



# INSTITUTIONAL BIOSAFETY COMMITTEE

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UNIVERSITY of WASHINGTON

## Meeting Minutes

**Date:** Wednesday, March 15, 2017

**Time:** 10:00 AM – 12:00 PM

**Location:** Foegen N-130A

- Members Present:**
1. Thea Brabb, Comparative Medicine (*Animal Containment Expert*)
  2. H.D. "Toby" Bradshaw, Biology (*Plant Expert*)
  3. Richard Grant, Washington National Primate Research Center
  4. Garry Hamilton (*Community Member*)
  5. Kevin Hybiske, Allergy and Infectious Diseases
  6. Stephen Libby, Laboratory Medicine (*IBC Chair*)
  7. Scott Meschke, Environmental & Occupational Health Sciences
  8. Matthew R. Parsek, Microbiology
  9. David Scarsella, Pacific Northwest Diabetes Research Institute (*Community Member*)
  10. Jason Smith, Microbiology (*IBC Vice Chair*)
  11. Eric Stefansson, Environmental Health & Safety (*Biosafety Officer, Animal Containment Expert*)
  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) Vice Chair called the meeting to order at 10:07 am. A quorum was present.
2. **REMINDER:** The IBC Vice 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 Vice Chair sought a motion to approve the minutes from the February 15, 2017 meeting.
  - A member made a motion to approve the February 15, 2017 minutes. Another member seconded the motion.
  - The committee voted unanimously, with three abstentions, to approve the February 15, 2017 meeting minutes.
4. **OLD BUSINESS**
  - At the January IBC meeting, Dr. DePaolo's BUA was approved pending a the biosafety officer's review of the IACUC protocol, and the industrial hygienist verifying correct waste disposal procedures for the azoxymethane. All of these outstanding items were resolved and the letter was sent out.
  - At the January IBC meeting, Dr. Shendure's BUA was approved pending a demo of the air sampler. This is still pending.
  - At the February IBC meeting, Dr. Morishima's BUA was approved pending biosafety officer review of the BSL-2 with BSL-3 practices SOP. This is still pending.
  - At the February IBC meeting, Dr. Phillip's BUA was approved pending biosafety officer review of the IACUC protocol submission. The protocol has not yet been submitted.
  - At the February IBC meeting, Dr. Rosenfeld's BUA was approved pending completion of the lab inspection and bloodborne pathogen training. The lab was successfully inspected, and the investigator completed all required trainings. The 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
    - One member declared a conflict of interest due to his own project appearing on the Biosafety Officer Report.
    - Dr. Jayadev added a new room to her approval.
    - Dr. Van Voorhis added the cell analysis facility to his approval.
    - Dr. Murry added a new imaging center to his approval.
    - Dr. Fuller added the administration of human IgG (immunoglobulin G) to mice to her approval letter. This agent is administered to mice at ABSL-2 but the mice can then be housed at ABSL-1.
    - Dr. Woodrow moved some agents from one BUA letter to another.
    - Dr. Frascch received a new BUA letter involving work with pregnant sheep. Pregnant sheep are known to shed *Coxiella burnetii* and can pose a Q fever risk. The sheep will be contained at ABSL-2 until it can be verified that they are not shedding *Coxiella burnetii*. Animals must have a negative Q fever titer prior to housing in the

vivarium. After a two week quarantine period there will be a second serological test for Q fever. If the results are still negative then the animals may be housed at ABSL-1. During quarantine period, all EHS approved SOPs must be followed including required respiratory protection.

- Dr. Grant received a new approval involving non-recombinant baboon cytomegalovirus, simian retrovirus, and human and non-human primate cells.
- The IBC Vice 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 voted unanimously, with one abstention, to approve this month's Biosafety Officer Report.

