INSTITUTIONAL BIOSAFETY COMMITTEE

UNIVERSITY of WASHINGTON

Meeting Minutes

Date: Wednesday, February 18, 2015
Time: 10:00 AM – 12:00 PM

Location: Health Sciences Building T-269

Members Present:

1. Michael Agy, Washington National Primate Research Center
2. H.D. "Toby" Bradshaw, Biology *(Plant Expert)*
3. Lesley Colby, Comparative Medicine *(Animal Containment Expert)*
4. Elizabeth Corwin (*Human Gene Transfer Expert; IBC Vice Chair*)
5. Jean Haulman, UW Travel Clinic
6. Stephen Libby, Laboratory Medicine (*IBC Chair*)
7. Jeanot Muster, Pharmacology
8. Matthew R. Parsek, Microbiology
9. Angela Rasmussen, Microbiology
10. Mei Y. Speer, Bioengineering
11. Eric Stefansson, Environmental Health & Safety (*Biosafety Officer*)

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 21, 2015 minutes meeting.
   - A member made a motion to approve the January 21, 2015 minutes. Another member seconded the motion.
   - The committee voted unanimously to approve the January 21, 2015 meeting minutes.

4. **BIOSAFETY OFFICER (BSO) REPORT***:* The BSO report is for project reviews involving infectious agents and for projects falling under Section III-E and III-F of the *NIH Guidelines*.

   a. Biosafety Officer Report
      - The IBC Chair sought a motion to approve this month's Biosafety Officer Report.
      - Dr. Swisher received a new approval to work with human source material.
      - Dr. Lee added new rooms to his approval.
      - Dr. Gottlieb received approval to work with non-recombinant strains of SIV (simian immunodeficiency virus).
      - Dr. Mefford received a new approval to work with human source material.
      - Dr. Rieke added a new room to his approval.
      - Dr. Liu moved some animals from one vivarium to another.
      - Dr. Klatt received approval to work with non-recombinant strains of SIV.
      - Dr. Neumann renewed a BUA involving work with human source material.
      - Dr. Tang added the use of enhanced gene delivery methods.
      - Dr. Frevert received approval for a new agent, *Salmonella typhimurium*.
      - Dr. Dodd received approval for two new agents, *Klebsiella pneumoniae* and *Staphylococcus aureus*.
      - Dr. Juul renewed a BUA involving human and non-human primate source material.
      - 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. **INDIVIDUAL PROJECT REVIEWS**

   1. Adams-Waldorf, Kristina, renewal, *Experimental Model for Chorioamnionitis and Preterm Labor*
      - The assigned IBC Primary Reviewer presented the Primary Review.
      - The lab researches the relationships among intrauterine infection, inflammatory responses, and preterm birth. A non-human primate model is used. The lab also investigates new therapeutics to inhibit preterm labor.
      - Agents used on this project include pathogenic strains of *Escherichia coli (E. coli)* and recombinant strains of *Streptococcus agalactiae*.

- The lab inspection has been completed and the training records are in place.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Adams-Waldorf. A second is not needed since he is the Primary Reviewer.
- The Committee voted unanimously to approve the draft BUA for Dr. Adams-Waldorf.

2. Altemeier, William, renewal, *Inflammatory Response Modulation by Mechanical Ventilation*

- The assigned IBC Primary Reviewer presented the Primary Review.
- The lab studies lung injuries. The goals of the project are to understand mechanisms by which lung inflammation, injury, and resolution of injury occur in response to a variety of acute injuries, including mechanical ventilation, microbial pathogens, and allergic sensitization.
- Agents used on this project include adenoviral vectors and *Staphylococcus aureus*.
- The draft BUA letter was shown.
- There are still deficiencies that need to be corrected from the lab inspection.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Altemeier. A second is not needed since he is the Primary Reviewer.
- The Committee voted unanimously to approve the draft BUA for Dr. Altemeier, contingent upon correction of the deficiencies found during the lab inspection.

