meeting comments: Cells are suspended in collagen and other Extracellular Matrix (ECM) components to make 3D models of tissues in order to study cell signaling in healthy and wounded tissues. Fluorescent dyes, biosensors, and	

optogenetic controllers help assess cell to cell communication to maintain homeostasis or heal tissue gaps. Primary human, other primary mammalian, or immortalized human, and other immortalized mammalian cell lines are obtained from commercial sources. Calcium, electrical and kinase responses after wounding is studied. These data may help to develop methods to optimize wound healing. It was noted that fluorescent biosensors and optogenetic controllers are generated in plasmids propagated in E. coli K-12 strains (BSL1). Replication-deficient 2nd and 3rd generation lentiviral vectors are used in HEK293FT cells. Following transfection (Lipofectamine 3000), cells are harvested (within 24 hours), and filtered for use. No concerns were voiced. Site Assessment: Has an ECP; one (1) personnel needs ROHP clearance; training is current; and the BSC and fume hood are certified.					
Motion: Approve	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

7. rDNA/Bhz – Three-year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2193		Connecting Single-Cell Signaling to Collective Behavior in Microbial Multicellular Systems	1	N/A	CRC

Primary Reviewer: Ed Loechler	Secondary Reviewer: Ron Morales			
Applicable NIH Guidelines: Section III-D-2-a				
Meeting comments: The goal of this project is to understand how single cells work together in groups. The lab is interested in studying the connecting properties of single cells and their way of communicating to group-wide behaviors. • Clarify the purpose of use of *B. subtilis* in the protocol. • Full sharps containers should be closed tightly and disposed of in biohazard boxes, they should not be autoclaved. • Use of a face shield should be checked and cryogenic protective gloves should be added to the list of PPE for handling of samples stored in liquid nitrogen dewar. Site Assessment: No findings.				
Motion: Conditional Approval (Administrative Review)	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

8. rDNA/Bhz – New Protocol

BUA	(PI)	Title	BSL	ABSL	Campus
2447		Role of Intercellular Communication in Pathogenesis of Diabetic Retinopathy	2	2	BUMC

Primary Reviewer: Inna Afasizheva	Secondary Reviewer: Rao Varada			
Applicable NIH Guidelines: Section III-D-4-a, Appendix G-II-A, Appendix E-III, Appendix G-II-A, Appendix Q-II-A				
Meeting comments: This is a new submission that seeks to study the cause of increasing cell death in the retinal blood capillaries in diabetic patients. The study focuses on the channel-mediated gap junction intercellular communication mechanism, the most direct and quickest pathway to connect through channels the cytoplasm of adjacent cells. It is known that high glucose decreases the expression level of Cx43 (connexin) and downregulates intracellular communication. Based on recent findings, the PI proposes to investigate the role of small molecules (danegaptide) in enhancing the intercellular communication pathway and preventing vascular lesions associated with diabetic retinopathy. Diabetic rats will be used as an in vivo model. Experimental work includes manipulation of rDNA such as plasmid isolation, transfections and intravitreal injections for direct plasmid delivery. Experiments with animals are described in detail. It was noted that the IACUC protocol covering the animal work is under review. Members discussed that the appropriate BSL/ABSL for the proposed work should be BSL-1/ABSL-1. • The PI should clarify why this is listed as a BSL-2/ABSL-2 protocol, this appears to be a BSL-1/ABSL-1 protocol – the BSL/ABSL should be listed consistently throughout. • Provide the source of plasmids. • Provide additional details of personnel experience. • Section VIII-4 PPE: lab coats, disposable gloves, safety glasses, surgical mask, shoe cover to be used. Site Assessment: The BSC is certified and the PI is working on updating ROHP clearance.				
Motion: Conditional Approval (Administrative Review)	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 3

9. rDNA/Bhz – Three-year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1904		BMP9 as a juvenile protective factor in cognitive aging	1	1	BUMC

