INSTITUTIONAL BIOSAFETY COMMITTEE

UNIVERSITY of WASHINGTON

Meeting Minutes

Date: Wednesday, September 18, 2024
Time: 10:00 a.m. – 12:00 p.m.

Location: Zoom

Members Present:
1. Jim Boonyaratanakornkit, Allergy and Infectious Diseases
2. Jason Cantera *(Community Member)*
3. Lesley Colby, Comparative Medicine *(Animal Containment Expert)*
4. Lesley Decker, Environmental Health & Safety (*Biosafety Officer*)
5. Erin Heiniger, Department of Bioengineering *(Laboratory Specialist*)
6. Richard Grant, Washington National Primate Research Center
7. Scott Meschke, Environmental & Occupational Health Sciences
8. Susan Parazzoli *(Community Member)*
9. Jason Smith, Microbiology (*IBC Chair*)
10. Paul Swenson, Seattle-King Co. Dept. of Public Health (*Community Member*)

Commonly Used Abbreviations
AAV: adeno-associated viral vector
BSL: biosafety level
BSL-2w/3: BSL-2 with BSL-3 practices
BSO: biosafety officer
BUA: Biological Use Authorization
DURC: Dual Use Research of Concern
IACUC: Institutional Animal Care and Use Committee
IBC: Institutional Biosafety Committee
iPSCs: induced pluripotent stem cells
NHP: non-human primate
NIH: National Institutes of Health
PI: Principal Investigator
rDNA: recombinant or synthetic DNA/RNA
RG: Risk Group
SOP: standard operating procedure
Source material: blood, tissue, body fluids, and cell lines

1. **CALL TO ORDER:** The Institutional Biosafety Committee (IBC) Chair called the meeting to order at 10:03 a.m. A quorum was present.

2. **REMINDER:** The IBC Chair reminded attendees that any notes that they retain are subject to public disclosure. A statement was also made about conflict of interest and voting on research proposals as described in the IBC Charter. This includes sharing a grant or a familial relationship.

3. **FOR YOUR INFORMATION:**
   - A short presentation was given about updated federal regulatory oversight of Dual Use Research of Concern (DURC) and pathogens with enhanced pandemic potential (ePPP). The updated framework needs to be implemented by May 2025.
   - EH&S has submitted the following rDNA incident to the NIH for review:
     - There was a bite from a mouse that had been previously exposed to a recombinant, attenuated vaccine strain of *Salmonella enterica* Typhimurium at ABSL-2. The employee performed first aid and consulted with the Employee Health Center. The final report was sent to the NIH on September 16, 2024.

4. **APPROVAL OF MINUTES:**
   - The IBC Chair sought a motion to approve the minutes from the August 21, 2024, meeting.
   - A member made a motion to approve the August 21, 2024, meeting minutes. Another member seconded the motion.
   - The committee voted unanimously to approve the August 21, 2024, meeting minutes.

5. **OLD BUSINESS:**
   - At the August 21, 2024 meeting, Dr. Gale's BUA was approved pending the successful completion of the inspection. This BUA has been sent.
   - At the August 21, 2024 meeting, Dr. Paredez's BUA was approved pending response to the lab inspection. This BUA has been sent.
   - At the August 21, 2024 meeting, Dr. Greninger's BUA was approved pending the successful completion of the inspection. This BUA is still pending.

6. **BIOSAFETY OFFICER (BSO) REPORT***:* The Biosafety Officer Report includes projects involving: (1) recombinant or synthetic nucleic acids covered under Sections III-E and III-F of the *NIH Guidelines,* (2) non-recombinant biological agents requiring BSL-2 with BSL-3 practices containment or lower, and (3) administrative updates, such as room additions.
   a. Biosafety Officer Report
      - Dr. Maly added new rooms for in vitro work with previously approved agents on the BUA *Study of Intracellular Protein Kinases.*
      - Dr. Zhang started new in vitro work with adenovirus, human source material, influenza virus, NHP source material, and Sindbis virus at BSL-2 on the BUA *Development of peptoid-based nanomembranes as anti-virus medical countermeasures.*
      - Dr. Perkel renewed in vivo work with AAV and lentiviral vectors that was previously approved at an IBC meeting in July 2024 on the BUA *Comparative Studies of Vocal Control.* (III-D)
      - Dr. MacLellan transferred agents and rooms from Dr. Murry's BUA, including in vitro and in vivo work with human source material, transduced human cells in rats at ABSL-2, and in vitro work with E. coli on the BUA *Cardiac Development, Growth, and Regeneration.* (III-D, III-F)