3. Bothwell, Mark, renewal, *Neurotrophin Receptor Interactions*

- The assigned IBC Primary Reviewer presented the Primary Review.
- The lab studies signaling mechanisms of cell surface receptors that control neural function. Human iPS (induced pluripotent stem) cells are used. The cells are acquired from a collaborator.
- Agents used on the protocol include lentiviral vectors and human iPS cells.
- Training records are in place and the lab inspection has been completed.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Bothwell. A second is not needed since she is the Primary Reviewer.
- The Committee voted unanimously to approve the draft BUA for Dr. Bothwell.

4. Bryers, James, new, *Periodontal Biomaterials with BITE (NIDCR)*

- The assigned IBC Primary Reviewer presented the Primary Review.
- The goal of the project is to develop a series of polymeric biomaterials that will promote tissue regeneration by controlling immune cell responses.
- Plasmid DNA in mice is used. Several species of risk group 2 bacteria, including *Pseudomonas aeruginosa* and *Staphylococcus aureus*, are also used.
- The training needs to be completed. There are some minor lab deficiencies that need to be corrected.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Bryers. A second is not needed since he is the Primary Reviewer.
- The Committee voted unanimously to approve the draft BUA for Dr. Bryers, contingent upon completion of training and resolution of the lab inspection deficiencies.

5. Kimelman, David, renewal, *Early Fish Development*

- The assigned IBC Primary Reviewer presented the Primary Review.
- The lab uses transgenic zebrafish. The lab studies the early development of the zebrafish embryo as a model system for human development.
- Human cell lines are also used on this project.
- Training records are in place, and the lab inspection has been completed.
- The draft BUA letter was shown.
- A discussion occurred regarding whether or not work with embryonic zebrafish that will never mature into live zebrafish should be listed on the BUA letter. The committee decided that since embryonic zebrafish are not live animals, work with the embryos should be considered akin to work with zebrafish tissue or cells. The committee decided that the embryonic zebrafish that will never mature into live zebrafish should not be on the BUA letter. The biosafety officer will edit the letter accordingly.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Kimelman. A second is not needed since he is the Primary Reviewer.
- <u>The Committee voted unanimously to approve the draft BUA for Dr. Kimelman, contingent upon removing the room with embryonic zebrafish from the BUA letter.</u>

6. Paik, Jisun, renewal, *Nutrition, Inflammation, and Obesity*

- The assigned IBC Primary Reviewer presented the Primary Review.
- The overall goal of the research is to develop inhibitors for retinoic acid biosynthesis. These inhibitors could potentially be used to treat obesity, or used as male contraceptives.
- Agents used on the project include human cells and lentiviral vectors. Non-exempt *E. coli* is also used. A brief discussion about this agent occurred. The *E. coli* used on this project is non-pathogenic and worked with at BSL-1, but only K-12 derivative strains are specifically exempted from the NIH Guidelines. This strain is not a K-12 derivative and so it falls under section III-E of the NIH Guidelines.
- There are a couple of answers on the BUA application that should be clarified (question 23 and 32).
- The draft BUA letter was shown.
- The lab inspection is scheduled for later this week.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Paik. A second is not needed since he is the Primary Reviewer.
- <u>The Committee voted unanimously to approve the draft BUA for Dr. Paik, pending correction of the BUA application and successful completion of a lab inspection.</u>

7. Rubel, Edwin, renewal, *Development, Function, and Regeneration of the Auditory System + in Ovo Gene Expression*

- The assigned IBC Primary Reviewer presented the Primary Review.
- The lab researches the auditory system. The overall goal of the research is to understand how the various parts of the auditory system develop normally, in order to be able to therapeutically intervene in cases of congenital hearing loss.
- AAV (adeno-associated viral vectors) are used in chickens and chicken embryos.
- Diphtheria toxin and tetrodotoxin are also used. The investigator is working on SOPs for these agents.