Primary Reviewer: Carmela Abraham	Secondary Reviewer: Susana Kurnick

Applicable NIH Guidelines: N/A

Meeting comments: Cholinergic neurons, which produce the neurotransmitter acetyl choline, are important for memory and learning and their function decreases with aging and in Alzheimer's disease (AD) and mouse models of AD. The PI discovered that the bone morphogenic factor 9 (BMP9) is a differentiating factor for cholinergic neurons and uses BMP KO mice. Aim 1 is to characterize the behavioral, cognitive, cellular and molecular phenotypes of the BMP KO mice. Aim 2 is to test the efficacy of icv BMP9 administration in ameliorating brain dysfunction using wild type and transgenic AD mice. Members discussed inconsistencies in the protocol regarding biosafety level (mention of both BSL-1 and BSL-2) and that work appears to be appropriate for BSL-1 but perhaps is designated as BSL-2 due to shared space; it was noted that the use of transgenic mice is ABSL-1 if commercially available/purchased.

- Clarify if BSL-1 or BSL-2 and ensure consistency throughout.
- Remove plating, colony counting.
- VIII 7 – remove the information regarding the studying of fungi (this appears unrelated) and indicate that a final concentration of 10 % bleach will be used.
- IX. "Work involving the use of biohazardous materials or recombinant DNA in live animals" is checked but this use does not apply - clarify why checked or uncheck.
- VII #3- update IACUC protocol number.
- VIII - check animal handling and cage changing.

Site Assessment: ROHP questionnaires were submitted for two (2) people; training is current; and BSC is certified.

Motion: Conditional Approval (Administrative Review)	For: 12	Recuse: 0	Against: 0	Abstain: 0	Absent: 4

10. rDNA/Bhz – Three-year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1296		In vitro studies of the amyloidogenic natures of transthyretin and immunoglobin light chain proteins	2	N/A	BUMC

Primary Reviewer: Inna Afasizheva	Secondary Reviewer: Tom Winters

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

Meeting comments: This is a 3-year resubmission that seeks to understand the role of TTR (transthyretin) and LC (light chain immunoglobulin) plasma proteins in formation of amyloid deposits in hearts and kidneys of patients with amyloidosis. The PI proposes to use two approaches: 1) Purification of the proteins from clinical samples including plasma/serum, urine and tissue specimens obtained from patients. IRB numbers are provided. Isolated proteins will be used for proteome analysis; and 2) In vitro studies aim to analyze biochemical and biophysical properties of proteins in test tubes and in cell lines. Methods include histology of fixed in formalin samples (never fresh) and immunohistochemistry. Cell based studies include measurement of viability using several common techniques. Stable mouse cell line (Sp2/0) secreting targeted proteins will be used to study immunoglobulins interaction.

- In the laboratory procedures section, the description of work with serum and plasma from the repository does not include BSL-2 practices with aerosols (such as leak proof centrifuge lid and BSC), please update.
- In the laboratory procedures section, explain what is meant by: "appropriate storage of clinical samples in BU Amyloidosis Center Research Laboratory".
- According to the application cell-based studies use multiple cell-lines; include all cell lines that the lab is using and provide detailed source information.
- Update the protocol to include a description of cell work.
- Clarify if a BSC is being used and if so, for what procedures.
- Clarify centrifuge use.

Site Assessment: The lab has an ECP; some personnel need ROHP clearance; training is current for all; and the BSC and fume hood are certified.					
Motion: Conditional Approval (Administrative Review)	For: 11	Recuse: 0	Against: 0	Abstain: 0	Absent: 5

11. rDNA/Bhz – Three-year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
793		Bacterial lysis on a microfluidic device Protozoa lysis on a microfluidic device	2	N/A	CRC

Primary Reviewer: Ron Morales	Secondary Reviewer: Jim Keeney
Applicable NIH Guidelines: III-D-2-a, Appendix C-II, Appendix B-II-A	
Meeting comments: The PI has been studying the development of a rapid and low-cost point of care (POC) infectious disease diagnostic device that can identify the presence of bacterial or protozoal infections in patient samples. The device can detect the presence of these agents through the amplified sample of their DNA from the lysed microorganism within a single hour. This helps the health care provider perform a rapid diagnosis to treat the patient appropriately. The lab is studying the development of this diagnostic device for Chlamydia, Gonorrhea, and Trichomonas which cause STDs and protozoal agents that cause malaria. Samples (urine, urethral and vaginal swabs, blood, and saliva) are obtained from patients and pass through a microfluidic chip. The captured cells are lysed by heat, the DNA is amplified and any agent that may be present is identified via antibody-based detection. The lab describes the different controls being used and their sources, the maintenance of microbial agents being used, and the de-identified samples used from John Hopkins Center for POC tests for STDs and MR4 or BEI Resources. The work is performed in the BSL-2 and agents handled in a BSC, solid and liquid waste treatment and disposal are well described including spent plastic microfluidic chips which are soaked in 10% bleach solution and discarded into sharps containers. It was clarified as part of the site assessment that training is current for listed personnel. Site Assessment: Training is current and the BSC is certified.	

