INSTITUTIONAL BIOSAFETY COMMITTEE

UNIVERSITY of WASHINGTON

Meeting Minutes

Date: Wednesday, July 16, 2014
Time: 10:00 AM – 12:00 PM

Location: Health Sciences Building T-269

Members Present:
1. Michael Agy, Washington National Primate Research Center
2. Thea Brabb, Comparative Medicine
3. Lesley Colby, Comparative Medicine
4. Elizabeth Corwin, Community Member
5. Jean Haulman, UW Travel Clinic
6. Stephen Libby, Laboratory Medicine
7. Scott Meschke, Environmental & Occupational Health Sciences
8. Mei Y. Speer, Bioengineering
9. Eric Stefansson, Environmental Health & Safety
10. Paul Swenson, Community Member, Seattle-King Co. Dept of Public Health
11. Valerie Yerkes, Community Member

Members Absent:
12. H.D. "Toby" Bradshaw, Biology
13. Jeanot Muster, Pharmacology
14. Matthew R. Parsek, Microbiology

Guests Present:
1. David Anderson, Executive Director, Health Sciences Administration
2. Linda Arnesen, Biosafety Officer, EH&S Research & Occupational Safety
3. Andrea Badger, IBC/Research Coordinator, EH&S Research & Occupational Safety
4. Jacqui Bales, Biosafety Officer, EH&S Research & Occupational Safety
5. Michael Bobola, Review Scientist, Office of Animal Welfare
6. Judy Cashman, Occupational Health Nurse, EH&S Research & Occupational Safety
7. Gabe Han, Summer Intern, EH&S Research & Occupational Safety
8. Tony Han, Biosafety Officer, EH&S Research & Occupational Safety
9. Katia Harb, Assistant Director, EH&S Research & Occupational Safety
10. Lesley Leggett, Biosafety Officer, EH&S Research & Occupational Safety
11. Glenn McLean, Biosafety Officer, EH&S Research & Occupational Safety

1. **CALL TO ORDER:** Steve Libby called the meeting to order at 10:04. A quorum was present.

2. **REMINDER:** Steve Libby 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. **INDIVIDUAL PROJECT REVIEWS** *(IBC member Primary Reviewer Reports and Biological Use Authorization (BUA) letters available as separate documents)*

    1. Atkins, William, new, *Analytical Biopharmacy Core Facility*
    - Eric Stefansson served as the Primary Reviewer and Linda Arnesen served as the Biosafety Officer Reviewer. Eric Stefansson presented the Primary Reviewer Report.
    - This application is for a new core facility that will study the interactions between proteins and other materials.
    - Each investigator who wishes to use this new facility will have to obtain their own BUA letter.
    - The investigator still needs to finish completing all SOPs for this new facility. The SOPs will need to be reviewed by the biosafety officer.
    - Mei Speer entered the meeting at 10:12.
    - The draft BUA letter was shown.
    - Eric Stefansson made a motion to approve the draft BUA for Dr. Atkins. A second is not needed since he is the Primary Reviewer.
    - <u>The Committee voted unanimously to approve the draft BUA for Dr. Atkins, with the condition that the investigator finish completing SOPs.</u>

    2. Bornfeldt, Karin, change, *Cardiovascular Disease and Diabetes*
    - Paul Swenson served as the Primary Reviewer and Jacqui Bales served as the Biosafety Officer Reviewer. Paul Swenson presented the Primary Reviewer Report.
    - This change requests the addition of adeno-associated viral vectors.
    - The lab inspection and training are up to date.
    - The draft BUA letter was shown.
    - Paul Swenson made a motion to approve the draft BUA for Dr. Bornfeldt. A second is not needed since he is the Primary Reviewer.
    - <u>The Committee voted unanimously to approve the draft BUA for Dr. Bornfeldt.</u>

