

Boston University Institutional Biosafety Committee (IBC) March 19, 2024 Meeting Minutes

Members Present: R. Ingalls, B. Slack, E. Muhlberger, R. Davey, I. Afasizheva, V. Gouon-Evans, P. Liu (joined

12:08 PM), T. Winters, R. Morales, N. Dey, S. Niemi, J. Keeney, V. Britton (joined 12:07

PM), S. Ghosh

Guests Present: J. Connor, A. Ellis, A. Ahmad, A. Broos-Caldwell, P. Richmond, J. Wood, M. Fitzgerald, T.

Killeen

Staff Present C. McGoff, L. Campbell

I. Review of February 16, 2024 IBC Meeting Minutes (R. Ingalls)

No concerns were voiced.

Motion: Approved

For: 12; Against: 0; Abstain 0; Absent: 2

II. Chair's Report: Nothing to report

III. New Business:

- A. IBC Office Updates: Members were presented with an overview of the changes made to the RIMS online application form.
- B. Incident Report: Nothing to report.
- C. Review of Research Occupational Health Program (ROHP) Report: Nothing to report.
- D. Environmental Health and Safety (EHS) Report: Nothing to report.

IV. Protocol Review

1. rDNA/Bhz – Annual Renewal

2442 Investigating the role of viral proteins	in disease 3	N/A	BUMC
pathogenesis			

Primary Reviewer: John Connor Secondary Reviewer: Ron Morales

Applicable NIH Guidelines: See sections III-D-1-b, III-D-2-a, III-D-3-b; Appendix B-III-D and G-II-C for experiments described in this protocol.

Meeting Comments: The committee decided to defer the decision on the proposed move of poliovirus work to BSL3 containment without hearing clarification from the NEIDL EHS and NEIDL management about why this move is necessary and how this move is going to impact the work of other PIs who also work in the same BSL-3 labs. The committee recommended that all of the changes pertaining to moving poliovirus work to BSL3 lab be removed so that the regular annual renewal of the protocol can be approved without any concerns. The committee will inform the PI once the aforementioned clarification is available, at which time the PI will be asked to submit an IBC amendment which should include plan to move poliovirus work in BSL3 lab. In the meantime, the following will be communicated to the PI:

- In the context of inactivation procedure to be used, it is stated that "All of the procedures will be performed according to the following recently submitted SOPs.....". These SOPs are now approved. Please provide specific SOP numbers.
- Typo 'Fir' should be 'For'.

 It is stated that 'I am also encouraging my lab members to receive a bivalent SARS-CoV-2 vaccine.' Please update this to state whether there are new procedures or if the vaccination remains ongoing? Clarify if this is relevant to the current state of circulating virus and the strains used in the laboratory.
- Section VIII.6 Describe safety precautions to be practiced for using sharps.

 Please comment on the following concern: Mohoney polio strain listed in the Hazardous biological agent section is PV type 1, which has not been eradicated. Are labs allowed to use the eradicated strains anymore?

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

2. rDNA –New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2636		Project 1: Microbial devices for sensing and	1	N/A	CRC
		actuation			

Primary Reviewer: Rob Davey Secondary Reviewer: Jim Keeney

Applicable NIH Guidelines: Section III-F-8

Meeting Comments: The goal is to make sensors based on microorganism-electronic interfaces. Bacteria and yeast are modified to express sensor proteins as well as markers such as luciferase or fluorescent proteins and incorporated into electronic systems such that their reaction to environmental changes can be detected. The main risk components are recombinant DNA-based and production of recombinant organisms. The bacteria and yeast will be *E. coli* and *S. cerevisiae* respectively. To mitigate the risk they will decontaminate liquids with bleach (10% final) for at least 30 minutes, and will use biohazard boxes for solids. PPE used are lab coats, disposable gloves and safety glasses, which are appropriate for the work. Sharps are disposed on in sharps containers. Recombinant plasmids will be made for expression of fluorescent proteins (GFP) as well as transcription factors or signal transduction proteins using standard E. coli and yeast vectors. These include tetR – tetracycline resistance and estrogen receptor and GPCRs from humans. No mammalian cell culture or animal work was proposed. Personnel are trained by the PI, who has appropriate experience.

BUA Site Assessment: This is a new lab which is in the process of getting set up. No biosafety cabinet will be used in this protocol. The lab freezers are in which is contiguous to Sharps containers available.

