INSTITUTIONAL BIOSAFETY COMMITTEE

UNIVERSITY of WASHINGTON

Meeting Minutes

Date: Wednesday, July 17, 2019
Time: 10:00 AM – 12:00 PM

Location: Foege N130A

Members Present:
1. Thea Brabb, Comparative Medicine *(Animal Containment Expert)*
2. Lesley Colby, Comparative Medicine *(Animal Containment Expert)*
3. Richard Grant, Washington National Primate Research Center
4. Garry Hamilton (*Community Member*)
5. Stephen Libby, Laboratory Medicine (*IBC Chair*)
6. Scott Meschke, Environmental & Occupational Health Sciences
7. Susan Parazzoli (Community Member)
8. Jason Smith, Microbiology (*IBC Vice Chair*)
9. Eric Stefansson, Environmental Health & Safety (*Biosafety Officer, Animal Containment Expert*)
10. Paul Swenson, Seattle-King Co. Dept. of Public Health (*Community Member*)

Commonly Used Abbreviations
IBC: Institutional Biosafety Committee
BSO: Biological Safety Officer
BUA: Biological Use Authorization
BSL: biosafety level
PI: Principal Investigator
IACUC: Institutional Animal Care and Use Committee
NIH: National Institutes of Health
DURC: Dual Use Research of Concern
SOP: standard operating procedure

1. **CALL TO ORDER:** The Institutional Biosafety Committee (IBC) Chair called the meeting to order at 10:01 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. **APPROVAL OF MINUTES:**
   - The IBC Chair sought a motion to approve the minutes from the June 19, 2019 meeting.
   - A member made a motion to approve the June 19, 2019 minutes. Another member seconded the motion.
   - The committee voted unanimously to approve the June 19, 2019 meeting minutes. There was one abstention.

4. **OLD BUSINESS:**
   - At the July 2018 meeting, Dr. Patel's BUA was approved pending a lab inspection. This is still pending.
   - At the October 2018 meeting, Dr. Stuber's BUA was approved pending a lab inspection and room changes to the BUA letter. This is still pending.
   - At the November 2018 meeting, Dr. Bornfeldt's BUA was approved pending additions to the BUA letter. This is still pending.
   - At the February 2019 meeting, Dr. Nahmani's BUA was approved pending a lab inspection and verification of third generation lentiviral vectors. This is still pending.
   - At the March 2019 meeting, Dr. Bajjalieh's BUA was approved pending additional information to the BUA. This is still pending.
   - At the March 2019 meeting, Dr. Moreno's BUA was approved pending a successful lab inspection and training completion. These items have been completed, and the BUA letter has been sent out.
   - At the June 2019 meeting, Dr. Buckner's BUA was approved pending a change to the BUA application. This change was made, and the BUA letter was sent out.
   - At the June 2019 meeting, Dr. Darvas's BUA was approved pending changes to the BUA letter. These changes were made, and the BUA letter was sent out.
   - At the June 2019 meeting, Dr. Moritz 's BUA was approved pending a change to the BUA letter. This change was made, and the BUA letter was sent out.
   - At the June 2019 meeting, Dr. Plymate's BUA was approved pending IACUC submission. IACUC review was completed, and the BUA letter was sent out.

5. **BIOSAFETY OFFICER (BSO) REPORT***:* The Biosafety Officer Report includes (1) projects involving recombinant or synthetic nucleic acids covered under section III-E and III-F of the *NIH Guidelines,* (2) proposals involving non-recombinant biohazardous agents requiring BSL-1 and BSL-2 containment, and (3) administrative updates, such as room additions.

   a. Biosafety Officer Report
      - Dr. Trikudanathan added an administrative site for the BUA *Diabetes AutoimmunitY withdrawn in established patients (DAY).*
      - Dr. Trikudanathan added an administrative site for the BUA *DiabeteS AUtoimmunNity WithdRawn In New OnSEt and In Established Patients (SUNRISE).*
      - Dr. Adams Waldorf added a new BSL2 lab space to the BUA *Experimental Model for Chorioamnionitis and Preterm Labor.*