## 6. INDIVIDUAL PROJECT REVIEWS

### 1. Klavins, Eric, new, *Hydra Engineering*

- The assigned IBC Primary Reviewer presented the Primary Review.
- This is a new project from an established investigator. The project involves creating, breeding, and using transgenic *Hydra vulgaris* (a species of sea anemone).
- The project was reviewed by an ad-hoc reviewer who specializes in aquatic animal containment.
- The lab has been inspected and all SOPs have been completed. The floor drain filters and covers are on order. A final inspection will be performed by the IBC reviewer and the biosafety officer once the drain filters and covers are in place.
- Question 32 on the BUA application ("use of recombinant or synthetic DNA/RNA in animals") needs to be completed.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Klavins, pending the final lab inspection and the correction of the BUA application.
- The Committee voted unanimously to approve the draft BUA for Dr. Klavins, pending the final lab inspection and the correction of the BUA application.

### 2. Horwitz, Marshall, renewal, *Genetics of Hematopoietic Malignancy: 1) Cyclic and Severe Congenital Neutropenia; 2) Familial Hodgkin Lymphoma*

- The assigned IBC Primary Reviewer presented the Primary Review.
- The committee discussed the use of potential oncogenes in amphotropic gammaretroviral vectors. The investigator was present at the IBC meeting, and confirmed that he will be upregulating tumor suppressor genes rather than knocking down oncogenes. This would not require enhanced practices.
- The lab successfully passed the lab inspection, and the trainings are all up to date.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Horwitz.
- The Committee voted unanimously to approve the draft BUA for Dr. Horwitz.

### 3. Sellers, Drew, renewal, *Stem Cells and Regeneration of the Spinal Cord*

- The assigned IBC Primary Reviewer presented the Primary Review.
- A question was raised about the lentiviral vectors used on this project. The investigator was present to answer questions, and confirmed that virtually all

lentiviral vectors used in his lab are third generation. Third generation vectors will be added to the BUA letter.

- The draft BUA letter was shown.
- Some rooms on the IACUC application do not match those on the BUA application. The PI will modify his IACUC application.
- The lab successfully passed the lab inspection and the trainings are all up to date.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Sellers, pending the modification of the BUA letter to list third generation lentiviral vectors.
- The Committee voted unanimously to approve the draft BUA for Dr. Sellers, pending the modification of the BUA letter to list third generation lentiviral vectors.

4. Berndt, Andre, new, *Screening and engineering of fluorescent biosensors*

- The assigned IBC Primary Reviewer presented the Primary Review.
- A discussion occurred about the baculoviral vectors. If these vectors enter mammalian cells, they cannot continue to replicate and are not known to cause any human disease, so BSL-1 containment is appropriate.
- The BUA letter should list AAV with oncogenic inserts at BSL-2 containment. The biosafety officer will change this.
- The lab successfully passed the lab inspection and the trainings are all up to date.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Berndt, pending modification of the BUA letter to list AAV vectors at BSL-2 containment.
- The Committee voted unanimously to approve the draft BUA for Dr. Berndt, pending modification of the BUA letter to list AAV vectors at BSL-2 containment.

5. Cao, Hung, change, *Microsensors to Study Heart Regeneration in Zebrafish*

- The assigned IBC Primary Reviewer presented the Primary Review.
- This is a change request. The investigator is adding transgenic strains of zebrafish.
- The lab has recently been inspected and the trainings are all up to date.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Cao.
- The Committee voted unanimously to approve the draft BUA for Dr. Cao.

6. Grant, Richard, change, *Primate Diagnostic Services Laboratories*

- One member declared a conflict of interest and left the room.
- The assigned IBC Primary Reviewer presented the Primary Review.
- This laboratory is geared to provide materials and diagnostic support to the researchers associated with the primate center. Samples derived from primates, including primates experimentally exposed to primate lentiviruses such as SHIV, will be received and processed.
- Some rooms are still being set up, and the final lab inspection is pending. The SOPs are in the process of being finalized and reviewed by the biosafety officer.
- All 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, pending a final lab inspection and finalized SOPs.
- The Committee voted unanimously, with one abstention, to approve the draft BUA for Dr. Grant, pending a final lab inspection and finalized SOPs.

7. Jayadev, Suman, renewal, *Inflammatory Mediators of Neurodegeneration*
  - The assigned IBC Primary Reviewer presented the Primary Review.
  - Lentiviral vectors and murine stem cell virus are used in vitro.
  - The draft BUA letter was shown.
  - The lab successfully passed the lab inspection and the trainings are all up to date.
  - The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Jayadev.
  - The Committee voted unanimously to approve the draft BUA for Dr. Jayadev.
  
