INSTITUTIONAL BIOSAFETY COMMITTEE

UNIVERSITY of WASHINGTON

Meeting Minutes

Date: Wednesday, February 17th, 2016
Time: 10:00 AM – 12:00 PM

Location: Foege N-130A

Members Present:
1. Thea Brabb, Comparative Medicine *(Animal Containment Expert)*
2. H.D. "Toby" Bradshaw, Biology *(Plant Expert)*
3. Lesley Colby, Comparative Medicine *(Animal Containment Expert)*
4. William Glover, Washington State Public Health Laboratories (*Community Member*)
5. David Koelle, Allergy and Infectious Diseases
6. Stephen Libby, Laboratory Medicine (*IBC Chair*)
7. Scott Meschke, Environmental & Occupational Health Sciences
8. Matthew R. Parsek, Microbiology
9. Angela Rasmussen, Microbiology
10. Jason Smith, Microbiology
11. Eric Stefansson, Environmental Health & Safety (*Biosafety Officer*)
12. 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 10:04 am. 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 January 20, 2016 minutes meeting.
   - A member made a motion to approve the January 20, 2016 minutes. Another member seconded the motion.
   - The committee voted unanimously to approve the January 20, 2016 meeting minutes with two abstentions.

4. **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. Stella, Dr. Blau, and Dr. Monnat each added the pathology flow cytometry core facility to their respective BUA approvals.
      - Dr. Hawkins renewed a BUA involving human and non-human primate blood, tissue, body fluids, and cell lines.
      - Dr. Dhaka renewed a BUA involving human source material.
      - Dr. Oganesian moved her lab from SLU Lab South to SLU Brotman.
      - Dr. Campbell added new lab space at Harborview to her BUA approval.
      - Dr. Raskind added the Harborview vivarium to her BUA approval.
      - The IBC Chair sought 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.

5. **CATEGORY III-D AMENDMENTS**

   1. Cookson, Brad, change, *Development of Reactive T-cells after Vaccination*
      - The biosafety officer presented the project.
      - Dr. Cookson is requesting to add new recombinant strains of Salmonella. He is already approved for Salmonella Typhimurium.
      - The assigned IBC member endorsed the biosafety officer's review.
      - The draft BUA letter was shown.
      - The assigned IBC member made a motion to approve the draft BUA letter for Dr. Cookson. A second is not needed since he endorsed the review.
      - The Committee voted unanimously to approve the draft BUA letter for Dr. Cookson, with one abstention.

2. Kwon, Ronald, change, *Neuromuscular Regulation of Bone in Zebrafish*

- The biosafety officer presented the project.
- Dr. Kwon has worked with zebrafish for many years. He is already approved to breed and use transgenic zebrafish, and now he is requesting to create transgenic zebrafish by using CRISPR/Cas9 technology.
- The assigned IBC member endorsed the biosafety officer's review.
- The draft BUA letter was shown.
- The assigned IBC member made a motion to approve the draft BUA letter for Dr. Kwon. A second is not needed since he endorsed the review.
- <u>The Committee voted unanimously to approve the draft BUA letter for Dr. Kwon.</u>