Motion: Approve	For: 11	Recuse: 0	Against: 0	Abstain: 0	Absent: 5

12. rDNA/Bhz – Three-year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
896		Environmental PPAR Agonists: Disruption of Adipose, Liver and Bone Function	2	1	BUMC

Primary Reviewer: Barbara Slack	Secondary Reviewer: Susanna Kurnick
Applicable NIH Guidelines: Sections III-D-1-a, III-D-2-a, III-E-1, III-D-4-a, Appendix B-II-D, Appendix G-II-B	

Meeting comments: This protocol investigates the effect of environmental toxins such as polychlorinated biphenyls (PCB) and organotin compounds on adipose tissue and bone cells. They use primary human adipocytes and bone marrow cells from commercial sources as well as from mice. Other human cell lines and non-human primate cell lines are also used. Lentivirus vectors packaged in-house are also used for delivering transcription factor expression or shRNA to the cells and animal bones. They also introduce high hazard chemicals to animals using EHS approved SOPs through gavage for which they provided a detailed description in the protocol. Treatment effects will be evaluated using standard assays such as RNA-seq, western blot, PCR and others. Members discussed whether the BSCs used exhaust one hundred percent to the outside for high hazard chemical use; EHS will confirm. If so, it was indicated that conditional approval with administrative review is sufficient.

- The PIs Laboratory Safety Training is not current.
- Section VIII.1 - check 'animal inoculations' (lentivirus to be injected into bone marrow) and add 'animal exposure - gavage' under 'Other'.
- Section IX-Materials Used in Research. 'Live Animal Use' should be checked. (Animals will be treated with high hazard chemicals (CCL3) via gavage, and injected with lentiviral vectors, according to Section A and rDNA table); ABSL-2 should be checked at the bottom of this section.
- Section A. Cos7 cells (monkey) should be added to table. HK-2 cells are human, not non-human primate as stated on form; please correct.

- Section A and rDNA table indicate that lentivirus encoding shRNAs will be injected into animal bone marrow. The procedures and safety precautions used should be briefly described in the Lab Procedures section.
- Section F. Regarding handling of high hazard chemicals - description refers several times to 'the above PPE' which is not specified. Please list the PPE to be used for these procedures at the top of the table.
- VII- #3 Elaborate on animal experiments. Will gavage be performed under a BSC? Will anesthesia be used?
- If mice will be gavaged with the high hazard organotins mentioned, then ABSL-2 needs to be checked rather than ABSL-1. The same holds true for lentivirus use in animals.
- Provide any relevant IRB numbers and update the IACUC approval numbers.

Site Assessment: Have an ECP; all personnel have been cleared; one (1) personnel needs to complete BSL-1/2 training; and the BSC is certified.

Motion: Conditional Approval (Administrative Review)	For:11	Recuse: 0	Against: 0	Abstain: 0	Absent: 5

13. rDNA/Bhz – Three-year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2168		MUC1* Chimeric Antigen Receptor T Cells Targeting Breast Cancer	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-a, III-E-1; Appendix B-II-D, G-II-B

Meeting comments: This protocol investigates the efficacy of chimeric antigen receptors expressing T cells as cancer therapeutics by injecting autologous T-cells expressing MUC1* antibody fragments into animals. These animals will have xenograft tumors of various cancer origin. Some work will be done at Minerva Biotechnologies, Waltham, and some at BUSM. Xenografts and imaging will be done at BU using ATCC cell lines. It was noted that all the lab work is done in Waltham and that only the animal work is done at BU.

