Boston University
Institutional Biosafety Committee (IBC)
January 26, 2021 Meeting Minutes
Location: Zoom and/or by phone
Start time: 12:00 PM End time: 2:06 PM

Members Present: C. Abraham, I. Afasizheva, E. Muhlberger, B. Slack, R. Davey, E. Loechler, R. Morales, T. Winters, R. Varada, C. Thurman (left 1:35 PM), J. Keeney, R. Timmerman, V. Britton (joined 12:12 PM), J. Barton
Guest Present: T. Killen, A. Ahmad, J. Davis, K. Tuohey, N. Yun, P. Richmond, B. Whitfield, J. Wood, M. Fitzgerald
Staff Present: S. Ghosh, C. McGoff, L. Campbell

I. Review of December 15, 2020 IBC Meeting Minutes

No comments or questions were voiced.
Motion: Approve
For: 13; Abstain: 0; Absent: 1

II. EHS Special Report

Research Safety Director discussed recent findings on identification positive PCR test results for SARS-CoV-2 in researchers working in laboratories involved in working with SARS-CoV-2 nucleic acids or plasmids expressing viral gene products. The issue originally was brought to light when back in September 2020, regular SARS-CoV-2 screening tests turned positive for few members of labs working with SARS-CoV-2, although they were asymptomatic all along. This led to the discussion between BU and BPHC whether those could be because of the use of SARS-CoV-2 amplicons. Since then, few more similar cases have been identified. Last month BPHC has asked BU to conduct environmental sampling of five select laboratories to test such hypothesis. Such sampling from those five labs showed a large number of those samples positive for SARS-CoV-2. Resampling was also done to confirm the results. Last week, BPHC asked BU to pause research in those labs and conduct thorough cleaning and then perform resampling. In consultation with BPHC, EHS put together a SOP for cleaning the labs and they are working with these labs to make sure that the cleaning is done properly. In the meantime, those labs confirmed that they have paused their work. After this ongoing rigorous cleaning, EHS will again test environmental samples from these labs. Those results and other associated information will be provided to BPHC. Some members expressed concerns that discussions with BPHC and subsequent decisions should be more open to the PIs so that they are aware of what is going on and can provide scientific support to the mitigation plans. The Medical Director clarified that BU now has ways to test samples in additional assay platforms, which can provide much clearer diagnosis about whether the positivity is due to real infection or laboratory contamination. Members insisted that positive results from individuals working in SARS-CoV-2 research labs should be quickly cross-validated via secondary testing platforms before being reported to the BPHC.

III. IBC Self-Assessment

Sajal Ghosh conducted the IBC Self-Assessment review. The NIH requires that the IBC is set up as an institutional body that will be responsible for overseeing the recommendations of the NIH guidelines for recombinant and synthetic nucleic acids in all applicable research work. For the evaluation of the function of this committee the NIH recommends that NIH-recommended best practices regarding implementation of the guidelines be reviewed with key personnel such as IBC members and administrators, biological safety officers, veterinarians, and animal care staff, as well as investigators and laboratory staff. The self-assessment tool that includes the NIH recommendations and institutional response to each of the recommendations was sent out to each member ahead of time. In the meeting Sajal presented the entire deck of NIH recommendations and institutional responses and discussed in particular the sections that deal with administrative policies and practices that members may not be as familiar with. Clarification was provided for all questions from the members. Overall, it was noted that this IBC follows all NIH recommendations and, on few items, where we are unable, we follow allowable alternate approach.

IV. New Business

A. Safety & Quality Assurance Program (SQAP) Report
Susanna Kurnick is no longer an IBC member as she left BU last week. Colleen Thurman will serve as an Animal Research expert and she is now an IBC voting member.

B. Research Occupational Health Program (ROHP) & Environmental Health and Safety (EHS) Report
ROHP Report: Since the last IBC meeting on 12/15/20, two researchers in the NEIDL tested positive for SARS-CoV-2 on asymptomatic screening.

12-23-20: ROHP received notification that a PhD student researcher for the NEIDL tested positive on asymptomatic COVID-19 screening on 12/22/20. He does work with SARS-CoV-2 but informed that he has no COVID-19 symptoms and felt well. This individual had been symptomatic for COVID-19 (although never tested) back in March 2020 when 3 out of 5 members in his household tested positive for the virus at that time. On 8/16/20 he tested positive for SARS-CoV-2 on asymptomatic screening which later was determined to be from amplicons. On 11/2/20 he was tested positive for anti-SARS-CoV-2 IgG (indicating previous exposure to the virus), but was negative for anti-SARS-CoV-2 IgM (indicating no current acute infection). This PhD student researcher has been back in the screening process since 11/15/20. He clarified that he follows all the necessary precautions and work practices recommended by the ROHP and EHS.
For his last screening result, he denies any known breaches or exposures but does report that he did perform a plaque assay using ultraviolet lights to inactivated SARS-CoV-2 virus using a new light device on 12-18-20. Healthway arranged for repeat testing using a Fisher Assay and repeat SARS-CoV-2 PCR testing. A biological research laboratory report form was submitted to BPHC. It was later determined that his positive test results were related to amplicons.