8. Lee, Chi Fung, new, *Protein Acetylation in Cardiac Function*
  - The assigned IBC Primary Reviewer presented the Primary Review.
  - The lab studies the role of protein acetylation in cardiac function. Cardiomyocytes are isolated from transgenic rodents and exposed to adenovirus-expressing modified proteins.
  - The work with adenoviral vectors will be conducted at BSL-2.
  - The lab successfully passed the lab inspection and the trainings are all up to date.
  - The draft BUA letter was shown.
  - The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Lee.
  - The Committee voted unanimously to approve the draft BUA for Dr. Lee.
  
9. Maggio-Price, Lillian, renewal, *Inflammatory Bowel Disease, Colon Cancer, Diet and the Microbiome*
  - The assigned IBC Primary Reviewer presented the Primary Review.
  - Two members declared a conflict of interest due to shared funding sources.
  - This lab studies the interactions between gut flora, enteric bacteria and viruses, and host genetics and the role these play in the development of inflammatory bowel disease and colon cancer.
  - Recombinant Helicobacter species are used at ABSL-1. Human cells, tissue, and feces are also used at BSL-2.
  - The lab successfully passed the lab inspection and the trainings are all up to date.
  - The draft BUA letter was shown.
  - A member pointed out that the letter should be corrected to list human cells and human feces under NIH section NA rather than III-D\*. The letter will be corrected.
  - The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Maggio-Price, pending correction of the BUA letter.
  - The Committee voted unanimously to approve the draft BUA for Dr. Maggio-Price, pending correction of the BUA letter.
  
10. Mefford, Heather, change, *Genomic Approach to Epilepsy*
  - The assigned IBC Primary Reviewer presented the Primary Review.
  - This is a change request to add lentiviral vectors. No oncogenic inserts are used.
  - The draft BUA letter was shown.
  - The lab has recently been inspected and the trainings are all up to date.
  - The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Mefford.
  - The Committee voted unanimously to approve the draft BUA for Dr. Mefford.
  
11. Mullins, James, renewal, *HIV-1 and Host Cell Changes in Disease Progression*
  - The assigned IBC Primary Reviewer presented the Primary Review.

- Recombinant primate lentiviruses are used in vitro. The work is conducted at BSL-2 with BSL-3 practices.
- The lab successfully passed the lab inspection. Most trainings are up to date, however, the PI needs to retake the biosafety training.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Mullins, pending completion of the PI's biosafety training.
- The Committee voted unanimously to approve the draft BUA for Dr. Mullins, pending completion of the PI's biosafety training.

**12. Parichy, David, renewal, *Development of adult phenotypes in zebrafish and its relatives***

- The assigned IBC Primary Reviewer presented the Primary Review.
- This is a renewal of an existing project. The investigator studies the developmental genetics of pigment pattern formation and scale development. Transgenic zebrafish are created, bred, and used on the protocol.
- The lab successfully passed the lab inspection and the trainings are all up to date.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Parichy.
- The Committee voted unanimously to approve the draft BUA for Dr. Parichy.

**13. Reniere, Michelle, change, *Redox regulation and virulence in bacterial pathogens***

- The assigned IBC Primary Reviewer presented the Primary Review.
- This is a change request. The investigator has previously been approved for wildtype and recombinant strains of *Listeria monocytogenes* in vitro, and now a mouse model will be used.
- The draft BUA letter was shown.
- A member noted that the *Listeria* is inadvertently listed twice on the BUA letter. This will be corrected.
- The lab has recently been inspected and the trainings are all up to date.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Reniere, pending correction of the BUA letter.
- The Committee voted unanimously to approve the draft BUA for Dr. Reniere, pending correction of the BUA letter.