- Clarify what work will be done at Minerva and what work will be done at BU and by whom.
- Will the human T cells be transduced with the virus at Minerva? How will the virus be removed from the cells?
- IX. 2. Clarify if any of the human cancer cell lines to be used are commercial cell lines and if they could cause human disease if injected accidentally.
- VIII. 4. Add laboratory coats; 5. Add certification date of BSC; 7. Revise to state that bleach will be added to a final concentration of 10% for a minimum of 30 minutes before disposal.
- VIII- Review the PPE section and check off animal handling as well as any other relevant laboratory procedures.
- Include approved IACUC protocol number.

Site Assessment: It was noted that this is a tenant lab that works closely with the ASC and follows PPE requirements for entering the facility; new personnel need to complete training; need to update ECP; personnel need to be cleared; two (2) personnel have left (and need to be removed); and one (1) person needs to be added.

Motion: Conditional Approval (Administrative Review)	For: 11	Recuse: 0	Against: 0	Abstain: 0	Absent: 5

14. rDNA/Bhz – Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
1166		IPCP-HTM and Seminal HIV-1 Shedding and Drug Resistance in HIV-1/HSV-2 Coinfected Men on HAART	2+	N/A	BUMC

Primary Reviewer: Elke Muhlberger	Secondary Reviewer: Bob Timmerman

Applicable NIH Guidelines: Sections III-D-1-a; Appendix B-II-D; Appendix G-II-B

Meeting comments: The PI is proposing to add cell lines.

- Clarify if the tUEC cell line is identical with THUEC (transduced Human Urethral Epithelial Cells). If this is the case, change the name for clarity.
- Remove mouse hybridoma cells from the Hazardous Biological Agents list.
- Human cell lines are classified as BSL-2, change in table.
- Remove hybridoma cell line from rDNA section.
- Clarify if Dr. Sulis was contacted and provide the information requested in the application.

Motion: Conditional Approval (Administrative Review)	For: 11	Recuse: 0	Against: 0	Abstain: 0	Absent: 5

15. rDNA/Bhz – Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
1487		CLASSIFICATION OF STUDIES: 1. Human Studies-IMPAACT/ACTG 2. Human Studies-NIH, industry and internally sponsored 3. IACUC/Animal Protocols *Specific titles are listed in Section VII.	2	2	BUMC

Primary Reviewer: Barbara Slack	Secondary Reviewer: Valeda Britton

Applicable NIH Guidelines: N/A

Meeting comments: This is an amendment to an IBC protocol that covers multiple clinical and animal studies. The amendment removes a number of studies and adds three (3); no procedural changes have been made.

- IRB approval number for third newly added study (Pfizer B7471013) is pending- update status if not still pending.
- Update the BSC certification date (date listed is 2017).
- LST, BBP, BSL1/BSL2 training up to date for all personnel except D. Lee – ensure that training is current for all listed personnel.
- Ensure requested IRB and IACUC approval information has been provided and is current.

Motion: Conditional Approval (Administrative Review)	For: 11	Recuse: 0	Against: 0	Abstain: 0	Absent: 5

16. Bhz – Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
2388		1) H-37773: MOM NEST Study: Safety, Efficacy, Pharmacokinetics, and Pharmacogenetics of Naltrexone in Pregnant Women with Opioid Use Disorder 2) NIDA Clinical Trial Network Protocol 0080: MOM Protocol - Randomized Trial of Buprenorphine for Pregnant Women with Opioid Use Disorder. 3) COVID-19 Placental Project	2+	N/A	BUMC

Primary Reviewer: Inna Afasizheva	Secondary Reviewer: Ron Morales

Applicable NIH Guidelines: N/A

Meeting comments: The PI is proposing to conduct research on samples obtained from placental tissue of COVID-19 positive women to understand maternal to infant transmission of the virus. Samples will be subject to RNA isolation, histology of unfixed samples, and immunoglobulin testing of cord blood. The PI indicated that work will be done at BSL-2 with special practices of BSL-3. It was noted that the virus should be listed in the hazardous biological agents table, there was further discussion regarding whether listing work with infectious material in the other potentially infectious materials section is sufficient; this will be further evaluated by the reviewers upon resubmission to ensure that use of infectious samples is clearly indicated. The BSO indicated that the safety specialist for this lab will work closely with the lab to ensure that appropriate practices of BSL-3 are being followed.