- Dr. Adams Waldorf added HIV, SIV, West Nile Virus, and Japanese encephalitis virus (Nakayama strain) using BSL2 with 3 practices containment to the BUA *Experimental Model of Viral-Induced Brain Injury.*
- Dr. Unadkat renewed the BUA *Mechanisms of drug disposition* using human blood, tissue, body fluids, and cell lines in vitro.
- Dr. Wang renewed the BUA *Organic Cation Transporter PMAT: Physiological Function and Role in Drug Disposition* using human blood, tissue, body fluids, and cell lines in vitro and in mice and recombinant or synthetic DNA/RNA (non-viral) enhanced gene delivery methods in vitro.
- Dr. Zagotta renewed the BUA *Gating Mechanisms of Ion Channels* working with Baculovirus, Pichia pastoris, human blood, tissue, body fluids, and cell lines, and recombinant or synthetic DNA/RNA (non-viral) enhanced gene delivery methods in vitro.
- Dr. Oberst is adding the use of Chromobacterium violaceaum in mice and in vitro. The biosafety officer will verify that the strain being used is appropriate at BSL1. This approval is pending.
- Dr. Kawasumi added rooms for in vitro work with previously approved BSL2 agents to the BUA *Skin Cancer Research.*
- Dr. Bakker's BUA has not yet been approved, and is to be removed from this report.
- Dr. Heath was approved for a new BUA *Identifying effective combination therapy for metastic cancers* using human blood, tissue, body fluids, and cell lines in mice.
- The IBC Chair sought a motion to approve this month's Biosafety Officer Report pending the removal of Dr. Bakker's BUA and the verification of Chromobacterium violaceaum strains being used in Dr. Oberst's BUA.
- A member made a motion to approve this month's Biosafety Officer Report pending the changes above. Another member seconded the motion.
- <u>The Committee unanimously voted to approve this month's Biosafety Officer Report pending the changes above.</u>

6. DURC REPORT:

- Dr. Hofstetter's project *Spinal Cord Injury and Bladder Malfunction* received approval for use of Botulinum neurotoxin. The lab is injecting Botulinum Standard neurotoxin into the detrusor muscle of the rat bladder after spinal cord injury. This is an FDA approved usage of Botox in human patients after SCI, allowing for relaxation of the overactive detrusor muscle. The toxin will be used as prescribed for patients.
- The DURC Institutional Review Entity (IRE) voted to approve this work.
- The Committee unanimously voted to approve the DURC application for Dr. Hofstetter.

7. ADMINISTRATIVE POLICY STATEMENT 12.3 REVISION:

- The director of EH&S presented revisions to the Administrative Policy Statement (APS) 12.3. The APS is a University policy regarding review of research projects involving biohazards and recombinant DNA.
- The Committee unanimously voted to approve the July 2019 revisions made to the APS 12.3.

8. SECTION III-D AMENDMENTS

a. Subramanian, Naeha, new, *A systems approach to understanding NLR function*

- The assigned IBC Primary Reviewer presented the Primary Review.

- The Institute for Systems Biology (ISB) is closing its vivarium, so the PI is requesting to move their mice to other UW vivariums.
- This project uses wildtype Salmonella Typhimurium and Sendai virus in mice.
- The vivariums are part of a core facility, so a lab inspection is not required.
- All of the required trainings have been completed.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Subramanian.
- The Committee voted unanimously to approve the draft BUA for Dr. Subramanian.

9. INDIVIDUAL PROJECT REVIEWS

b. Bornfeldt, Karin, renewal, *Cardiovascular Disease and Diabetes*

- The assigned IBC Primary Reviewer presented the Primary Review.
- This lab studies the mechanisms of diabetes-accelerated atherosclerosis. They work with Lymphocytic choriomeningitis virus (LCMV), adeno-associated viral vectors, and gammaretroviral vectors in mice and in vitro.
- The greatest identified hazard is work with LCMV.
- Lab policies cannot prevent pregnant women to work with LCMV.
- The lab was inspected and no deficiencies were identified.
- All of the required trainings have been completed.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Bornfeldt pending removal of a lab policy from BUA application.
- The Committee voted unanimously to approve the draft BUA for Dr. Bornfeldt pending the above BUA application change.

c. Darvas, Martin, renewal, *Genetic analysis of mouse behavior*

- The assigned IBC Primary Reviewer presented the Primary Review.
- This lab works to understand the influence of genes on neural activity and connectivity in order to gain insight into how the brain processes information related to attention, learning, memory, social cognition, motor coordination and motivation as well as how disruption of specific neural circuits can lead to developmental and neurodegenerative disease, cognitive impairment, addiction, social impairment and psychoses.
- The greatest hazards involve work with HSV1 and human cells, lentivirus, and recombinant E. coli.
- The lab was inspected and no deficiencies were identified.
- All of the required trainings have been completed.
- The IACUC protocol has not yet been submitted.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Darvas pending IACUC protocol.
- The Committee voted unanimously to approve the draft BUA for Dr. Darvas pending the IACUC protocol.

d. Dhaka, Ajay, renewal, *Dhaka Zebrafish*

- The assigned IBC Primary Reviewer presented the Primary Review.

