Boston University
Institutional Biosafety Committee (IBC)
March 21, 2023 Meeting Agenda
Location: Zoom and/or by phone
Start time: 12:03 PM End time: 1:24 PM

Members Present:	R. Ingalls, B. Slack, V. Gouon-Evans, W. Lu, P. Liu (joined 12:05 PM), R. Morales, T. Winters, S. Niemi, J. Keeney, V. Britton (joined 12:07 PM), N. Dey, S. Ghosh
Guests Present:	A. Ahmad, G. Madico, J. Wood, T. Killeen, M. Fitzgerald, P. Richmond
Staff Present:	C. McGoff, L. Campbell

I. Review of February 14, 2023 IBC Meeting Minutes

No concerns were voiced.
Motion: Approve
For: 12; Against: 0; Abstain: 0; Absent: 0

II. Chair's Report:

Members were provided with an update on a protocol previously discussed the February 2023 meeting. Members were reminded to propose or volunteer to present topics for the quarterly didactic lectures.

III. New Business:

A. Review of Research Occupational Health Program (ROHP) Report: There were no incidents to report; no updates from ROHP provided.

B. Environmental Health and Safety (EHS) Report:
R. Morales informed the committee that the annual rDNA permit for Boston University, the NEIDL, Boston Medical Center and the Arietis tenant laboratory has been approved by BPHC. Members were also informed that EHS began management of the Biosafety Cabinet (BSC)

IV. Protocol Review

1. Bhz – Three-Year Renewal

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

Primary Reviewer: Robin Ingalls	Secondary Reviewer: Tom Winters Additional Reviewer: Guillermo Madico
Applicable NIH Guidelines: N/A	
Meeting Comments: This is a protocol for storage, propagation, and distribution of BSL3 pathogens at the NEIDL. They are obtained from BEI, WRCEVA (World Reference Center for Emerging Viruses and Arboviruses) and investigators including BMC clinicians. Compared to the previous iteration of this protocol, personnel have been updated, the repository has been simplified, and the insectary has been removed. Training is up to date. Procedures include storage of BSL3 pathogens listed (18 currently listed in biohazard table but only 4 RG3 viruses are in storage currently); cell culture and viral propagation, including viral quantitation; PCR and sequencing of inactivated samples; handling of pathogens received by NEIDL; inventory management including BSL3 agent inventory, spreadsheet with virus characteristics, and distribution to qualified investigators. Cell culture and viral propagation are performed under BSL-3 conditions and the description of methodology is provided. Shipping, transport, handling, and storage has been in place among security, EH&S and researchers since 2020. Viral quantification is done using several methodologies. A method to validate identity of viral studies is in place. Select agent and non-select agent work is separated by rooms and equipment used. PPE is appropriate including BSL 3 conditions with PAPR's. Liquid and solid waste are handled properly. Disinfection is done with 5% Microchem Plus, then cleaning done with 70% ethanol or 10% fresh bleach. Transport to labs is carried out in leak proof / shatter proof containers after wiped down by 10%	

fresh bleach or 5% Microchem Plus with 10 minute contact time. No concerns with procedures described, inactivation or waste handling. IRB-approval is current. The following will be communicated to the PI:

- Please downgrade the BSL status of West Nile Virus and St. Louis Encephalitis Virus to BSL2 in the hazardous biological agent list.

BUA Site Assessment: Among the viruses listed, Eastern Equine Encephalitis virus and Venezuelan equine encephalitis virus are both Select agents see Select Agents and Toxins List | Federal Select Agent Program. These two pathogens will be added to NEIDL Select agent registration and be approved by the Federal Select agent Program before acquisition of these virus. New NEIDL Director is added to the protocol, who will be going through additional safety training in BioRAFT. Biosafety cabinets were certified last on April 2022 by EHS. BSL-3 labs were las inspected January 2023.

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

2. rDNA/Bhz – Annual Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2352	Anthony Griffiths	Propagation and Characterization of viruses Pathogens	4	N/A	BUMC

Primary Reviewer: Rob Davey	Secondary Reviewer: Elke Muhlberger

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

Meeting Comments: This protocol covers PI's research on several RG4 viruses and coronaviruses and countermeasures against them that has been reviewed several time and as recent as last month. The only difference in this annual renewal submission is that the personnel list has been updated and biosafety cabinet certification date has been updated. Training of the added personnel is current. EHS confirmed that the lab was inspected just last month and there is no concern.