    3. Frevert, Charles, new, *A Transgenic Mouse Model of Scrapie*
    - Thea Brabb served as the Primary Reviewer and Lesley Leggett served as the Biosafety Officer Reviewer. Thea Brabb presented the Primary Reviewer Report.
    - The investigator is breeding mice that over-express the normal (non-infectious) prion protein of sheep. This makes the mice susceptible to the prion that causes scrapie. However, the mice do not have any prion disease and are not infectious.
    - The mice can be housed at ABSL-1.
    - The draft BUA letter was shown.
    - Thea Brabb made a motion to approve the draft BUA for Dr. Frevert. A second is not needed since she is the Primary Reviewer.
    - <u>The Committee voted unanimously to approve the draft BUA for Dr. Frevert.</u>
    - *Post-Meeting Update: Because the IBC review determined that ABSL-1 housing was sufficient, the only agent that would appear on Dr. Frevert's BUA letter is standard*

transgenic mice, which are exempt. The IBC does not issue BUA letters for research projects that involve only exempt work, and therefore, Dr. Frevert will not be issued a BUA letter for this project.

4. Hajjar, Adeline, renewal, *Linking Innate and Adaptive Immunity*

- Scott Meschke served as the Primary Reviewer and Glenn McLean served as the Biosafety Officer Reviewer. Scott Meschke presented the Primary Reviewer Report.
- The lab studies the innate immune response to a variety of pathogens.
- Many risk group 2 are used, including *Salmonella typhimurium*, *Bordetella pertussis*, and *Listeria monocytogenes*.
- There is an error on the BUA letter. Human feces is listed as BSL-2 and III-D*. The III-D* notation is used for wild-type agents in transgenic mice, but "human feces" is not an "agent" according to the *NIH guidelines*. The NIH section should be NA.
- The draft BUA letter was shown. A footnote needs to be added to the BUA letter.
- Scott Meschke made a motion to approve the draft BUA for Dr. Hajjar. A second is not needed since he is the Primary Reviewer.
- The Committee voted unanimously to approve the draft BUA for Dr. Hajjar, contingent upon correction of the BUA letter.

5. Keel, Sioban, renewal, *Mechanisms of Anemia*

- Steve Libby served as the Primary Reviewer and Lesley Leggett served as the Biosafety Officer Reviewer. Steve Libby presented the Primary Reviewer Report.
- The lab's research involves attempting to determine why red blood cell development fails when a phosphate protein is dysfunctional. The lab also studies red blood cell development in general.
- The agents used include various types of viral vectors, and human cells.
- The lentiviral vectors used in this project are third generation, and so the work with oncogenes can proceed at BSL-2. The documentation regarding the lentiviral vectors were shown to the committee. The committee decided the documentation was sufficient.
- Steve Libby will amend his review to indicate the work with oncogenes.
- The draft BUA letter was shown.
- Steve Libby made a motion to approve the draft BUA for Dr. Keel. A second is not needed since he is the Primary Reviewer.
- The Committee voted unanimously to approve the draft BUA for Dr. Keel.

6. Ladiges, Warren, change, *Mouse Genomics Program*

- Matt Parsek served as the Primary Reviewer and Linda Arnesen served as the Biosafety Officer Reviewer. On behalf of Matt Parsek, Steve Libby presented the Primary Reviewer Report.
- This change is requesting to add the use of adeno-associated virus.
- The draft BUA letter was shown.
- Steve Libby made a motion to approve the draft BUA for Dr. Ladiges. A second is not needed since he endorsed the primary review.
- The Committee voted unanimously to approve the draft BUA for Dr. Ladiges.

7. Monnat, Raymond, new, *Small Molecule Protection of Bone Marrow Hematopoietic Stem Cells*

- Mei Speer served as the Primary Reviewer and Jacqui Bales served as the Biosafety Officer Reviewer. Mei Speer presented the Primary Reviewer Report.
- The lab works to find new approaches to prevent or delay bone marrow failure or leukemia in people who are at risk of these outcomes.
- The investigator uses lentiviral vectors to knock down genes, and the target protein is FANCG, which is listed as an oncogene in the Cancer Gene Census. When defective, it increases the risk of developing tumors.
- The lentiviral vectors are third generation, which means the work with the oncogenic inserts can proceed at BSL-2. The committee reviewed the documentation submitted by the investigator and decided it was sufficient.
- The draft BUA letter was shown.
- Mei Speer made a motion to approve the draft BUA for Dr. Monnat. A second is not needed since she is the Primary Reviewer.
- The Committee voted unanimously to approve the draft BUA for Dr. Monnat.