1-19-21: A Research Scientist tested positive for SARS-CoV-2 on asymptomatic screening on 1/16/21. She remains asymptomatic and denies any known positive Covid 19 contacts. She denies working directly with SARS-CoV-2. She follows all ROHP and EHS recommendations for working in a lab that is involved in working with SARS-CoV-2. She wears a lab coat, one pair of gloves and a new surgical face mask that she puts on as she enters the lab (removing her own personal mask) and removes these PPE on exiting. She does work on a bench running gels, diluting plasmids, work on protein samples and plasma that contain the protein but not the sequence or the virus of SARS-CoV-2. Her last day of work was 1/16/21. She did clarify that she shares space in a tissue culture room with others that maybe working with plasmids that contain sequences of SARS-CoV-2 but not the full virus. She reports that researchers are spaced at least 6 feet apart and there is strong ventilation in the room.
Dr. Winters was in touch with both Healthway and this researcher to determine if her results from 1/16/21 are possibly related to SARS-CoV-2 amplicon from environmental contamination. It was later determined that her results were indeed related to amplicons. A Biological Research Laboratory Report was submitted to BPHC.

EHS Report: On the morning of 12/24/20, an animal care staff member discovered a cage in with no mice present and reported the finding to the animal care supervisor who notified the corresponding lab and ASC vet services and operations staff. ASC set up more traps within the room to trap these three mice, which were reported to be prion-infected. On the morning of 12/26/20, one mouse was caught by an animal care staff and subsequently euthanized by a vet tech per vet instructions due to numerous limb injuries.
EHS investigation revealed that these wild type mice C57BL6 were sent from an external vendor and had been inoculated intra-cerebrally on 11/30/20 with mouse-adapted RML prions (a standard laboratory strain). There is a strong barrier to inter-species transmission of prions, so this strain poses little threat to humans. In addition, this strain is not known to be shed by the animals (it remains in the CNS), so the risk to other mice is also minimal. Prions are not casually transmissible (for example, by respiratory or fecal routes), and even the oral route requires the ingestion of tissues of the central nervous system. Finally, these mice are only 30 days into the incubation period, which normally lasts 150 days, so the titer of infective prions in their brains of these escaped mice is extremely low. Given all these considerations, it was believed that these three mice pose little risk to the health and safety of ASC and other personnel, to other laboratory animals, or the community. No recombinant DNA or

synthetic nucleic acids were administered to them. By 12/29/20 the other two mice were caught and humanely euthanized.

The three mice made an inch-wide hole and escaped out of the cage by tearing through the filtered top. The feeding bottles that had been used to administer the liquid diet were either accidentally pushed too far back giving the mice access to the filter cage top or it is also possible the mice pushed it back themselves. ASC has already made corrections and worked with the lab so this mishap can be avoided in the future. All the cages now have food hoppers, cutting off access to the filtered top.

V. Protocol Review

1. Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1981		Correlation of THBS1 polymorphisms and TSP-1 expression	2	2	BUMC
Primary Reviewer: Inna Afasizheva		Secondary Reviewer: Colleen Thurman			
Applicable NIH Guidelines: N/A					

Meeting Comments: The 1981 protocol focuses on studying eye surface inflammation pathways that are regulated by thrombospondin 1 (TSP1) protein. Reduced level of TSP1 is associated with increased risk of developing chronic dry eye syndrome. Protocol describes experimental approaches establishing relation between expression level of TSP1 protein and variations in the THBS1 gene that encodes this protein in conjunctiva, blood and saliva samples. Experiments include peripheral blood samples collected from human volunteers (covered by current IRB protocol), conjunctiva and isolation of DNA and RNA using commonly used kits and sequence analysis at Molecular Core Facility. Animal model studies determine the role of TSP1 in inflammation of the ocular surface in uveitis model in mice induced by pertussis toxin injection. Additional experiments with human saliva are supported by two approved amendments. Although the laboratory procedure part of the protocol is described well, several inconsistencies were noted. It is indicated that lab members will collect samples and process them for downstream experiments, the personnel list only includes PI and another faculty (Dr. whose involvement is only for the animal work. The animal work approval expired long ago but the protocol has not been updated.