6. INDIVIDUAL PROJECT REVIEWS

3. Yang, Xiaoming, change, *Interventional Oncology*

- The assigned IBC Primary Reviewer presented the Primary Review.
- This is a change request. The overall goal of the research is to develop new technologies of radiofrequency heating enhanced gene therapy or chemotherapy.
- The investigator is requesting to add a new oncolytic virus, Talimogene laherparepvec, also known as T-VEC. This virus was engineered from a herpes simplex virus (HSV-1). The T-VEC virus has been attenuated so that it no longer causes herpes, and other genetic modifications have been made to increase the selectivity for cancer cells & to secrete the cytokine GM-CSF.
- The manufacturer's safety data sheet suggests BSL-1 containment for small volumes and medical facilities, and BSL-1 or BSL-2 for research and development up to 10 liters. The PI will be using much less than 10 liters of the virus. The committee discussed the appropriate containment level for this virus.
- The manufacturer's safety data sheet states that treatment with T-VEC is contraindicated in persons who are immunocompromised, including cancer patients, people with HIV or AIDS, and pregnant women. These are fairly standard recommendations for risk group 2 organisms.
- The IBC Primary Reviewer recommended discussing with the Employee Health Center the possibility of offering a pathway to expedited (within a few hours) antiviral therapy to staff in case of exposure.
- The draft BUA letter was shown.
- The IBC Primary Reviewer recommends that "Personnel with contraindicating conditions as listed above should not use T-VEC or care for treated animals." The committee discussed this recommendation and decided that it would be more appropriate for the committee to ensure that personnel are counseled about the potential risks of working with this agent. The committee decided to approve the draft BUA letter as written, without any language prohibiting immunocompromised lab researchers or animal care personnel from working with the T-VEC or T-VEC infected animals. The IBC Primary Reviewer and/or the Employee Health Physician will review the occupational health recommendations that the employees will receive, and ensure that the language properly conveys the risk to immunocompromised staff.
- The training has been completed, and the lab has been recently inspected.
- The IBC Primary Reviewer made a motion to approve the draft BUA letter for Dr. Yang. A second is not needed since he is the Primary Reviewer.

- The Committee voted unanimously to approve the draft BUA letter for Dr. Yang. The letter will be sent after the IBC Primary Reviewer and/or the Employee Health Physician reviews the occupational health recommendations associated with this project.

4. Gale, Michael, renewal, *The Host Response to Virus Infection*

- The assigned IBC Primary Reviewer presented the Primary Review.
- This is a renewal. The Gale lab studies how viral and host factors impact innate immune defenses to determine the outcome of virus infection. Additional studies focus on development of antiviral therapies, immune adjuvants, or vaccine strategies to control virus infection.
- The Gale lab works with a wide variety of viruses, including Hepatitis C virus, influenza, Dengue, Sindbis, vaccinia, and West Nile virus. Lentiviral vectors and ecotropic gammaretroviral vectors are also used. The research with these viruses is conducted at BSL-2 with BSL-3 practices.
- The Gale lab is also working with three strains of Hantavirus: Seoul, Hantaan, and Sin Nombre. These viruses require BSL-3 containment and practices. An IBC subcommittee was formed in September 2015 to review these Hantavirus strains for Dr. Gale.
- This same subcommittee summarized the risk assessment that was performed.
- The subcommittee evaluated the containment requirements, occupational health recommendations for laboratory workers, and the appropriate PPE when using Hantavirus. The subcommittee also discussed potential environmental exposure risks and what methods can be utilized to prevent those risks. Respirators, a standard requirement for BSL-3 work, will be used.
- An occupational health consult has occurred for all employees who work with Hantavirus. Employee Health Center has been informed of the viruses that are worked with, in case any researcher on this project needs to seek medical attention after an exposure or an illness.
- Wallet cards have been provided to researchers on this project. The cards include information about what kind of symptoms researchers should seek medical attention for. The cards also include the 24-hour pager number of the Employee Health physician.
- Research involving Zika virus is being added to the protocol. Zika virus is transmitted primarily through the bite of an infected mosquito. It may also be sexually transmitted. Clinical symptoms are usually mild and last several days, however, there have been reports of a serious birth defect of the brain called microcephaly and other poor pregnancy outcomes in babies of mothers who were infected with Zika virus while pregnant.
- A medical management plan has been developed in anticipation of this research. The committee reviewed the plan. Those who have direct contact with Zika virus must receive in-person medical counseling before beginning work with Zika virus. Direct contact is defined as working directly with viral cultures, infected material, or any items that have come in contact with Zika virus, caring for infected animals (including handling bedding of infected animals), and working in rooms or facilities where animals and procedures are not in primary containment devices (for example, in non-human primate rooms). Medical counseling is available, but not required, for those who don't have direct contact with Zika virus but are present in the same laboratory where work with Zika virus is occurring.