- Dr. Kollman started new work with human source material at BSL-2, E. coli, and rDNA including enhanced gene delivery methods on the BUA *Allosteric Regulation of Metabolic Enzymes.* (III-E, III-F).
- Dr. Marchand added in vitro work with wildtype Risk Group 1 species of *Streptomyces* on the BUA *Development of synthetic biology tools for non-standard nucleic acids.*
- Dr. Nyangahu added in vivo work with Citrobacter rodentium in mice at ABSL-2 and moved all in vivo work to a previously approved room on the BUA *Gut Microbiota, Inflammation, and Enteric Pathogens.*
- Dr. Lingappa renewed work with human source material at BSL-2 on the BUA *International Clinical Research Lab and Repository.*
- Dr. Yager added work with wildtype E. coli K-12 derivative strain and bacteriophage in already approved rooms on the BUA *Point-of-Care Diagnostics.* (III-F)
- Dr. Stokes transferred agents and rooms from Dr. Gale's BUA, including in vivo work with several Risk Group 2 viruses and rDNA including enhanced gene delivery methods in mice at ABSL-2 on the BUA *Pathogenic mechanisms of flavivirus encephalitis.* (III-D)
- Dr. Doty renewed work with transgenic poplar plants on the BUA *Transgenic plants for remediation.* (III-E)
- Dr. Mustelin renewed in vitro work with human and NHP materials at BSL-2, lab strains of E. coli, and rDNA including enhanced gene delivery methods on the BUA *Molecular mechanism of Rheumatoid Arthritis and Lupus*. (III-E, III-F)
- Dr. Sparkman-Yager added in vitro work with human source material at BSL-2 in a new room and rDNA to a previously approved room on the BUA *High throughput screening to discover RNA-targeting small molecule therapeutics.* (III-F)
- Dr. Cao added work with wildtype Bacteroides fragilis at BSL-2 in new rooms on the BUA *Mucosal Immunoengineering and Microbiome Pharmaceutics*.
- Dr. An started a new project using human source material at BSL-2 and human cells in rats at ABSL-2 on the BUA *Aging Tooth Regeneration with hIPSCs in CA Scaffolds.*
- Dr. Paik transferred agents and rooms from Dr. Nyangahu's BUA, including in vivo work with Citrobacter rodentium, pathogenic E. coli, and human feces in mice at ABSL-2 on the BUA *Gut Microbiota, Inflammation and Enteric Pathogens.*
- The IBC Chair a motion to approve this month's Biosafety Officer Report.
- A member made a motion to approve this month's Biosafety Officer Report. Another member seconded the motion.
- The Committee unanimously voted to approve this month's Biosafety Officer Report with one abstaining.

7. INDIVIDUAL PROJECT REVIEWS

a. Bornfeldt, Karin, renewal, *CRISPR, Vector and Transgenic Mouse Core (CVTMC)*

- NIH Guidelines Sections III-D, III-E, and III-F
- The assigned IBC Primary Reviewer presented the Primary Review.
- The Bornfeldt lab engineers and produces plasmids and viral vectors for the University of Washington research community for use in in vivo and in vitro work.
- The lab works with third generation lentiviral vectors, AAV, and human source material at BSL-2. They also work with E. coli and rDNA including enhanced gene delivery methods.

- The lab inspection is scheduled for after the IBC meeting.
- All required trainings are complete.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Bornfeldt.
- The Committee voted unanimously to approve the draft BUA for Dr. Bornfeldt, pending successful completion of the lab inspection.

b. Deng, Xinxian, renewal, *Studies of dosage regulation of X-linked genes and their roles in health and disease*

- NIH Guidelines Sections III-D, III-E, and III-F
- The assigned IBC Primary Reviewer presented the Primary Review.
- The Deng lab studies how gene dosage regulation affects X-linked genetic diseases. They genetically modify human and animal cell lines using molecular methods.
- The lab uses third generation lentiviral vectors with oncogenic inserts, Sendai viral vectors with oncogenic inserts, and human source material at BSL-2. They also work with E. coli K-12 strains, rDNA including enhanced gene delivery methods, and animal cell lines.
- The lab was inspected, and all deficiencies have been corrected.
- All required trainings are complete.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Deng.
- The Committee voted unanimously to approve the draft BUA for Dr. Deng.

c. Giacani, Lorenzo, change, *Studies on the pathogenesis of syphilis and human treponematoses*