Committee expressed concerns that the protocol has not been updated properly for this 3-year renewal. It must be updated based on what is being done at present and what will be done in near future. Personnel list does not include other lab members who might be part of this protocol. Further, the animal work approval has long been expired but the protocol suggests that this animal work is ongoing. Dr. currently does not have any IACUC protocol for the proposed work. Further, PI has indicated to the EHS that she may remove Dr. Masli from the protocol if her training is not updated. However, the protocol indicates that she is the only person performing the animal model work proposed in the protocol. That raises further concern about the current status of the animal work. A thorough revision of experiments currently being done and appropriate clarification are required.

- Please indicate which lab members "with training in phlebotomy" will perform blood draw. Personnel list includes two personnel only. One is co-PI on the animal project. If PI will draw blood by herself it should be mentioned in the protocol. If other members are involved in the laboratory work, please update the personnel list.
- Dr. Carol Sulis is not the contact person for IRB protocols any longer. Please change the name to Dr. Anwaar Ahmad.
- The animal protocol describing mice infection with Bordetella pertussis toxin is not current. The only approved IACUC protocol for is PROTO201800256, which is a breeding protocol. Experimental animal protocol PROTO201800282 (formerly AN-15400) was closed 3/3/2020. If animals are being approved in this IBC submission, provide approved or pending IACUC application information and update the following:
  - VIII. 1. Check animal handling
  - VIII. 4. Clarify lab coat vs disposable scrubs for animal work
  - Check Live animal use box in the Materials Used in Research Section

Animal Science center informed that anyone working in the animal house must be properly trained and should be registered in the approved IACUC protocol. Handling of animals by any unauthorized personnel would constitute violation of ASC policy. BUA Site Assessment: ROHP clearance, BSL1/2 and BBP training is due for one personnel.					
Motion: Conditional Approval (Administrative Review)	For: 14	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

2. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1974		Targeting the AHR to intercept lung cancer; Endogenous and Environmental AHR Ligands in Head and Neck Cancer Aggression and Immunosuppression; AHR-mediated immunosuppression in glioblastoma; A simple platform for expanding human hematopoietic stem cells	2	2	BUMC

Primary Reviewer: Barbara Slack	Secondary Reviewer: Colleen Thurman
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: Goal of the protocol is to study the role of aryl hydrocarbon receptor (AHR) in tumor migration and invasion. The models they use for their study include human and murine cancer cell lines and mouse xenografts where they inject human cancer cell lines. They use replication incompetent lentivirus vectors, siRNAs and CRISPR/Cas9 technology to manipulate gene expression in cells. Protocol includes standard cloning experiments and propagation of plasmids in bacteria. The protocol also includes use of three high hazard chemicals (HHC) that they have been using for many years. They have appropriate SOPs for their use and their safe handing using respirator and face shields and preparation of solutions of HHCs in chemical fume hoods are well described.

- and need to update BSL1/2 and Chemical Safety training and PI needs to update rDNA/IBC Policy Training.
- Section VIII.1 Check animal handling; check plating, colony counting (for plasmid propagation)
- Section VIII. 2. Check Others
- Section VIII. 3. Check Other. Work is done in BSC or chemical fume hood. Is respirator/N95 required?
- Section VIII. 4. Check Other. Is N95/respirator required if work is done in a BSC?
- Section VIII.6. Please indicate that sharps containers, when full, will be placed in double red bag-lined biohazard boxes for disposal.
- Section VIII.7 Please indicate that bleach at a final concentration of 10% will be used to treat liquid waste.
- Section A. Lentiviral vectors should be added to table. Table should indicate that human cancer cell lines are capable of causing human disease (for example, if accidentally injected)
- Add MCF-10, SUM149, 293T cell lines to Section A (these are human cell lines listed in the rDNA table).
- Section H. IACUC Approval number is PROTO201800289. Please update.

BUA Site Assessment: Site Assessment is not done yet and is scheduled for tomorrow (1/27/21).

Motion: Conditional Approval (Administrative Review)	For: 14	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

3. Bhz – Annual Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2352		Propagation and characterization of viruses	4	N/A	BUMC

Primary Reviewer: Elke Muhlberger	Secondary Reviewers: Nadya Yun
Applicable NIH Guidelines: N/A	

Meeting Comments: This protocol receives, grows and characterizes viruses that cause severe disease and require Biosafety Level 4 containment; specifically, filoviruses including Ebola virus, arenaviruses including Lassa virus,

bunyaviruses including Crimean-Congo hemorrhagic fever virus, and paramyxoviruses including Nipah virus and virus' that require BSL3 containment such as SARS-CoV-2. In this annual renewal biosafety cabinet certification dates have been updated but no other changes made. This is a nicely written protocol and has been amended and reviewed several times in recent past. No concerns were noted.