- A committee member asked if a note could be added to the BUA letter stating that they need to contact the Comparative Medicine Facility Director before beginning animal work with the Zika virus.
- The draft BUA letter was shown.
- The training has been completed, and the lab has been inspected by the biosafety officer.
- The IBC Primary Reviewer made a motion to approve the draft BUA letter for Dr. Gale. A second is not needed since he is the Primary Reviewer.
- The Committee voted unanimously to approve the draft BUA letter for Dr. Gale, contingent upon adding a statement to the BUA letter directing the investigator to contact Comparative Medicine before beginning animal studies with Zika virus.

5. Trapnell, Cole, change, *Trapnell lab general operations*

- The assigned IBC Primary Reviewer presented the Primary Review.
- A researcher from the Trapnell lab came to the IBC meeting and introduced himself.
- This is a change request. The overall goal of the Trapnell laboratory is to discover novel regulators that govern cellular transitions (i.e., cell differentiation, reprogramming, etc.) by utilizing single-cell genomics.
- The lab is requesting to add single-cycle infectious influenza A virus. This is similar to other replication deficient viral vector systems that the committee often reviews, except that an influenza virus is used as the backbone, rather than the more common lentiviruses or retroviruses.
- The BUA letter is worded to restrict the research to the backbone A/WSN/33-ΔHA, (a mouse-adapted H1N1 influenza A virus). A change request would need to be submitted if the Trapnell lab wanted to use any additional strains in the future. This technology could be used with strains that are more pathogenic than A/WSN/33-ΔHA, and the IBC would need to perform another risk assessment in the event that a different backbone influenza virus strain is proposed.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA letter for Dr. Trapnell. A second is not needed since he is the Primary Reviewer.
- The Committee voted unanimously to approve the draft BUA letter for Dr. Trapnell.

6. Horwitz, Greg, renewal, *Neurophysiology of Vision*

- The assigned IBC Primary Reviewer presented the Primary Review.
- The overall goal of the research is to understand the neural mechanisms underlying trichromatic visual perception. Adeno-associated viral vectors, lentiviral vectors and a herpes simplex viral vector are used in a macaque model.
- The draft BUA letter was shown.
- The primary review mentions that the investigator should uncheck III-E. This has already been done.
- The biosafety officer inspected the lab and everything was in order. The required training been taken.
- The IBC Primary Reviewer made a motion to approve the draft BUA letter for Dr. Horwitz. A second is not needed since she is the Primary Reviewer.
- The Committee voted unanimously to approve the draft BUA letter for Dr. Horwitz.

7. Chait, Alan, renewal, *Lipoproteins, Inflammation and Atherosclerosis*

- The assigned IBC Primary Reviewer presented the Primary Review.
- Dr. Chait's research focuses on lipoprotein-proteoglycan interactions in atherogenesis; the role of diabetes in the pathogenesis of macrovascular disease; and the links amongst obesity, inflammation, insulin resistance and atherosclerosis.
- The correction to the application mentioned in the review (complete question 98) has already been made.
- Lentiviral vectors with no oncogenic inserts are used. Adeno-associated viral vectors and human blood and cells are also used.
- The biosafety officer inspected the lab and all identified issues have been corrected. The required training has been taken.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA letter for Dr. Chait. A second is not needed since she is the Primary Reviewer.
- <u>The Committee voted unanimously to approve the draft BUA letter for Dr. Chait.</u>

8. Disis, Mary, renewal, *UW Gene and Cell Therapy Core located in Clinical Research Center*

- The assigned IBC Primary Reviewer presented the Primary Review.
- This is a 3 year renewal application requesting approval for ongoing services provided by the UW Gene and Cell Therapy Core facility. The principal investigator for this core facility has changed from Ann Stapleton to Mary Disis.
- The facility capabilities include processing apheresis products, blood separation, stem cell enrichment, T cell subset selection or deletion, manufacturing of gene modified cells as well as ex-vivo manipulation, including viral vector transduction, of cells for novel gene and cell therapy products intended for clinical research use.
- Laboratory procedures involving biohazardous materials include purification of human stems cells and T cells using the CliniMacs or other closed system, culturing of human stem cells, T cells, or other blood cells, transduction of human cells with viral vectors as specified by individual protocols, and cryopreservation of human cells for future expansion or infusion.
- Individual research protocols involving viral vectors requesting services from the core will require prior IBC approval.
- The draft BUA letter was shown.
- The facility has been inspected by the biosafety officer, and all the training has been completed.
- The IBC Primary Reviewer made a motion to approve the draft BUA letter for Dr. Disis. A second is not needed since she is the Primary Reviewer.
- <u>The Committee voted unanimously to approve the draft BUA letter for Dr. Disis.</u>