- The investigator should clarify how transgenic mice are used on this project. It appears that they will be used to generate inner ear cell culture systems for transduction with AAV vectors or transfection with plasmids expressing genes of interest. This could be explained more clearly in the BUA application.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Rubel. A second is not needed since she is the Primary Reviewer.
- <u>The Committee voted unanimously to approve the draft BUA for Dr. Rubel, contingent upon submitting toxin SOPs, and clarifying how transgenic mice are used on the project.</u>

8. Schwartz, Michael, change, *Neuro-Endocrine Control of Energy Balance*

- The assigned IBC Primary Reviewer presented the Primary Review.
- The investigator is requesting to add a modified rabies virus vector for use in mice.
- The rabies virus vector is avian pseudotyped. This means that it does not have the correct capsid gene to infect mammalian cells. The rabies virus vector is also missing the glycoprotein that would allow the virus to spread across synapses.
- The mice cannot shed the rabies virus vector. The rabies vector can only infect and replicate inside a single neuron.
- If this rabies virus vector were to be accidentally injected into a human, no immune response or disease would occur because humans lack Cre recombinase.
- A discussion occurred regarding the biosafety level of the rabies virus vector.
- A question was raised about the wording on the BUA letter, RVΔG-EnvA. The strain name is SAD. The IBC member wondered if 'SAD' should be incorporated into the agent name on the BUA letter.
    - EH&S will research this and make sure we are using the correct wording.
- The draft BUA letter was shown.
- The lab inspection has been completed and training records are in place.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Schwartz. A second is not needed since he is the Primary Reviewer.
- <u>The Committee voted unanimously to approve the draft BUA for Dr. Schwartz.</u>

9. Wong, Rachel, renewal, *Development of the retina (fish)*

- The assigned IBC Primary Reviewer presented the Primary Review.
- The PI studies neural development and regeneration. Two transgenic zebrafish lines are used. *E. coli* is also used to clone genes.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Wong. A second is not needed since he is the Primary Reviewer.
- <u>The Committee voted unanimously to approve the draft BUA for Dr. Wong, contingent upon completion of the lab inspection.</u>

10. Wong, Rachel, renewal, *Development of the retina (mouse)*

- The assigned IBC Primary Reviewer presented the Primary Review.
- This is very similar to Dr. Wong's previous project except that it involves mice instead of zebrafish. Dr. Wong has two IACUC protocols and so there is a different BUA letter that corresponds to each protocol.
- Transgenic mice are used and plasmid DNA is administered to the mice.

- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Wong. A second is not needed since he is the Primary Reviewer.
- The Committee voted unanimously to approve the draft BUA for Dr. Wong, contingent upon completion of the lab inspection.

SUBCOMMITTEE REPORTS:

11. Disis, Mary, renewal, *A Phase I Trial of the Safety and Immunogenicity of a DNA Plasmid Based Vaccine Encoding the Amino Acids 1-163 of Insulin-Like Growth Factor Binding Protein-2 (IGFBP-2) in Patients with Advanced Ovarian Cancer*

- Three members of the IBC served as the Subcommittee Reviewers. One of the Subcommittee Reviewers presented the Subcommittee Report, which is attached.
- The draft BUA letter was shown.
- This is a renewal application. The intent of the research is to study the safety of this vaccine as a potential treatment for ovarian cancer cells.
- The trial began in March 2012 and is no longer accruing new subjects, but is still monitoring patients and collecting blood samples from them.
- The study has been reviewed by the RAC (recombinant DNA advisory committee).
- A member made a motion to approve the draft BUA letter for Dr. Disis. Another member seconded the motion.
- The Committee voted unanimously to approve the draft BUA for Dr. Disis.

12. Kiem, Hans-Peter, new, *A Phase-I trial of gene modified stem-cells to generate HIV-resistant cells in conjunction with standard chemotherapy for treatment of lymphoma in patients with HIV infection*

- Three members of the IBC served as the Subcommittee Reviewers. One of the Subcommittee Reviewers presented the Subcommittee Report, which is attached.
- This study seeks to determine whether an autologous stem cell transplant with stem cells modified to confer HIV resistance is safe and feasible in HIV-positive patients with Hodgkin on Non-Hodgkin Lymphoma who have completed first-line treatment and are in remission. The study also seeks to determine whether in vivo selection with a low dose of chemotherapy will increase the level of gene modified cells.
- The RAC performed an initial review of this proposal, but determined that no in-depth review or public RAC discussion was required.
- Third-generation lentiviral vectors are used. The vectors are created by an outside company. The activities performed at UWMC (UW Medical Center), including handling and re-infusion of transduced cells, require BSL-2 containment.
- The informed consent documents were reviewed by the subcommittee appear to clearly state the objectives of the study, as well as the risks, some of which are unknown. The consent forms will also be reviewed by the Fred Hutchinson Cancer Research Center IRB (institutional review board).
- The draft BUA letter was shown.
- A discussion occurred regarding the wording of the agent used.
- A member made a motion to approve the draft BUA letter for Dr. Kiem. Another member seconded the motion.
- The Committee voted unanimously to approve the draft BUA for Dr. Kiem.