A motion was made not to require annual review of this protocol.
For: 14; Against: 0; Abstain: 0; Absent: 0

Motion: Approval	For: 14	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

4. Bhz – Annual Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2361		Testing medical countermeasures against high consequence pathogens in rodents	4	4	BUMC

Primary Reviewer: Rob Davey Additional Reviewer: Nadya Yun	Secondary Reviewers: Rao Varada

Applicable NIH Guidelines: N/A

Meeting Comments: This protocol determines the efficacies of vaccines and therapies against high consequence pathogens (risk group 3 and 4 pathogens) using animal models, including rodents. It provides detail description of procedures for safe handling of those pathogens. This annual renewal only updates biosafety cabinet certification dates. ASC director confirmed that the protocol is supported by four well written and active IACUC protocols. Committee discussed whether there is need to update the personnel list.

- Please remove Susanna Kurnick from the personnel list as she has left the institution.

A motion was made not to require annual review of this protocol.
For: 14; Against: 0; Abstain: 0; Absent: 0

Motion: Conditional Approval (Administrative Review)	For: 14	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

5. rDNA – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2018		Core Curriculum Labs	1	N/A	CRC

Primary Reviewer: Ed Loechler	Secondary Reviewer: Jim Keeney

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

Meeting Comments: This protocol supports laboratory training of undergraduate students in Core Curriculum Natural Science class. Using an educational kit from Bio-Rad, students learn how DNA (a plasmid) is introduced into bacteria to produce novel proteins. They study the origins of life, including origins of DNA, RNA, and proteins. Specifically, the lab shows how a gene confers resistance to the antibiotic ampicillin, as well as how a reporter gene (GFP) can be used to determine whether DNA was successfully introduced into the bacteria. Standard microbiological techniques are used. Typical bacterial plates are used (for example, LB, with and without ampicillin, and with and without arabinose). The plasmid pGLO is transformed into *E. coli* K-12. Standard microbiological safety procedures are followed. Surfaces are decontaminated with fresh 10% bleach. Staff (not students) prepare plates, etc. Precautions are carefully described when using equipment (for example, UV lights). Training for the PI and assistant are appropriate and up to date.

BUA Site Assessment: All members have ROHP clearance and all required training are current for all members. Biosafety cabinet is not required for this protocol.

Motion: Approval	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

6. Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2501		Spectral and Metabolic Basis of Visual Responses	2	2(?)	BUMC

Primary Reviewer: Rob Davey	Secondary Reviewer: Tom Winters

Applicable NIH Guidelines: N/A

Meeting Comments: This team seeks to understand mechanisms that regulate visual sensitivity under different conditions of ambient illumination and different conditions of retinal light adaptation. To accomplish this the team plans to study the absorbance spectra of primate monkey rod and cone retinal pigment and correlate it with previously obtained data from other vertebrate species. The eyes of Rhesus monkeys will be obtained from the BU Department of Anatomy lab, and the eyes of marmosets will be obtained from a collaborator from Johns Hopkins University and sent to the Cornwall lab. The BU primates have been tested for Herpes B on an annual schedule. The eyes of Rhesus monkeys will be removed by lab postdoc after the monkeys are euthanized during scheduled surgeries in the Rosene lab. The eyes will be placed in a sealed tube, which will then be placed in a light-tight box and transported to the Cornwall lab. No one in the lab will come into contact with live monkeys. After receipt of both tissue types in the lab dissecting room, the eyes will be hemisected, the retinas will be removed, and placed in salt solution, then dissected, and transported to an adjacent room for electrical and microspectrophotometric measurements. Lab members have received BioRAFT training on working with NHP. Full PPE (lab coat, disposable gloves, goggles/safety glasses, surgical mask) will be worn in all rooms during dissection and experiments. Prep lab and experimental labs will have chemical spill kits. Sharps are also used in the protocol. All lab spaces will be decontaminated following their use for experiments: a) Benchtops will be sprayed with 10% bleach, b) Dissecting instruments will be washed with 70% isopropyl alcohol, c) Waste will be placed in biohazard boxes double lined with biohazard bags, d) Sharps will be placed in a biohazard sharps disposal container and sprayed with bleach and e) Bleach at >10% will be added to liquid waste and allowed to stand for 30 minutes prior to pouring down drain. Committee discussed the possible Herpes B virus contamination in the NHP samples and how those issues are dealt with. The ASC director clarified that the ASC has annual Herpes B virus screening program for all NHPs and also during any NHP-bite or scratch incidents. Because a NHP identified as negative for the virus may shed the virus at a different time, it is suggested that always treat them as if they are infected. Committee suggested that protocol should have clearer description of Herpes B virus risk mitigation procedures.