9. Fang, Ferric, renewal, *Salmonella Pathogenesis and Immunity*

- The IBC Chair declared a conflict of interest, turned the meeting over to another member, and left the room.
- The assigned IBC Primary Reviewer presented the Primary Review.
- The lab researches the interaction of bacterial pathogens with the host immune system. Several species of Salmonella are used, as well as other Risk Group 2 bacteria such as *Listeria monocytogenes* and *Francisella novicida*.
- The draft BUA letter was shown.

- The IACUC protocol has not yet been submitted. The BUA letter will be not be issued until the biosafety officer has reviewed the IACUC protocol.
- The required trainings have been completed, and the biosafety officer inspected the lab and everything was in order.
- The IBC Primary Reviewer made a motion to approve the draft BUA letter for Dr. Fang. A second is not needed since he is the Primary Reviewer.
- The Committee voted unanimously to approve the draft BUA letter for Dr. Fang, pending the biosafety officer's review of the IACUC protocol.
- The IBC Chair re-entered the room.

10. Reniere, Michelle, new, *Redox regulation and virulence in Listeria monocytogenes*

- The assigned IBC Primary Reviewer presented the Primary Review.
- This is a new project. The goal of the project is to study the regulation virulence factors in *Listeria monocytogenes* and *Staphylococcus aureus*.
- Recombinant strains of *Listeria monocytogenes* and *Staphylococcus aureus* are used on the project.
- The draft BUA letter was shown.
- The lab inspection and trainings were up to date.
- The IBC Primary Reviewer made a motion to approve the draft BUA letter for Dr. Reniere. A second is not needed since he is the Primary Reviewer.
- The Committee voted unanimously to approve the draft BUA letter for Dr. Reniere.

11. Noss, Erika, new, *Understanding Fibroblasts Role in Autoimmune Disease*

- The assigned IBC Primary Reviewer presented the Primary Review.
- This is a new project. The goal of the project is to investigate the role of fibroblasts in autoimmune diseases such as rheumatoid arthritis and inflammatory bowel disease.
- Lentiviral vectors are used on the project. Human and mouse cell lines will be transfected with plasmids for transient or stable gene expression.
- A discussion occurred regarding the oncogene database. It can be difficult to determine which genes are true oncogenes. Sometimes genes will appear in the oncogene database because they are overexpressed in certain cancers or tumors, but they are not necessarily causing cancer or acting as oncogenes.
- In this case, several genes the investigator is using are found in the cancer gene census database, and these genes will be overexpressed in plasmids for interaction studies, however, these genes alone are not sufficient to transform a cell.
- The draft BUA letter was shown.
- The biosafety officer has inspected the lab, and the training was completed.
- The IBC Primary Reviewer made a motion to approve the draft BUA letter for Dr. Noss. A second is not needed since he is the Primary Reviewer.
- The Committee voted unanimously to approve the draft BUA letter for Dr. Noss.

12. Rostomily, Robert, renewal, *Xenotransplant Model for Epithelial Mesenchymal Transition in Gliomas*

- The assigned IBC Primary Reviewer presented the Primary Review.
- The overall goal of the research is to investigate the role of TWIST1 in cancer stem cell function, glioma invasion, and glioma development. In vitro and mouse models are used.