13. Kiem, Hans-Peter, new, *Autologous transplantation and stem cell based-gene therapy with LVsh5/C46 (CAL-1), a dual anti-HIV lentiviral vector, for the treatment of HIV-associated lymphoma*

- Three members of the IBC served as the Subcommittee Reviewers. One of the Subcommittee Reviewers presented the Subcommittee Report, which is attached.
- This study seeks to determine whether an autologous stem cell transplant with Cal-1 modified stem cells is safe and feasible in HIV-positive patients with Hodgkin on Non-Hodgkin Lymphoma. Cal-1 seeks to make target cells (CD4+ T lymphocytes) resistant to HIV infection. The research participants who participate in the study are already eligible to receive an autologous stem cell transplant as standard of care.
- The RAC performed an initial review of this proposal, but determined that no in-depth review or public RAC discussion was required.
- Third-generation lentiviral vectors are used. The vectors are created by an outside company. The activities performed at UWMC (UW Medical Center), including handling and re-infusion of transduced cells, require BSL-2 containment.
- As with the previous study, the informed consent documents were reviewed by the subcommittee appear to clearly state the objectives of the study, as well as the risks, some of which are unknown. The consent forms will also be reviewed by the Fred Hutchinson Cancer Research Center IRB (institutional review board).
- The draft BUA letter was shown.
- A member made a motion to approve the draft BUA letter for Dr. Kiem. Another member seconded the motion.
- <u>The Committee voted unanimously to approve the draft BUA for Dr. Kiem.</u>

FOR YOUR INFORMATION:

- The RAC reviewed the consent language for Dr. Disis's clinical trial *A Phase I Trial of the Safety and Immunogenicity of a Multiple Antigen Vaccine (STEMVAC) in HER2 Negative Advanced Stage Breast Cancer Patients*. This is not the same project that the committee discussed earlier this meeting. The RAC review noted that the target population for this trial is likely to be infertile, and stated that the consent form should be clearer that pregnancy is an unlikely event. The RAC also commented that the consent language should clarify that withdrawal from the study means withdrawal from future monitoring and not from any potential effects of the gene transfer agent. The RAC also stated that the use of the term 'vaccine' may lead participants to think that this is an established approach and suggested that modified wording like 'experimental vaccine' or 'study vaccine' should be used instead.
    - Dr. Disis revised the consent language and sent it to the IBC for review. The subcommittee who originally reviewed the project *A Phase I Trial of the Safety and Immunogenicity of a Multiple Antigen Vaccine (STEMVAC) in HER2 Negative Advanced Stage Breast Cancer Patients* reviewed the revised consent wording and decided that it addressed all of the RAC's concerns.
- In December, the committee reviewed Dr. Alvin Liu's project and decided to table the vote until we received more information about the lentiviral vectors and the proposed facilities. Dr. Liu has decided to use plasmid DNA for a vector rather than lentiviral vectors, and so BSL-2 containment is appropriate. The revised BUA letter was shown. A member made a motion to approve the draft BUA letter for Dr. Liu. Another member seconded the motion. The Committee voted unanimously to approve the draft BUA for Dr. Liu.

- We have received a response to an NIH report that was sent in October. A researcher experienced a splash to the face from the syringe when administering recombinant *Listeria monocytogenes* during a tail vein injection into a mouse. Proper post-exposure protocols were followed. The PI purchased additional personal protective equipment to help prevent an incident like this from occurring in the future. Staff members were also retrained regarding how to perform tail vein injections safely. The NIH reviewed the report and determined that the actions the university took in response to the incident were sufficient. The NIH does not require any further information.

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

MEETING ADJOURNED AT APPROXIMATELY 11:47 am.