- NIH Guidelines Sections III-D
- The assigned IBC Primary Reviewer presented the Primary Review.
- The Giacani lab proposes to add an experiment to study naturally occurring mutations of the 16S rRNA gene of Treponema pallidum. These gene mutations are described in literature, but isolates are not available. The lab aims to generate these mutations using rDNA techniques to assess in vitro if they are associated with decreased susceptibility to tetracyclines. No in vivo work is proposed.
- There was a discussion regarding the potential for this work to fall under NIH Section III-A as this experiment involves potential conference of resistance to second line antibiotic treatments for syphilis. The NIH has been contacted for consultation. If the project requires Section III-A review by the NIH, it will be reviewed by an IBC subcommittee at a future IBC meeting.
- A lab inspection was not required as the lab was recently inspected.
- All required trainings are complete.
- A medical management plan is in place for T. pallidum, and a new medical management plan will be developed for potential tetracycline resistant strains.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Giacani.
- The Committee voted unanimously to approve the draft BUA for Dr. Giacani, pending determination by the NIH that Section III-A does not apply and development of the medical management plan for resistant strains.

d. Khaing, Zin, new, *A Noninvasive Neurotrophic Factor Treatment to Repair the Injured Spinal Cord*

- Section III-D
- The assigned IBC Primary Reviewer presented the Primary Review.
- The Khaing lab studies the mechanisms of the inhibition of axon regeneration following brain and spinal cord injury.
- The lab will administer AAV to rats.
- The lab was inspected, and all deficiencies have been corrected.
- All required trainings are complete.
- The IACUC protocol is still pending.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Khaing.
- The Committee voted unanimously to approve the draft BUA for Dr. Khaing.

e. Laursen, Willem, new, *Mosquito taste*

- Sections III-D and III-F
- The assigned IBC Primary Reviewer presented the Primary Review.
- The Laursen lab studies the cellular and molecular mechanisms underlying mosquito taste-driven behaviors. They also aim to identify and characterize target candidates for these mechanisms using genetic analysis, enabled by cell-specific mutagenesis and modified gene expression.
- The lab proposes to create and work with transgenic *Aedes aegypti* mosquitoes at arthropod containment level 2 (ACL-2). This species of mosquito cannot survive in the Seattle climate, and no pathogenic agents will be used with the mosquitoes. They also work with human source material at BSL-2 and transgenic Drosophila, E. coli K-12 strains, and rDNA at BSL-1.
- The lab inspection is scheduled for after the IBC meeting.
- All required trainings are complete.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Laursen.
- The Committee voted unanimously to approve the draft BUA for Dr. Laursen, pending successful completion of the lab inspection.

f. Mack, David, renewal, *Stem cell-derived Disease-in-a-Dish Models to Study Neuromuscular Conditions*

- Sections III-D and III-F
- The assigned IBC Primary Reviewer presented the Primary Review.
- The Mack lab studies Duchenne Muscular Dystrophy (DMD) patient heart cells generated from iPSCs in comparison to heart cells from healthy individuals to identify potential drugs to treat DMD patients using RT-PCR, immunocytochemistry, and flow cytometry.
- The lab works with human source material including iPSCs, third generation lentiviral vectors, and Sendai viral vectors at BSL-2. They also work with AAV, rDNA, and baculoviral vectors at BSL-1.
- A lab inspection has been performed and is still pending a response.
- All required trainings are complete.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Mack.

- The Committee voted unanimously to approve the draft BUA for Dr. Mack, pending responses to the lab inspection.

g. Oberst, Andrew, renewal, *Programmed Cell Death and Immunity*

- NIH Guidelines Sections III-D, III-E, and III-F
- The assigned IBC Primary Reviewer presented the Primary Review.
- The Oberst lab studies the mechanisms that control programmed cell death and the immunological effects of the different types of programmed cell death in vivo.
- The lab works with several Risk Group 2 pathogens in vitro and in vivo in mice including influenza A virus, murine cytomegalovirus, West Nile virus, and Zika virus at (A)BSL-2. In vitro work is performed with human and NHP source material, vaccinia virus, ecotropic gammaretroviral vectors with and without oncogenes, and amphotrophic gammaretroviral vectors at BSL-2. Other agents they work with include AAV, third generation lentiviral vectors, and Plasmodium species.
- The lab was inspected, and all deficiencies have been corrected.
- All required trainings are complete.
- There are occupational health requirements for work with Zika virus, influenza virus, diphtheria toxin, and vaccinia virus.
- The IACUC protocol is still pending.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Oberst.
- The Committee voted unanimously to approve the draft BUA for Dr. Oberst, pending BUA application edits.