**14. Soge, Olusegun, renewal, *Horizontal Gene Transfer in Chlamydia***

- One member declared a conflict of interest.
- The investigator studies the genetics of Chlamydia pathogenesis.
- The laboratory will be using lateral gene transfer of the tetC gene from tetracycline resistant strains of *Chlamydia suis* to strains of *Chlamydia trachomatis*. The tet-resistant strains will then be used as drug selection markers in further recombination experiments.
- The investigator has already obtained NIH director approval to conduct these studies. A medical management plan is in place.
- Some hazardous chemicals are used on the project, including cycloheximide and sodium azide. An industrial hygienist consulted with the lab to ensure this work was conducted in a fume hood and that proper SOPs were in place.
- The lab successfully passed the lab inspection and the trainings are all up to date.
- The assigned IBC Primary Reviewer presented the Primary Review.

- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Soge.
- The Committee voted unanimously to approve the draft BUA for Dr. Soge.

**15. Stetson, Daniel, renewal, *Mechanisms and Consequences of Innate Immune Detection of Nucleic Acids***

- The assigned IBC Primary Reviewer presented the Primary Review.
- The investigator uses a variety of viruses and viral vectors, including herpes simplex type 1, encephalomyocarditis virus, mouse adenovirus, murine cytomegalovirus, adenoviral vectors, and adeno-associated viral vectors.
- A question was raised about whether the murine cytomegalovirus and mouse adenovirus were used in a mouse model. The mouse adenovirus is administered to mice on this project, but the murine cytomegalovirus work only occurs in vitro.
- The investigator still needs to submit the IACUC renewal application for this work. The approval will be pending the biosafety officer's review of the IACUC protocol.
- The lab successfully passed the lab inspection and the trainings are all up to date.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Stetson, pending completion of the IACUC renewal.
- The Committee voted unanimously to approve the draft BUA for Dr. Stetson, pending completion of the IACUC renewal.

**SUBCOMMITTEE REPORTS:**

**16. Bleakley, Marie, new, *Phase I study of adoptive immunotherapy with CD8+ and CD4+ memory T cells transduced to express an HA-1-specific T cell receptor (TCR) for children and adults with recurrent acute leukemia after allogeneic hematopoietic stem cell transplantation (HCT)***

- Three members of the IBC served as the Subcommittee Reviewers. One of the Subcommittee Reviewers presented the Subcommittee Report.
- This is a new application.
- In patients who receive hematopoietic stem cell transplantation (HCT) to treat leukemia, approximately 30% will relapse. One way to prevent relapse is to strengthen the graft vs leukemia (GVL) response of the transferred cells, so that they kill residual disease. The risk is graft vs host disease (GvHD), wherein the infused lymphocytes attack the patient's healthy cells.
- This trial will test a strategy whereby T cells from a donor that are engineered to be specific for an antigen (called HA-1) on the recipient's cancer cells will be infused into patients.
- This is a dose escalation study to primarily assess feasibility and safety. Secondary objectives will assess persistence, localization, and function of the infused cells and their effects on leukemia burden.
- T cells will be isolated from donors. They will be engineered at FHCRC with a lentiviral vector (3rd generation, VSV-G pseudotyped) called "HA-1 TCR LV" encoding the alpha and beta chains of a TCR specific for HA-1, a marker that can be used to purify the transduced cells (RQR), CD8 to increase the killing potential of transduced cells, and a "kill switch" called "iCasp9" that leads to apoptosis of transduced cells upon treatment with a drug (Rimiducid). The "kill switch" is a safeguard against severe GvHD. The transgenic T cells will then be infused into patients following chemotherapy, with

increasing doses for each cohort. Bone marrow and peripheral blood will be sampled to evaluate the therapy.

- The draft BUA letter was shown.
- The trainings are all up to date.
- A member made a motion to approve the draft BUA letter for Dr. Bleakley. Another member seconded the motion.
- The Committee voted unanimously to approve the draft BUA for Dr. Bleakley.

**17. Liao, John, new, *A Phase II Study of Concurrent IGFBP-2 Vaccination and Neoadjuvant Chemotherapy to Increase the Rate of Pathologic Complete Response at the Time of Cytoreductive Surgery***

- Three members of the IBC served as the Subcommittee Reviewers. One of the Subcommittee Reviewers presented the Subcommittee Report.
- This is a new study, but almost identical to one previously reviewed by the IBC in 2015 under PI Mary Disis.
- The purpose of the trial is to vaccinate patients with advanced ovarian cancer with a plasmid vaccine encoding amino acid 1-163 of IGFBP-2 (insulin-like growth factor binding protein 2). This protein is highly expressed in tumors. The idea to create a vaccine to this protein which activates T-cells that recognizes this protein and attack the tumor cells expressing it.
- The draft BUA letter was shown.
- The trainings are all up to date.
- A member made a motion to approve the draft BUA letter for Dr. Liao. Another member seconded the motion.
- The Committee voted unanimously to approve the draft BUA for Dr. Liao.