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

3. rDNA/Bhz - Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1605		Cell Wall Integrity Signaling in Yeast	1	N/A	BUMC

Primary Reviewer: Valerie Gouon-Evans Secondary Reviewer: Bob Timmerman

Applicable NIH Guidelines: Section III-F-3, III-F-8, App E-II-A, E-III-A

Meeting Comments: The goal of the project is to understand how yeast cells maintain the structural integrity of their cell walls to identify molecular targets for the development of antifungal agents that display selective toxicity against fungal cells. Model genetic organisms, such as baker's yeast, *Saccharomyces cerevisiae*, will be used to study the molecular mechanisms of stress signaling, especially the mechanisms by which various stress signals are transmitted to Stress Activated Protein Kinases (SAPK) and downstream pathways. Some of the stressors used include arsenate, arsenite, acetic acid, genomic damage, and curcumin. Genetic modifications in yeast cells will be done by variety of methods including gene knock-outs, gene replacements, plasmid-based gene expression, plasmid library screens for complementation or suppression, mutant screens and selections, etc. They use nonpathogenic E. coli to clone and express recombinant proteins and to make variety of plasmids for introducing foreign genes into yeasts. The lab generates point mutants and deletion mutants of various genes using PCR-mediated random and directed mutagenesis. The list of genes mutated in the past are provided and indicate that other genes to be mutated will depend on the results of the screens. The following will be communicated to the PI:

- Check vigorous mixing, blending
- Check Laboratory Coats
- Remove N95. It is not required for the proposed procedures.
- Please add a sentence for the liquid biohazard disposal that all liquid wastes will be treated with bleach at a final concentration of 10% for a minimum of 30 minutes before disposal down the drain.

BUA Site Assessment: Add procedure: Vigorous mixing/blending Add PPE: Laboratory coats, Remove PPE: N-95							
respirator. BSC not needed for proposed work.	respirator. BSC not needed for proposed work. can be removed from the protocol as it is an autoclave and						
washing room. No biohazardous material transportation is anticipated in this protocol.							
Motion: Conditional Approval (Administrative Review)	For: 14	Recuse: 0	Against: 0	Abstain: 0	Absent: 0		

4. rDNA/Bhz – Amendment

BUA	(PI)	Title		BSL	ABSL	Campus
2566		Biorepository in systemic sclerosis		2	N/A	BUMC
		Systemic sclerosis research studies				
Primary Reviewer: Inna Afasizheva		Secondary Revie	ewers: Va	lerie Gouon	ı-Evans	

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

Meeting Comments: The goal of this study is to investigate how immune cells move through the skin layer in systemic sclerosis (Scleroderma) and to cellular signaling pathways that contribute to the abnormal immune cell function. Specifically they use biological samples from scleroderma patients including heart and lung tissues. This amendment to add new procedures by which the group will explore the role of specific transcription factor in Scleroderma. They will lentivirus vectors to manipulate expression of this transcription factor in human cancer cell lines and try to correlate their findings with what is observed in clinical samples. The following will be communicated to the PI:

- Since the protocol now involves rDNA work (lentivirus work), a "Not applicable to this project" response for rDNA training is not appropriate for any of the listed personnel (such as experienced" or "Will not handle or work on this part of the project" may be chosen instead.
- All listed members must complete the rDNA/IBC policy training in BioRAFT, even when someone will not be doing any rDNA work. This is mandatory.
- VIII. 1: add "pipetting infectious liquid
- VIII.5: Please provide a recent certification date of the biosafety cabinet.
- VIII.8: Please list the disinfectants to be used.
- VIII.10 and VIII.11: please answer (How and where are biohazardous materials stored and transported such as human cancer cell line, lentivirus stock)
- Please add lentivirus in the hazardous biological agent list
- Please update IRB approval dates: : 4/24/2025; : 3/14/2025.
- Replace the current statement in the Applicable NIH guidelines question with "Section III-D-1-a, and III-E-1."