It was proposed that a regular annual renewal is no longer needed for this protocol. All members agreed to this proposal (For: 12; Recuse: 0; Against: 0, Abstain: 0; Absent: 0).

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

3. rDNA/Bhz – Annual Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2286	Elke Muhlberger	Biomolecule Production Core – Propagating BSL4 pathogen	4	N/A	BUMC

Primary Reviewer: Robin Ingalls	Secondary Reviewer: Sajal Ghosh

Applicable NIH Guidelines: Section III-D-1-a, III-D-1-b, III-D-1-c

Meeting Comments: This NEIDL Biomolecule Production core protocol is responsible for storage and handling of BSL-4 viruses. The service of the core is to provide viruses to NEIDL BSL-4 researchers for their experiments and to perform BSL-4 infection studies for the research community. The only difference in this annual renewal submission is that the personnel list has been updated and training of the added personnel is current. EHS confirmed that the lab was inspected just last month and there is no concern.

It was proposed that a regular annual renewal is no longer needed for this protocol. All members agreed to this proposal (For: 12; Recuse: 0; Against: 0, Abstain: 0; Absent: 0).

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

4. rDNA/Bhz – Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus

785	Benjamin Wolozin	Molecular and Pharmacological studies of neurodegenerative diseases	2	1+	BUMC
Primary Reviewer: Barbara Slack			Secondary Reviewer: Steve Niemi Additional Reviewer: Bob Timmerman		
Applicable NIH Guidelines: Section III-D1, III-D4, Appendix B-II, B-III					

Meeting Comments: The goal of this protocol is to study the mechanism and pathophysiology of neurodegenerative diseases such as Amyotrophic Lateral Sclerosis (ALS), Parkinson's disease (PD), and Alzheimer's disease (AD), with particular attention to aggregation of specific proteins in tissues. Genes linked to AD, PD, ALS, or related pathways will be manipulated in primary neurons (from rats and mice) and cultured human cell lines by lentiviral vectors or by the use lenti-CRISPR vectors. Appropriate precautions are well described. Their in vivo experiments include use of transgenic or knockout mice lacking neurological disease related genes where animals will receive AAV or lentiviral vectors expressing light-responsive chimeric proteins. Induced pluripotent stem cells (iPSCs) from controls and AD patients will also be cultured in lab, analyzed by RNAseq, biochemical, and immunocytochemical methods. Further, human brain tissues obtained from different brain banks will also be used in the study and will be handled inside biosafety cabinet considering them as infectious. Sonication, slicing or lysing of brain tissues will be done in chemical fume hood. A 40% bleach will be used for decontamination. Re-usable instruments will be autoclaved. The following will be communicated to the PI:

- Section I.2- Please remove all comments from the “summary changes” box. This box is only for amendments and 3-yr renewals are reviewed de novo.
- Section III.2-Please update the personnel list to reflect those who are currently working in the protocol. [redacted], [redacted], [redacted], [redacted], [redacted] and [redacted] need update each of LST, BSL1/2, BBP and Chem Safety training. [redacted] and [redacted] need to update BBP training. [redacted] and [redacted] need to update rDNA/IBC policy training.
- Except for the PI, ROHP clearance is inactive for all personnel and must be updated.
- Section IV – Add rooms [redacted] and [redacted] to the list.
- Section VI. DURC- The response to the question #1 in the bottom of DURC section should be “Yes”. Please change the response.
- Section VII.3 – Please also include brief description of lentivirus injections in Rat or Mouse brain in the lab procedure section. The text currently mentions only AAV vector injections into animals.
- -Please indicate whether or not the brain banks supplying the tissue test for infectious diseases (for ROHP records- useful in the event of an exposure).
- Section VIII.I. – Please check ‘Animal handling, cage changing’.
- Section VIII.5. - Update BSC certification date (it shows an old 2019 date).
- Section VIII.6. -If a microtome will be used, please confirm that cut-resistant gloves will be worn.
- Section VIII.7B. - Please confirm that human brain tissue and tools that will be discarded as waste will be marked for incineration.
- Section IX. The rDNA table indicates that lentiviral vectors will be injected into rat or mouse brain, so the study should be conducted at ABSL2 level, and therefore the highest animal biosafety level should be ABSL2 not ABSL1+.
- Section A. Lentiviral and AAV vectors should be listed separately. Lentiviral vectors are handled at BSL2, not BSL1. Please amend the table in section A to indicate that lentiviral vectors will also be injected into animals (as stated in the rDNA table in section H).
- Section B- The risk of prion contamination associated with this protocol should be low, because neuropathologically characterized brain tissue from patients with ALS, PD, FTD, and controls will be used. The protocol describes appropriate precautions that will be taken when handling this material, but a few points need clarification:
- -Please confirm that instruments that will be re-used after contacting human brain material will be treated with 40% bleach, rinsed with water, and then autoclaved. (The text provided is a bit ambiguous).
- Section H. Animal Experiments – update IACUC approval date.