- Ecotropic and amphotropic gammaretroviral vectors are used, as well as lentiviral vectors. Parts of the application do not seem clear. Some oncogenes and tumor suppressor genes are identified on the application, but there is not information about how these genes will be used. It is unclear whether the tumor suppressor genes will be over-expressed or knocked down. The biosafety officer will ask the investigator for clarification.
- A few questions on the BUA application have not been filled in (question 34, 76, 87, and 97).
- The biosafety officer has inspected the lab and everything was in good order. The required trainings have been completed.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA letter for Dr. Rostomily, pending clarification of the oncogenes and completion of the BUA application. A second is not needed since she is the Primary Reviewer.
- The Committee voted unanimously to approve the draft BUA letter for Dr. Rostomily, pending completion of the blank BUA application questions and clarification of how the oncogenes and tumor suppressor genes listed on the project will be used.

13. Woodward, Joshua, new, *Staphylococcus aureus and Pseudomonas aeruginosa pathogenesis and host response*

- The assigned IBC Primary Reviewer presented the Primary Review.
- This is a new BUA application from an established investigator. Lentiviral and gammaretroviral vectors, as well as recombinant strains of *Pseudomonas aeruginosa* and *Staphylococcus aureus*.
- A few minor corrections to the BUA application are needed. The viral vectors have been previously approved on another BUA, but if they are going to be added to this BUA, they should be fully described in the gene delivery methods table of the BUA application. Risk Group 2 should be checked for *S. aureus* in the microorganism table. Question 89 about the lab safety manual should be answered.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA letter for Dr. Woodward. A second is not needed since he is the Primary Reviewer.
- The Committee voted unanimously to approve the draft BUA letter for Dr. Woodward, pending the corrections to the BUA application.

14. Xu, Libin, renewal, *7-Dehydrocholesterol-derived oxysterols in SLOS: role and therapy*

- The assigned IBC Primary Reviewer presented the Primary Review.
- The draft BUA letter was shown.
- This is a change request. Third-generation lentiviral vectors and human induced pluripotent stem cells are being added to study the pathophysiology of Smith-Lemli-Optiz syndrome.
- The training has been completed, and the lab has recently been inspected.
- The IBC Primary Reviewer made a motion to approve the draft BUA letter for Dr. Xu. A second is not needed since he is the Primary Reviewer.
- The Committee voted unanimously to approve the draft BUA letter for Dr. Xu.

15. Zhang, Miqin, renewal, *Molecular MR Imaging of Tumors*

- The assigned IBC Primary Reviewer presented the Primary Review.
- This is a renewal application investigating the targeting ability, transfection efficiency and therapeutic effect of a non-viral iron oxide and gadolinium nanoparticle system this lab has developed that demonstrates specific tumor targeting in prior studies of MR tumor imaging. These studies aim to determine the efficacy of in vivo targeting of ligand specific nanoparticles functionalized to efficiently deliver DNA to cancer cells in order to facilitate expression of cytotoxic and or immune-stimulatory genes.
- The letter needs to be corrected to list amphotropic gammaretroviral vectors with oncogenic inserts that have been replication competent virus tested at BSL-2. The biosafety officer will verify that oncogenic inserts are used in the amphotropic vectors, and the letter will be corrected.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA letter for Dr. Zhang. A second is not needed since she is the Primary Reviewer.
- The Committee voted unanimously to approve the draft BUA letter for Dr. Zhang, contingent upon the correction to the BUA letter.

FOR YOUR INFORMATION:

- A lab accident occurred involving *Burkholderia pseudomallei*. An employee accidentally bumped three plates, which fell out of the biosafety cabinet. The spill was contained in the room, and properly cleaned according to standard operating procedures. All required personal protective equipment was worn. A biosafety officer & the employee health center were contacted for assistance and evaluation. The incident was promptly reported to the CDC. A root cause investigation was done with the investigator, the research personnel, and the biosafety officer. Medical monitoring was followed per the standard operating procedures. The principal investigator has made changes to laboratory work practices as a means to prevent a similar incidents in the future.

ADMINISTRATIVE UPDATES:

- There will be a new IBC member joining as a representative from the Washington National Primate Research Center.

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

MEETING ADJOURNED AT APPROXIMATELY 12:05 p.m.