- Because a NHP identified as negative for the herpes B virus at a given time may shed the virus at a different time, please provide a clear statement in the laboratory procedure section that members of the protocol acknowledge that NHP samples should always be handled as if they are infected with herpes B virus, irrespective of the last screening result.
- Please provide description of who will transport the eyeballs from Dr. lab and how exactly they will be brought to your lab including PPE to be used.
- Describe how and where retina tissue dissection will take place. State whether biosafety cabinet will be used and if not, describe how the safeguard will be maintained in the dark room and what PPE will be worn during the work.
- Please make sure that the instruments are disinfected with hydrogen peroxide-based disinfectants instead of 70% ethanol.

BUA Site Assessment: There was no finding to report to IBC. EHS reviewed different disposal methods for solid, liquid biohazardous waste stream and sharp waste stream and no concerns were noted. EHS recommended use of 0.5% hydrogen peroxide-based disinfectants to use on any reusable tools and they have stock of such disinfectant.

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

7. rDNA/Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2505		Rod outer segment structure: determinants and its effect on the photon response	2	N/A	BUMC

Primary Reviewer: Elke Muhlberger	Secondary Reviewer: Bob Timmerman

Additional Reviewer: Ron Morales					
Applicable NIH Guidelines: N/A					
Meeting Comments: This protocol investigates the mechanism of stimulation of photoreceptors in the eye following exposure to light and especially the role of bicarbonate in the process. They use eye cups from rhesus monkeys and isolate retinas where the rod-cells are present and expose them to light in presence or absence of bicarbonate and measure their effect on transduction of message. They have described nicely all the biosafety concerns in their work. In response to several risk assessment questions, EHS clarified that members of this protocol and that of the previous protocol use one gloved hand to hold the NHP eyeball-transport container through freight elevator while using the other hand to operate elevator or open doors. It was discussed that Peroxyguard is the hydrogen peroxide-based EPA-approved disinfectant suitable for this protocol. They do not work with any cell line, but rather with the NHP tissues. In response to committee's concern on whether the slicing of tissues are being done in the biosafety cabinet, EHS clarified that it is difficult to perform those processes as they are done in a dark room under a microscope with the user wearing a headband with an infrared light source and cutting only about 5 mm long slices. • W4 rooms have been marked as ABSL2 and shared with only Dr. But no animal work is being done in those rooms. Please clarify or correct the statement. • Because a NHP identified as negative for the herpes B virus at a given time may shed the virus at a different time, please provide a clear statement in the laboratory procedure that members of the protocol acknowledge that NHP samples should always be handled as if they are infected with herpes B virus, irrespective of the last screening result. • Please provide description of how and where retina tissue dissection will take place. State whether the biosafety cabinet will be used and if not, describe how safeguards will be maintained in the dark room and what PPE will be worn during the work. • Please elaborate if instruments used to slice tissues are disposable or reusable. If reusable, please explain what precautions are taken when cleaning. • State how unwanted tissue samples are discarded. BUA Site Assessment: There was no finding to report to IBC. EHS reviewed different disposal methods for solid, liquid biohazardous waste stream and sharp waste stream and no concerns were noted.					
Motion: Conditional Approval (Administrative Review)	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

8. 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: Carmela Abraham			Secondary Reviewers: Ron Morales		
Applicable NIH Guidelines: Sections III-D-1-a; Appendix-B-II-D, Appendix G-II-B					
Meeting Comments: This protocol investigates what role sexually transmitted diseases play in HIV-1 transmission and in the development of drug resistant HIV-1. This line of studies have been carried out in the PI's lab for over a decade and members are all highly experienced in handling HIV-1 . In this amendment they are now adding cervicovaginal lavages from Rhesus monkeys to this protocol as part of their immunocontraception grant project work. This amendment was originally reviewed by the DMR process but one reviewer wanted it to be discussed in the full committee IBC meeting because of the Herpes B virus concerns in the rhesus monkey body fluid. It was noted that the PI provided detailed safety measures on handling those rhesus monkey samples. It was also discussed that the D-125 is in fact an approved disinfectant for HIV. No other concerns were noted.					
Motion: Approval	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 1