- Clarify if any of the personnel conducting the proposed work have experience working with infectious samples, providing details of relevant experience/training for the proposed work.
- Identify what procedures and special practices of BSL-3 will be used for conduct of the proposed work (RNA isolation, histology, and immunoglobin testing) so it is clear what will be done and that the appropriate BSL-3 practices will be used.
- Clarify if tissue grinding and homogenizing will be performed in a biosafety cabinet.
- The primary container holding tissue samples should be leak-proof and sealed.
- Sharps containers must not be autoclaved; they should be closed securely and discarded in the biohazard box.

• Biohazard boxes containing waste tissue material for disposal should be labelled with appropriate sticker labels for tissue disposal. • Work with positive SARS-CoV-2 samples must be performed in the BSL-2 lab following special practices of BSL-3; the labs EHS safety specialist should be consulted to ensure that appropriate practices will be followed.

Motion: Conditional Approval (Reviewers to Review)	For: 11	Recuse: 0	Against: 0	Abstain: 0	Absent: 5

17. rDNA/Bhz – Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
2113		Zika virus growth and characterization; development and evaluation of diagnostic tests for positive and negative sense RNA viruses.	2+	N/A	BUMC

Primary Reviewer: Tom Winters	Secondary Reviewer: Ron Morales
Applicable NIH Guidelines: Section III-D-1-a, III-D-2-a, and III-D-3-a; Appendix B-II-D, and G-II-B-3	
Meeting comments: The PI is adding procedures for diagnostics including rtPCR for SARS-CoV-2 and IRIS assays. Zika virus and Dengue virus lab methodologies are described in the currently approved registration. The proposed laboratory methodology described includes receipt of SARS-CoV-2 RNA cell lysate from BEI to use as a control. OP and NP samples (in transport media stored frozen in the laboratory of a NEIDL investigator) will be deidentified before use. In addition, deidentified samples from Boston Children's Hospital (BCH) will be used. RNA will be used in rtPCR reaction to quantify the SARS-CoV-2 RNA present. Lab precautions appear appropriate and work is done inside a BSC. Serum samples from SARS-CoV-2 positive patients from the bio bank will be received, deidentified, and frozen. Serial dilutions of serum are performed and used in a standard ELISA assay development. Laboratory precautions including BSC use and incubation of plates in leak proof secondary containment is described. Serum from patients who have recovered from COVID-19 infection will be studied from a bio bank, deidentified and frozen. Dilutions are performed and will be used in a standard ELISA assay development. It was noted that SARS-CoV-2 RNA work is done with BSL-2 precautions and appears consistent with CDC laboratory recommendations and work with serum and swab media done at BSL-2 with BSL-3 practices appears appropriate and consistent with CDC laboratory guidelines. Members discussed that work with SARS-CoV-2 positive clinical samples must be performed in the BSL-2 lab with special practices of BSL-3. EHS will work closely with the lab to ensure that the appropriate BSL-3 practices are being used.	

Motion: Approve	For: 10	Recuse: 0	Against: 0	Abstain: 0	Absent: 6

18. rDNA/Bhz – Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
1630		HIV transmission pathogenesis	2+	N/A	BUMC

Primary Reviewer: Barbara Slack	Secondary Reviewer: Jim Keeney
Applicable NIH Guidelines: Section III-D-1-b, Section III-D-2-a, Section III-D-3-b, Section III-E-1; Appendix B-III-D, Appendix G-II-C	
Meeting comments: The PI is proposing to incorporate a sequence encoding the SARS-CoV-2 spike protein into HIV virus pseudotypes with NL4-3 or Q23-17 backbones (capable of only one round of infection) in order to study transmission potential in human lung carcinoma cell lines and to assess antibody reactivity and neutralization. • Ensure that required training is current for all listed personnel; Laboratory Safety Training for Olson appears to have expired in 2017. • Update the BSC certification date. • Add Calu 3 and Calu 6 cell lines to the biohazard agent list (Section A). • Add cDNA encoding SARS-CoV-2 spike protein and human cell lines Calu 3 and Calu 6 to the rDNA table.	

Motion: Conditional Approval (Administrative Review)	For: 9	Recuse: 0	Against: 0	Abstain: 0	Absent: 7