- Strains of E. coli are used to engineer plasmids with various fluorescent reporter genes in order to create and breed transgenic zebrafish. The zebrafish are used to study how neural crest cells and cranial placode progenitors give rise to a diverse group of cells types during development as well as the molecular and genetic basis underlying the body's ability to detect and respond to noxious stimuli, with the goal of reaching a better understanding of acute and chronic pain. The lab also looks for genetic components associated with neurodevelopment disorders.
- A lab inspection is required.
- All of the required trainings have been completed.
- The IACUC protocol has not yet been submitted.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Dhaka pending BUA application changes, a lab inspection, and review of the IACUC protocol.
- <u>The Committee voted unanimously to approve the draft BUA for Dr. Dhaka pending the items above.</u>

e. Elkon, Keith, renewal, *Genetic, Cellular, and Molecular Studies in SLE (Apoptosis)*

- The assigned IBC Primary Reviewer presented the Primary Review.
- The goal of this research is to define the molecular basis of autoimmune diseases such as Lupus and Rheumatoid Arthritis. Work with lentiviral vectors, adenoviral vectors, and human-derived substances is done in vitro and in mice.
- The greatest risk declared by the PI is repeated exposure to BrdU.
- The lab was inspected and deficiencies were addressed.
- All of the required trainings have been completed.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Elkon.
- <u>The Committee voted unanimously to approve the draft BUA for Dr. Elkon.</u>

f. Gale, Michael, change, *The Host Response to Virus Infection*

- The assigned IBC Primary Reviewer presented the Primary Review.
- Recombinant strains of Group B Streptococcus are being added to this lab's work. The strains will come from another lab with current approval.
- The lab was recently inspected, so a new lab inspection was not required for this change.
- All of the required trainings have been completed.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Gale.
- <u>The Committee voted unanimously to approve the draft BUA for Dr. Gale.</u>

g. Grant, Richard, change, *Primate Diagnostic Services Laboratory*

- The assigned IBC Primary Reviewer presented the Primary Review.
- This lab is adding in vitro work with adeno-associated viral vectors. These viral vectors are produced by another lab with current approval.
- The lab was recently inspected, so a new lab inspection was not required for this change.
- All of the required trainings have been completed.
- The draft BUA letter was shown.

- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Grant.
- The Committee voted unanimously to approve the draft BUA for Dr. Grant. There was one abstention from a committee member who is the PI of this application.

h. Hybiske, Kevin, renewal, *Chlamydia pathogenesis and immune evasion*

- The assigned IBC Primary Reviewer presented the Primary Review.
- This lab applies molecular, genetic, and cellular strategies to investigate unique interactions between the intracellular bacterium Chlamydia and the host epithelial cells they infect. It also pursues functional genomic, proteomic, and structural analyses to advance our understanding of Chlamydia pathogenesis.
- All animal work with mice is done at the University of Kansas.
- A successful lab Inspection is required.
- All of the required trainings have been completed.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Hybiske pending a successful lab inspection.
- The Committee voted unanimously to approve the draft BUA for Dr. Hybiske pending a successful lab inspection.

i. King, Neil, new, *Neil King Lab Biological Use Authorization*

- The assigned IBC Primary Reviewer presented the Primary Review.
- This lab designs proteins based on computational algorithms and expresses these synthetic genes in E. coli and yeast for recombinant protein purification. In vitro work involves lentiviral vectors, non-pathogenic strains of E. coli, recombinant or synthetic DNA/RNA (non-viral) enhanced gene delivery methods, and human blood, tissue, body fluids, and cell lines.
- The lab was inspected and no deficiencies were identified.
- All of the required trainings have been completed.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. King.
- The Committee voted unanimously to approve the draft BUA for Dr. King.

j. Klavins, Eric, renewal, *Mammalian Cellular Computation and RoL:FELS:Exploring the adaptive possibilities of 'redundancy'*

- The assigned IBC Primary Reviewer presented the Primary Review.
- This lab works to design gene circuits and cell-cell communication systems that enable novel multicellular behaviors in bacteria or yeast. Lentiviral vectors, recombinant or synthetic DNA/RNA (non-viral) enhanced gene delivery methods, and human and non-human primate blood, tissue, body fluids, and cell lines are used in vitro.
- The lab was inspected and no deficiencies were identified.
- All of the required trainings have been completed.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Klavins.
- The Committee voted unanimously to approve the draft BUA for Dr. Klavins.

k. Lin, Shin, renewal, *Epigenomics of Heart Failure*

- The assigned IBC Primary Reviewer presented the Primary Review.