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

5. rDNA/Bhz –Amendment

BUA	(PI)	Title		BSL	ABSL	Campus
2350		Viruses pseudotyped with hemorhagic fever virus		2	N/A	BUMC
		glycoproteins and virus-like particles				
		infection mechanism.				
Primary Reviewer: Elke Muhlherger Seconda		Secondary Revi	ewer: Saia	al Ghosh		

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Applicable NIH Guidelines: III-D-1-a, III-D-2-a, III-D-3-a, III-E-1

Meeting Comments: The original goal of this protocol is to make pseudotyped viruses or virus like particles for their use as reporter systems to detect inhibitors of virus entry. The viruses are made by expression of virus proteins in cells. Each virus generated is replication defective, only able to infect cells but unable to assemble new viruses. A marker of infection is encoded within the recombinant virus genome such as a fluorescent protein or luciferase enzyme. In this amendment they propose to work with plasmids containing segments of filovirus, arenavirus and bunyavirus genomes. The virus types will be limited to arenaviruses, which include New World (Junin and Machupo) and Old World (Lassa) viruses as well as Crimean Congo Hemorrhagic fever virus (CCHFV) that have multi-segmented genomes, as well as parts of Ebolaviruses where the genome is normally on one segment. In each case, plasmids containing each segment will be cultivated in *E. coli* as plasmids. They will then be mutated to place

in point mutations that are expected to cause reductions in virus replication fitness to understand replication mechanism. For this protocol, at all times, the genome plasmids are handled independently of each other, never in combination and support plasmids (those needed to make the virus RNA replication complex) are kept away from each genome fragment and away from mammalian tissue culture. NIH has approved PI's request to perform these additional arenavirus genome cloning work in BSL2 lab. The committee requested few minor clarification on the research plan. The following will communicated to the PI:

- This amendment covers plasmid preparations of viral genome fragments and introducing mutations in these
 plasmids. It is not clear why the PI added this sentence: Each change would not be expected to increase virus
 virulence and if such were identified, we would stop work and notify the IBC and EHS, as detailed in our BSL4
 protocols." This refers to viruses generated with these constructs, but these are not part of this protocol.
 Needs clarification.
- It is stated that "We propose to perform the work at BSL2 in a space that is distinct from our tissue culture room with a normally closed door and engineering controls separating the spaces." This room is different from the full-length clone room, correct? Please clarify.
- It might be helpful to remove the generation of full-length filovirus plasmids from this protocol and add that this work is covered by IBC protocol 2109 (PI), the reason being that there are NIH regulations in place for handling full-length filovirus and henipavirus clones. Members of the PI's lab are listed on protocol 2109.
- The PI may wish to add that *E. coli* K12 bacteria will be used.
- Section VIII, 1: Check "Culture stirrers, shakers" and "Plating, colony counting".
- Section VIII, 6: If sharps are used to cut out agarose gel fragments, this should be added to section.
- rDNA section The PI states that fragments from "other filoviruses" will be generated. IBC recommends naming the other filoviruses.
- rDNA section, eukaryotic host strains: It is stated that some cell lines will be used "as recipients of recombinant viruses". Since no recombinant full-length virus is being put in cell culture in this protocol, clarify what this sentence mean. This sentence should be removed if it relates to BSL4 work.
- rDNA section, 8 and 11: Please confirm that no DNA fragments >200 nts will be ordered to generate viral fragments.

PI recused himself from approval discussion and voting.

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

6. rDNA/Bhz -Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
2562		Discovery and development of therapies and consumer products derived from the human microbiome	2	N/A	BUMC

Primary Reviewer: Robin Ingalls Secondary Reviewer: Inna Afasizheva

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

Meeting Comments: The goal of this protocol is to identify as many as possible individual human gut bacterium species that are believed to contribute to good health. They will screen diverse panels of human gut bacteria for activity against major disease targets. Once they have an understanding of which bacteria influence a specific disease target, they plan to engineer that bacteria to be able to use it as probiotic and for commercial development. In this amendment they propose for the first time, to add a recombinant DNA procedure by which they will be able to delete specific unwanted gene from the bacteroides species. The process includes plasmid manipulation by recombinant DNA technology, introduction of the plasmid into *E. coli* and subsequent transfer of the plasmid to the bacteroides species by bacterial conjugation. Specific cloning technology to be used in the protocol, will allow the bacteroides to expel the desired gene from its genome. The experimental procedures are described in detail and they do not appear to involve risk of exposure to hazardous materials. The following will be communicated to the PI:

- PI must complete rDNA/IBC Policy training in BioRAFT. All members of a protocol involving rDNA work must also complete the rDNA/IBC policy training.
- Please correct the typo on the sentence in the laboratory procedure section "However, since pARC [luck] a Bacteroides origin of replication.." This should be 'lacks'.
- Provide recent Biosafety Cabinet certification date.

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

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

A list of protocols that were reviewed by DMR was displayed in the meeting.