8. Oberst, Andrew, change, *Programmed Cell Death and Immunity*

- Michael Agy served as the Primary Reviewer and Jacqui Bales served as the Biosafety Officer Reviewer. Michael Agy presented the Primary Reviewer Report.
- The investigator is adding several strains of mouse adapted influenza virus.
- The draft BUA letter was shown.
- Michael Agy made a motion to approve the draft BUA for Dr. Oberst. A second is not needed since he is the Primary Reviewer.
- The Committee voted unanimously to approve the draft BUA for Dr. Oberst.

9. Rabinovitch, Peter, change, *Biology of Aging*

- Valerie Yerkes served as the Primary Reviewer and Linda Arnesen served as the Biosafety Officer Reviewer. Valerie Yerkes presented the Primary Reviewer Report.
- The investigator wishes to add adeno-associated viral vectors to his list of approved agents.
- The investigator has retaken the biosafety training.
- The draft BUA letter was shown.
- Valerie Yerkes made a motion to approve the draft BUA for Dr. Rabinovitch. A second is not needed since she is the Primary Reviewer.
- The Committee voted unanimously to approve the draft BUA for Dr. Rabinovitch.

10. Stamatoyannopoulos, George, new, *Insulators and enhancers for globin gene therapy vectors*

- Jeanot Muster served as the Primary Reviewer and Glenn McLean served as the Biosafety Officer Reviewer. On behalf of Jeanot Muster, Steve Libby presented the Primary Reviewer Report.
- The lab studies hemoglobin and blood cell development.
- The lab work involves a variety of agents, including gammaretroviral vectors, lentiviral vectors, and human cells.
- The draft BUA letter was shown.
- The training has lapsed for several lab members.
- The lab inspection revealed that the facility has a few deficiencies that need to be corrected.

- Steve Libby made a motion to approve the draft BUA for Dr. Stamatoyannopoulos. A second is not needed since he endorsed the primary review.
- The Committee voted unanimously to approve the draft BUA for Dr. Stamatoyannopoulos, pending completion of training and resolution of facility issues.

11. Stetson, Daniel, change, *Mechanisms and Consequences of Innate Immune Detection of Nucleic Acids*

- Matt Parsek served as the Primary Reviewer and Lesley Leggett served as the Biosafety Officer Reviewer. On behalf of Matt Parsek, Steve Libby presented the Primary Reviewer Report.
- The investigator is requesting to add the use of recombinant human cytomegalovirus, herpes simplex virus type 1, vaccinia virus, and mouse cytomegalovirus.
- Although mouse cytomegalovirus strains only require BSL-1 containment, the PI has chosen to use BSL-2 containment.
- The draft BUA letter was shown.
- The PI's training is current.
- Steve Libby made a motion to approve the draft BUA for Dr. Stetson. A second is not needed since he endorsed the primary review.
- The Committee voted unanimously to approve the draft BUA for Dr. Stetson.

12. Ware, Carol, change, *Human ES Cell Core*

- Steve Libby served as the Primary Reviewer and Glenn McLean served as the Biosafety Officer Reviewer. Steve Libby presented the Primary Reviewer Report.
- The investigator wishes to add the use of adeno-associated viral vectors.
- AAV vector work is a risk group 1 agent requiring BSL-1 containment, but the entire Ware core facility is operated at BSL-2.
- The draft BUA letter was shown.
- Steve Libby made a motion to approve the draft BUA for Dr. Ware. A second is not needed since he is the Primary Reviewer.
- The Committee voted unanimously to approve the draft BUA for Dr. Ware.

SUBCOMMITTEE REPORTS:

1. Human Cells Subcommittee

- The Human Cells subcommittee has an update regarding the proposal to lower biocontainment of animals currently housed at ABSL-2 after they have been administered human cells.
- The subcommittee members are in agreement about several key aspects of the proposal.
    - All subcommittee members agree that direct handling and administration of cells of human origin require BSL-2 containment.
    - Risk assessments would still be performed on a case-by-case basis by both the IBC and Institutional Animal Care and Use Committee (IACUC). For example, humanized animals would be excluded from the proposal.