BUA Site Assessment: Biosafety cabinet is duly certified. Add room [redacted] and [redacted]. Lab does not use 40% bleach for their work, rather they use universal precautions. Brain banks don't specifically check for prion but they did check for contamination with blood borne pathogens.					
Motion: Conditional Approval (Administrative Review)	For: 12	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

5. rDNA/Bhz – Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
2524	Michael Lafleur	Testing and target validation of novel antimicrobials	2	2	BUMC
Primary Reviewer: Weining Lu		Secondary Reviewers: Tom Winters Additional Reviewer: Steve Niemi			
Applicable NIH Guidelines: April 2019 NIH guidelines; Section III-D-1-a, III-D-2-a, III-F-8, Appendix B-I, BII-A, C-II					
Meeting Comments: The goal of this protocol is to discover and develop novel antimicrobial agents using cell culture and mouse models, especially for *S. aureus* and *H. pylori*. The Amendment asks to make three changes to the original IBC protocol: (1) add additional human cell lines for cytotoxicity testing. (2) add additional host strains and vectors for rDNA work. (3) to test a genetically engineered clpP deletion strain of S. aureus for virulence in mouse models of infection. They work with many bacteria, fungi, and human cell lines. They also work with MRSA and erythromycin-resistant S. aureus. BSL-2 work, and ABSL-2 work is done as described. PPE appears appropriate. Liquid and solid waste are disposed of properly. Disinfection appears appropriate. Transportation is done in double shatterproof containers. ASC director clarified that ABSL2 practices used in the protocol are appropriate for the work described. The following will be communicated to the PI: • Please update the personnel list if Royce Conlin is no longer working in the lab, otherwise update his ROHP clearance. • Please provide a brief description of how the use of clpP mutant but erythromycin and methicillin resistant *S. aureus* would help achieve the goal of this protocol. • It is stated that request is being made to add additional human cell lines. However, no new human cell lines have been added. • State if the use of this clpP mutant *S. aureus* strain require additional safe handling protocols. • Clarify who is the "other researcher" from whom the clpP mutant strain will be received. • Update biosafety cabinet certification date. • Note that IRB approval is not required for the use of Erythromycin and Methicillin resistant *S. aureus* strain. Please modify your response in hazardous agent list. • Note that ROHP provides vaccine for *S. pneumoniae* when requested. • Remove the reference of Appendix M from the applicable NIH guidelines.					
Motion: Conditional Approval (Re-review by R. Ingalls and T. Winters	For: 12	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

6. rDNA/Bhz – Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
662	Maria Kukuruzinska	The Role of E-cadherin N-glycans in Oral Cancer	2	2	BUMC
Primary Reviewer: Valerie Gouon-Evans		Secondary Reviewer: Jim Keeney Additional Reviewer: Steve Niemi			
Applicable NIH Guidelines: Section III-D-4-a					
Meeting Comments: This lab investigates the role of the cross talk between E-cadherin N-glycosylation status and Wnt/beta-catenin signaling in oral cancer development and progression to metastasis. They propose to integrate genomic, epigenetic, molecular and structural approaches to characterize the mechanisms responsible for the					

generation of aggressive oral cancer cells and to identify new strategies for improving treatments for oral cancer patients. The biohazards in the protocol includes Human OSCC (oral squamous cell carcinoma) cell lines from ATCC and patient-derived tumor cells and fixed human tissues from the BARC repository. An IACUC approved mouse model of OSCC will also be utilized where a chemical carcinogen fed through drinking water, will be used to create the tumor. The amendment is to use an inducible gene silencing lentivirus system to express shRNA in order to perform loss-of-function studies of the Wnt/beta catenin pathway. The following will be communicated to the PI:

- Animal Work PPE with mice: Please include surgical mask
- Biological safety cabinet needs to be certified. Last certification was 03/19/2022.
- Please specify how you transport from the lab to the mouse facility the following: cells to be transplanted into mice, lentiviruses to be injected into mice, carcinogen to be included in the drinking water.
- IRB approval is not required for Cancer cell lines and Retroviral vector. Please update these boxes.
- Update IACUC approval numbers with current numbers associated with each hazardous agents listed.
- Complete the description of the host-vector-donor system in prokaryotic system as the protocol involves plasmid transformation in competent cells, plasmid purification etc.
- Update current new format IACUC approval and provide current approval date.
- Are the lentiviruses used in this study defective? Correct your response.
- Are the lentiviruses used in this study replication competent? Correct your response.
- Applicable NIH Guidelines sections should be: Sections III-D-1-a, III-D-2-a; III-D-4-a; III-E-1.

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

7. rDNA/Bhz – Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
2522	Zeba Wunderlich	Uncovering mechanisms of gene expression control	2	N/A	CRC

Primary Reviewer: Sajal Ghosh	Secondary Reviewer: Robin Ingalls

Applicable NIH Guidelines: Sections III-D-1-a, III-D-4-a, III-F-1 and III-F-2

Meeting Comments: The original goal of this protocol is to understand how cellular gene expression are regulated during different physiological need such as during development or during infection by a pathogen when innate immune response needs to be kicked in. To study the role of various non-coding DNA segments on the chromosome, such as promoters, enhancers, they use either transgenic fruit fly cell lines or the flies directly as a model for infection studies. In this amendment they are adding new drosophila cell lines where they plan to introduce an easily exchangeable gene cassette for their different experimental goals. This they plan to do by CRISPR/Cas9 technology. The guide RNA and Cas9 for these edits are expressed from separate plasmids and introduced into cells using electroporation. There will be no gene-drive effect. They expect only few off target effects as the targets are non-coding sites in the genome that have been previously validated as inert. There will be no gene drive situation. Five new personnel have been added and all member are aware of the safety issues on the use of CRISPR/Cas9 reagents. The following will be communicated to the PI:

- Please change the submission type as “amendment” and add a line or two in the Summary Change box briefly stating the purpose of this particular amendment.
- Make sure that all members of this protocol update their ROHP clearances.
- Please add the vector and donor information for the CRISPR /Cas9 work in the Host-Vector-Donor information section of both the prokaryotic and eukaryotic experiments section.

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

V. List of Protocols reviewed by DMR (not discussed in the meeting)

List of protocols (below) that are currently being reviewed by DMR was displayed in the meeting.

Three-Year Renewals to be review by DMR:

8. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1729	Nader Rahimi	Role of protein ubiquitination in angiogenesis	2	2	BUMC
Primary Reviewer: Sajal Ghosh		Secondary Reviewer: Steve Niemi			
Applicable NIH Guidelines: Sections III-D-1-a, III-D-2-a; III-E-1; Appendix B-II					

9. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
796	John Celenza	Genetic and biochemical analysis of genes from Arabidopsis thaliana involved in root development and indole-3-acetic acid biosynthesis	1-P	N/A	CRC
Primary Reviewer: Ed Loechler External Plant rDNA research expert: Elena Kramer (Harvard)		Secondary Reviewer: Jim Keeney			
Applicable NIH Guidelines: 2019 NIH Guidelines Sections III-D-5 and III-E-2					

10. rDNA/Bhz – Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1013	Shelley Russek	GABA-A receptor subunit regulation and epileptogenesis; Mapping the Transcriptome of Age-Related Hippocampal Trisynaptic Circuit Dysfunction in a Rat Model for Alzheimer's Disease	2	2	BUMC
Primary Reviewer: Barbara Slack		Secondary Reviewer: Steve Niemi			
Applicable NIH Guidelines: Sections III-D-1-a, III-D-2-a, III-D-4-a, III-E-1 and Appendix G-II-B, Appendix M.					

rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
793	Catherine Klapperich	Bacterial lysis on a microfluidic device Protozoa lysis on a microfluidic device	2	N/A	CRC
Primary Reviewer: Pinghua Liu		Secondary Reviewer: Weining Lu			
Applicable NIH Guidelines: III-D-2-a, Appendix C-II, Appendix B-II-A					

VI. List of approved Protocols since last IBC meeting (since the 2/14/23 Meeting)

A complete list of protocols approved by the IBC since the last IBC meeting on 2/14/23 was provided to the members before the meeting and also was displayed in the meeting.