- This lab works to understand how the epigenome changes in failing hearts. Both human tissues and animal models are used in this research.
- The greatest risk declared is work with patient tissues and lentivirus/adenovirus transductions.
- The lab was inspected and deficiencies were addressed.
- All of the required trainings have been completed.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Shin.
- The Committee voted unanimously to approve the draft BUA for Dr. Shin.

l. Manoil, Colin, renewal, *Genetic analysis of Gram-negative bacterial pathogens*

- The assigned IBC Primary Reviewer presented the Primary Review.
- This lab uses genetic and genomic approaches to identifying targets for new antibiotics and antibiotic adjuvants, and to characterize new antibiotic resistance genes of Gram-negative pathogens and their nonpathogenic surrogates. This research involves in vitro work with various recombinant risk group 2 organisms.
- The lab was inspected and no deficiencies were identified.
- All of the required trainings have been completed.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Manoil.
- The Committee voted unanimously to approve the draft BUA for Dr. Manoil.

m. Oshima, Junko, renewal, *International Registry of Werner Syndrome*

- The assigned IBC Primary Reviewer presented the Primary Review.
- The goal of this research is to elucidate the genetic mechanisms of aging. The specific aim is to investigate the genetic causes and mechanisms of accelerated aging syndromes (progeroid syndrome).
- The greatest risks declared by the PI are work with lentiviral infection of human cells, Epstein Barr virus, amphotropic gamma retrovirus, and foamy viral vectors.
- The plasmids are in E. coli and not the viral supernatant. The PI identified an oncogenic gene insert, but it is not a true oncogene because it is not transforming. No increase in biosafety level is needed.
- The lab was inspected and no deficiencies were identified.
- All of the required trainings have been completed.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Oshima.
- The Committee voted unanimously to approve the draft BUA for Dr. Oshima.

n. Raible, David, renewal, *Regulation of Zebrafish Development*

- The assigned IBC Secondary Reviewer presented the Primary Review.
- This lab breeds and studies transgenic zebrafish to understand how mechanosensory hair cells develop, respond to damage, and regenerate. It involves in vitro work with recombinant or synthetic DNA/RNA (non-viral) enhanced gene delivery methods and human blood, tissue, body fluids, and cell lines.
- The lab was inspected and no deficiencies were identified.
- All of the required trainings have been completed.
- The draft BUA letter was shown.
- The IBC Secondary Reviewer made a motion to approve the draft BUA for Dr. Raible.

- The Committee voted unanimously to approve the draft BUA for Dr. Raible.

o. Stevens, Kelly, renewal, *Regenerative Technologies*
- The assigned IBC Primary Reviewer presented the Primary Review.
- This lab is developing cell-based therapies for patients with organ failure due to heart and liver disease. They use primary cells, ESCs and iPSCs from humans and rodents that have been transduced with viral vectors containing genes for fluoresecent marker, calcium indicators, and matrix metaloproteinases to study how cells assemble to form 3D organ tissue. The cells and engineered tissues are obtained from collaborator labs.
- The lab opted not to provide 3rd generation lentiviral vector verification, so it is listed at BSL2 on the BUA letter.
- The lab was inspected and no deficiencies were identified.
- All of the required trainings have been completed.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Stevens.
- The Committee voted unanimously to approve the draft BUA for Dr. Stevens.

p. von Moltke, Jakob, renewal, *Initiation of type 2 Immune Responses*
- The assigned IBC Primary Reviewer presented the Primary Review.
- This lab works to understand the initiation of type 2 immune responses that mammalian immune systems generate upon exposure to parasitic worms (helminths) or allergens. The research will infectmice with Influenza A PR8 to study type 2 immunity in tissue remodeling after flu infection.
- The lab was inspected and no deficiencies were identified.
- All of the required trainings have been completed.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. von Moltke.
- The Committee voted unanimously to approve the draft BUA for Dr. von Moltke.

q. Young, Jessica, renewal, *Modeling late-onset sporadic Alzheimer's disease using human stem cells*
- The assigned IBC Primary Reviewer presented the Primary Review.
- This lab uses human embryonic stem cells and human induced pluripotent stem cells to differentiate into neuronal lineages to study genes that increase risk for late-onset Alzheimer's disease.
- The greatest biohazard risk involves the production of high titer lentivirus.
- The lab was inspected and no deficiencies were identified.
- All of the required trainings have been completed.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Young.
- The Committee voted unanimously to approve the draft BUA for Dr. Young.