    - Housing of fish administered any human cell (primary human cells, immortalized human cell lines, or human cells passaged in-vivo) can safely be lowered to ABSL-1.
    - Mice and rats, guinea pigs, and rabbits can safely be housed at ABSL-1 following administration of immortalized human cell lines and human cells passaged in-vivo.
- There was not consensus among the subcommittee regarding housing containment required for mice and rats, guinea pigs, and rabbits following administration of primary human cells.
    - The argument for ABSL-1 housing is based on the low risk of a human tissue donor harboring an undetected infection which could then be successfully transmitted to produce a viable infection in the animal. Also, the containment practices at ABSL-2 don't offer significantly more protection against needlestick exposure events, which are the primary route of exposure for human bloodborne pathogens or for LCMV (lymphocytic choriomeningitis), than do ABSL-1 containment practices and personal protective equipment.
    - The argument for ABSL-2 housing is based on the potentially severe consequences should an unlikely transmission event of LCMV or human BBP occur. A viable infection in the mice could endanger personnel safety and endanger the vivarium colony. A widespread outbreak could devastate the animal colony and result in lost research time and lost resources.
- The IBC members provided input on these issues. Several members echoed the concerns regarding animal facility personnel safety and colony integrity.
- The committee was not given a draft proposal to review prior to the meeting. Also, the proposal still contains gaps and differences of opinion among the subcommittee members. Therefore, the proposal will not be voted on at today's meeting, with the exception of the fish section of the proposal. All subcommittee members are in clear agreement that it is safe to house fish at ABSL-1 after administration of all types of human cells.
- Steve Libby made a motion to approve only the fish section of the draft proposal, which states administration of human cells to fish will be conducted at ABSL-2, and then housing will be conducted at ABSL-1.
- <u>The Committee voted unanimously to approve only the fish section of the draft proposal.</u>
- The rest of the proposal will be tabled until the next IBC meeting.

2. Viral Vector Subcommittee

- The Viral Vector Subcommittee has a draft proposal regarding the bloodborne pathogen issue that was discovered when working on the lentiviral vector proposal, which was voted on during the April meeting.
    - The lentiviral vector proposal contained two determinations relating to bloodborne pathogens: (1) Viral vector products prepared with human cell lines are at very low risk of contamination with bloodborne pathogens (BBP) and other potentially hazardous infectious agents. (2) These viral vector products are nevertheless subject to WISHA BBP rules regarding products derived from human cells.
    - This bloodborne pathogen proposal acknowledges that viral vectors are subject to the WISHA BBP rules, but notes that the BBP standards do not call

for a specific biosafety level. Therefore, due to the extremely low risk of BBP contamination, the subcommittee has determined that, in general, viral vectors can continue to be worked with at BSL-1.
        - There are some exceptions and specifications to the proposal. At this time, only viral vectors generated specifically in HEK293T cells are eligible to be worked with at BSL-1. Viral vectors generated in any other cell lines must be reviewed on a case-by-case basis. Also, adenoviral vectors are exempted from the proposal due to a slightly higher risk and the potential that the E1 gene could be mobilized.
    - All lab work with human cells, for example, during the generation of viral vectors, must still be conducted at BSL-2. Work directly with HEK293T cells must be done at BSL-2. Only the resulting viral vectors (adenoviral vectors excluded) may be worked with at BSL-1.
- Steve Libby made a motion to approve the proposal, which is titled "A proposal and rationale to mitigate the impact of the Bloodborne Pathogen standards on research with recombinant viral vectors generated in established human cell lines" and dated July 11, 2014.
- The Committee voted unanimously to approve "A proposal and rationale to mitigate the impact of the Bloodborne Pathogen standards on research with recombinant viral vectors generated in established human cell lines," version dated July 11, 2014.

FOR YOUR INFORMATION:

- Andrea Badger presented the final edits that have been made to the BUA application and BUA change form. Questions have been modified in response to the lentiviral vector proposal. The form will be uploaded to the EH&S website and available for use in August.
- Steve Libby made a motion to approve the revised BUA application and BUA change form and the new change in PI form, with an understanding that minor revisions may still continue until the BUA is uploaded to the EH&S website.
- The Committee voted unanimously to approve the revised BUA application and revised BUA change form and new change in PI form.

MEETING ADJOURNED AT APPROXIMATELY 12:06.