**18. Till, Brian, new, *A Phase I/II Study to Evaluate the Safety of Cellular Immunotherapy Using Autologous T cells Engineered to Express a CD20-Specific Chimeric Antigen Receptor for Patients with Relapsed or Refractory B-cell Non-Hodgkin Lymphomas***

- Three members of the IBC served as the Subcommittee Reviewers. One of the Subcommittee Reviewers presented the Subcommittee Report.
- This is a clinical trial application. The goal of the study is to test the safety of administering T-cells engineered via a lentiviral vector with a synthetic “chimeric antigen receptor” or CAR that targets CD20, an antigen that is highly expressed on cancer cells.
- CD4 and CD8 positive T cells will be isolated from patients. The cells will be transduced at FHCRC with a lentiviral vector (3rd generation, VSV-G pseudotyped) expressing the CD20-specific CAR and a truncated CD19 that will be used to select transduced cells.
- The transgenic T cells will then be infused into patients following chemotherapy, with increasing doses for each cohort. Bone marrow, peripheral blood, and lymph node biopsies will be collected to evaluate the therapy.
- The lentiviral vector is 3rd generation. The transgene is not an oncogene. Transduction of differentiated T cells is unlikely to lead to transformation by insertional mutagenesis and has not been observed in other trials. Tests for replication competent viruses are included at the appropriate points in the protocol.
- The draft BUA letter was shown.
- The trainings are all up to date.
- A member made a motion to approve the draft BUA letter for Dr. Till. Another member seconded the motion.



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

**19. Hyde, Jennifer, new, *Contribution of virus-host interactions to viral pathogenesis***

- Three members of the IBC served as the Subcommittee Reviewers. Two ad-hoc viral experts also served as reviewers. One of the Subcommittee Reviewers presented the Subcommittee Report.
- This is a new application. The investigator is requesting to use wildtype herpes simplex virus types 1 and 2, as well as recombinant strains of Ross River virus and Sindbis virus.
- A recombinant strain of Venezuelan equine encephalitis virus (TC-83 strain, which is exempt from select agent regulations). A subcommittee was assigned to assess the genetic modifications that will be made to the VEEV.
- The investigator has several safeguards in place to ensure that virulent VEEV is not generated. No protein-coding mutations will be introduced into TC83. The 5'UTR of TC83 will not be mutated. Modifications will be made only in non-coding sequences of the E2 region.
- The PI provided a detailed list of mutations and known effects, as well as a narrative clarifying the genetic determinants of the alphavirus pathogenesis.
- Some questions on the BUA application (36, 43, and 45) need to be revised to make it clear that the investigator is not planning experiments that would increase the virulence of the TC-83 strain of VEEV.
- A discussion occurred about the VEEV vaccine and whether vaccination of lab staff or implementation of a medical management plan was necessary or appropriate. The subcommittee felt that the negative side effects of the vaccine would likely offset the benefits of the vaccination, but that consideration is warranted. The Employee Health Physician will examine this study and decide what, if any, medical management plan will be in place for this project.
- The lab successfully passed the lab inspection and the trainings are all up to date.
- The draft BUA letter was shown.
- A member made a motion to approve the draft BUA letter for Dr. Hyde, pending correction of the BUA application to clarify that the virulence of TC-83 will not be enhanced. Another member seconded the motion.
- The Committee voted unanimously to approve the draft BUA for Dr. Hyde, pending correction of the BUA application to clarify that the virulence of TC-83 will not be enhanced.

**ISSUES FROM THE FLOOR & PUBLIC COMMENTS:**

There were no issues from the floor, and no public comments.

**MEETING ADJOURNED AT APPROXIMATELY 11:54 a.m.**