h. Stuber, Garret, renewal, *Neural Circuits for Motivation and Reward*

- NIH Guidelines Sections III-D, III-E, and III-F
- The assigned IBC Primary Reviewer presented the Primary Review.
- The Stuber lab studies how neural structures contribute to maladaptive behaviors, such as substance abuse disorders and psychiatric diseases. Using various genetic tools, they identify and manipulate dysregulated neural circuits in vivo to assess which cell types, populations, and neural structures contribute to psychiatric illness.
- The lab works with rabies virus vectors in mice at ABSL-2. They also work with AAV and canine adenoviral vectors in mice at ABSL-1 and E. coli K-12 and rDNA including enhanced gene delivery methods at BSL-1.
- The lab was inspected, and all deficiencies have been corrected.
- All required trainings are complete.
- The IACUC protocol is still pending.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Stuber.
- The Committee voted unanimously to approve the draft BUA for Dr. Stuber.

8. SUBCOMMITTEE REPORTS:

i. Cowan, Andrew, new, *A Phase 3 Randomized Study Comparing Daratumumab, Bortezomib, Lenalidomide and Dexamethasone (DVRd) followed by Ciltacabtagene Autoleucel versus Daratumumab,Bortezomib, Lenalidomide and Dexamethasone (DVRd) followed by Autologous Stem Cell Transplant (ASCT) in Participants with Newly Diagnosed Multiple Myeloma who are Transplant Eligible*

- Section III-C
- Two members of the IBC served as the Subcommittee Reviewers. One of the Subcommittee Reviewers presented the Subcommittee Report.
- This is a new application for a multi-center, non-profit-sponsored, randomized, open-label, phase 3 trial of ciltacabtagene autoleucel (a BCMA CAR T-cell product) compared to autologous transplant for newly diagnosed multiple myeloma.
- Patient-derived CAR T-cells will be genetically modified ex-vivo with third generation lentiviral vectors and administered back to the human subjects.
- The draft BUA letter was shown.
- A member made a motion to approve the draft BUA letter for Dr. Cowen. Another member seconded the motion.
- The Committee voted unanimously to approve the draft BUA for Dr. Cowen.

j. Goss, Chris, new, *A Phase 1/2, Multicenter Study Evaluating the Safety, Tolerability, and Biodistribution of RCT2100 with Single-Ascending Doses in Healthy Participants and Multiple-Ascending Doses and Proof-of-Concept in Participants with Cystic Fibrosis*

- Section III-C
- Two members of the IBC served as the Subcommittee Reviewers. One of the Subcommittee Reviewers presented the Subcommittee Report.
- This is a multi-site, industry-sponsored, external IRB-approved, non-first-in-humans study of nebulized respiratory tract delivery of a mRNA in lipid nanoparticle (LNP) product that encodes CFTR protein and is designed to replete normal CFTR levels in relevant respiratory cells in patients with cystic fibrosis and a mutated CFTR gene.
- mRNA in an LNP will be administered to human subjects using a handheld nebulizer.
- There was a discussion regarding the model of nebulizer used to administer the mRNA, potential occupational health exposure, and a simulation study that had been performed to measure potential exposure. Overall, the committee agreed that the potential for exposure and health risk posed by the agent is minimal.
- A member made a motion to approve the draft BUA letter for Dr. Goss. Another member seconded the motion.
- The Committee voted unanimously to approve the draft BUA for Dr. Goss.

k. Lynch, Ryan, new, *A randomized, open-label study evaluating the efficacy and safety of cemacabtagene ansegedleucel in participants with minimal residual disease after response to first line therapy for large B-cell lymphoma (ALPHA3)*

- Section III-C
- Two members of the IBC served as the Subcommittee Reviewers. One of the Subcommittee Reviewers presented the Subcommittee Report.
- This is a new application for an industry-sponsored, multi-center, randomized, open-label phase 2 clinical trial to assess the efficacy and safety of cema-cel and ALLO-647 vs. observation in participants with large B cell lymphoma (LBCL) and minimal residual disease (MRD) after first-line therapy.
- Allogeneic CAR T-cells from healthy donors will be genetically modified ex-vivo with third generation lentiviral vectors and transcription activator-like effector nucleases (TALEN) and administered to human subjects.
- The draft BUA letter was shown.

- A member made a motion to approve the draft BUA letter for Dr. Lynch. Another member seconded the motion.
- The Committee voted unanimously to approve the draft BUA for Dr. Lynch.

9. **ISSUES FROM THE FLOOR & PUBLIC COMMENTS:** There were no issues from the floor, and no public comments.

10. **MEETING ADJOURNED AT APPROXIMATELY 11:40 a.m.**