10. SUBCOMMITTEE REPORTS:

r. Lee, Sylvia, new, *A Phase 1 Study Evaluating the Safety and Efficacy of HPV16 E7 T Cell Receptor Engineered T Cells (KITE-439) in HLA-A*02:01+ Subjects with Relapsed/Refractory HPV16+ Cancers*

- One member and one ad hoc reviewer served as the Subcommittee Reviewers. The ad hoc reviewer presented the Subcommittee Report.
- This is a Phase 1, first in human, multicenter, open-label trial using genetically engineered autologous T cells expressing a TCR that targets HPV16-expressing solid tumors. The primary objectives are to evaluate the safety of KITE-439, determine a recommended dose, and estimate overall response rates for subsequent trials.
- Infusion of the genetically modified cells will take place at UWMC.
- Safety issues are mainly limited to accidental sharp needle parenteral administration of KITE-439 T cells to hospital staff during cell product reconstitution or administration. Exposure to non-self cells even from parenteral administration is low risk as cells would be eliminated by the exposed person's immune system.
- The draft BUA letter was shown.
- The ad hoc reviewer made a motion to approve the draft BUA letter for Dr. Lee. A member seconded the motion.
- <u>The Committee voted unanimously to approve the draft BUA for Dr. Lee.</u>

s. Wagner, Michael, new, *A Phase 2 Single Arm Open-Label Clinical Trial of ADP-A2M4 SPEARTM T cells in subjects with Advanced Synovial Sarcoma or Myxoid/Round Cell Liposarcoma*

- One member and one ad hoc reviewer served as the Subcommittee Reviewers. The ad hoc reviewer presented the Subcommittee Report.
- This is a Phase 2, multicenter, open-label, single arm trial that will treat patients with advanced synovial sarcomas or liposarcomas. This study is testing a new treatment for metastatic sarcomas and inoperable liposarcomas that currently have limited or highly morbid treatment options. The objectives are to evaluate the efficacy, safety, and tolerability of the product.
- Infusion of the genetically modified cells will take place at UWMC.
- Safety issues are mainly limited to accidental sharp needle parenteral administration of the T cells to hospital staff during cell product reconstitution or administration. Exposure to non-self cells even from parenteral administration is low risk as cells would be eliminated by the exposed person's immune system.
- The draft BUA letter was shown.
- The ad hoc reviewer made a motion to approve the draft BUA letter for Dr. Wagner. A member seconded the motion.
- <u>The Committee voted unanimously to approve the draft BUA for Dr. Wagner.</u>

t. Hawn, Thomas, BSL3 Inactivation Petition to Waive Verification

- Three members of the IBC served as the Subcommittee Reviewers. One of the Subcommittee Reviewers presented the Subcommittee Report.
- This lab is requesting to waive the verification processes for several inactivation procedures of Mycobacterium tuberculosis to be able to expedite removal of this material from BSL3 containment. Additional validation testing for SOPs were submitted to support this request. All validation testing was performed in triplicate with positive

and negative controls. All cultures were held for 42 days to assure adequate time for growth. All validation testing samples were no growth after 42 days and all positive controls were reported as "TNTC".

- The subcommittee finds that the validation results are appropriate and no additional verification will be required for the four procedures reviewed. All material removed by these inactivation procedures must be handled following BSL2 practices in the Hawn lab or the core Immunology cell analysis facility. All SOPs must be followed as written and any changes to the SOPs will require additional review by the subcommittee. Verification of each inactivation protocol must be performed annually. Annual proficiency must be documented for all personnel performing the inactivation protocol
- .A member made a motion to approve the subcommittee's recommendations. A member seconded the motion.
- The Committee voted unanimously to waive verification for Dr. Hawn's BSL3 Inactivation with the above conditions.

10. FOR YOUR INFORMATION:

- **NIH Incident Report:** A researcher poked their finger while disposing of a bone marrow needle into a sharps container. The bone marrow needle had been used on a non-human primate that had been inoculated with SHIV. The NIH has been notified.
- **Harborview Research & Training (HR&T) Rooms on BUA Letters:** Due to the temporary closure of the building, new or renewal BUA letters will include temporary lab locations as well as HR&T lab locations. All HR&T rooms will be inspected and approved once the building has reopened.

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

12. MEETING ADJOURNED AT APPROXIMATELY 11:53 A.M.