



**NCI-FREDERICK
INSTITUTIONAL BIOSAFETY COMMITTEE**

Minutes
May 15, 2007
NCI-Frederick

The NCI-Frederick Institutional Biosafety Committee was convened at 12:10 p.m. in the Building 549 Executive Boardroom with the following members in attendance:

Ms. Theresa Bell, Secretary	Dr. Henry Hearn
Dr. Randall Morin	Dr. David Garfinkel
Ms. Alberta Peugeot	Dr. Mike Baseler
Dr. Bruce Crise	Dr. Stephen Creekmore
Ms. Dianna Boissey	Dr. Stephen Hughes
Dr. Jeanne Herring	

Members not in attendance: Dr. Melinda Hollingshead, Dr. Dan McVicar, Dr. David Garfinkel, and Mr. Lucien Winegar

Others in attendance: Ms. Cara Leitch, Dr. Robert Thomas, and Dr. Scott Keimig

INTRODUCTION

The March minutes were distributed during the meeting and a vote will be taken by email.

PROTOCOL REVIEWS

NEW BUSINESS

(07-25) Trinchieri/Noer

- Need more in-depth form for PIs submitting samples to complete for cell sorting requests
- No mo-flo or aerosol containment mentioned
- Containment machine in room w/ 2 other machines-everyone with potential for exposure must be informed and covered

- Judgment call for PI on whether to allow the material into facility (need procedure in place)
- Map test
- Need procedure in place that they are not generating an aerosol
- Are there viral sequences that have been knowingly added to the sample? – should be on sample receipt questionnaire form
- PI submitting samples should be required to submit SOP on how/where/who inactivated the pathogen/virus.
- Are there viral sequences that have been knowingly added to the sample? Add this to the form.
- Use Part B of the IBC form is a good template for additional questions to ask on the cell sorting form.
- Clearly define if materials will be accepted fixed or unfixed, infectious or non-infectious.
- PI giving samples must have an IBC registration. Change question “Any applicable IBC registration #” to “IBC Registration number”(mandatory)
- Are cells going to be screened for replication competence?
- Elaborate on the SOP (insert all specific information requested in this review)
- SOP should include this statement “These machines will not be operated by anyone other than ... (so it is clear who has the potential for exposure).”
- SOP for both mop-flo and other cell sorters should specify how the aerosol management system contains the aerosols? Please provide a procedure for this. How do you know aerosol-containment device is working?
- SOP should state how often the machine is tested (monthly, quarterly, etc.)?
- SOP should include machine testing when in clog or failure mode to see what happens to the particles.
- Reference the VRC website on how to test with Glo-germ and identify the frequency with which this test will be done.
- SOP should clarify that operator must constantly be able to see the gauges. Will operator be with the machine while running samples?
- B6a, B5h1, and SOP - Protective respirator is a good idea (N95 masks or N100). Should not leave PPE options up to the user - set a PPE standard for everyone.
- Part B “if anything tests +, will not be sorted/has to be fixed” should always fix to be on the safe side (will this ruin certain experiments)
- It is a judgment call for your group on whether to allow certain materials into your facility, so a specific procedure should be in place for this.
- Will you be sorting samples from NIH?
- Routine maintenance needed - run Clorox behind, replace lines, or do both?
- Lower risk: MoFlo - pressurized tube, splash guard
- Higher risk: FACSAria seal and pressurized chamber (no tubing should be used here)

Dr. Baseler made a motion to defer approval, Dr. Crise seconded and all were in favor.

RENEWALS

(07-26) Farrar

- Is this registration based on assumptions that the material is replication incompetent? (Phoenix cell lines are replication competent. If mice tumors)
- This is a complex registration with a lot of different work going on.
- B5h1 fumigated hood – is this addressing a Chemical Fume Hood or Biosafety Cabinet?
- Clarify D3b and D5

Dr. Creekmore made a motion to approve with the above stipulations resolved, Dr. Crise seconded and all were in favor.

(07-24) Hussain

- Verify how the C parvum is heat inactivated. It is a heat fixed live bug.
- C-10, 100 microliters is a small amount
- Clarify the material is purchased in vials then boiled and verified by plating it out on agar plates

Dr. Garfinkel made a motion to approve, pending resolution of the above issues, Dr. Baseler seconded and all were in favor.

(07-23) Oppenheim/Howard

- PI may want to initiate separate registrations according to materials used and procedures performed for easier understanding of work and to assist with future amendments.
- Does this submittal include any NEW work or is this only a combination of the work previously included in IBC 05-31 and Pathogen registration?
- (A1) Prokaryote and eukaryote expression vectors
- List and describe each expression vector system and what will be done with each, by whom and where.
- Common cell lines (human and mice)—each need to be described along with their application.
- Transfections (each of these will need to be described)? Are these only for making mice?
- Vector expression in pro and eu –karyote cell lines
- Gene gun delivery into mouse models should be described in detail
 - Gene Gun description (see Part E).
 - Transgenic animal production (to be included here or future amendment?)
 - Immortalization of primary mouse fibroblasts from Tg or KO mouse strains (where is this described?)
- Viruses, vectors, genes, and cells are all being combined. How each of these components will be combined is not clear. Please detail each experiment so it is clear which materials will be coming into contact with one another and where each is worked with and by whom.
- The involvement of mice is not clear. Please provide more detail as to what exactly will be done with the mice.

- On page 2, be sure to clearly state that sharps will not be used in areas where vectors are present. Sharps and virus must be kept separate. No sharps may be used with lentivirus.
- A5a, ensure tech's demonstrate proficiency in procedures before being released to work on their own.
- A6a, make note of the requirement for a primary and secondary sealed, leakproof container. You may also want to reference the EHS safetygram for intrafacility transport: <http://home.ncifcrf.gov/ehs/uploadedFiles/ISM-158.pdf>
- In Part B, address the potential for recombination of replication defective with endogenous retroviruses when mobilizable elements are present.
- B2c: Provide a detailed explanation of the gene gun delivery technique as well as the plasmid injection technique and how these are conducted safely.
- B5c: This response should be "yes". And all subsequent answers under B5c will need to be answered in response to each vector worked with. (It may be easier if a separate Part B is completed for each one).
- B5d: Will all vectors have less than half of the viral genome.
- B5e: SV 40 is also a viral vector. Please address the inherent hazards of these promoters used as viral vectors.
- B5e3: Both human and amphotropic viral vectors are being utilized—this response should be "yes".
- B5e4: The Tet-on system is both recombinant and an oncogene and should be addressed here. Describe both the pTet and pRNAT systems here.
- B5f: This response appears to be incorrect with an insufficient reply for B5f1. Please correct and clarify with respect to endogenous retroviruses when injected into mice.
- B5i: CMV and RSV are listed under oncogenic viruses. Describe their source and if that source is MLV based?
- B6c: states "none" regarding oncogenic virus, but B5i states there are oncogenic viruses. Please correct and clarify.
- B8b: There ARE hazards associated with the foreign proteins. Identify and describe them, and provide this response in B8b1.
- B10a: Remove "fume hood" and these procedures listed MUST be conducted in a BSC.
- In the second Part B, B2c, states "no" but mice are used and therefore, MLV vectors need to be addressed.
- B5: Are MLV-based vectors used and if so, again they need to be addressed.
- B5c: The answer is no but pLenti4 is an HIV vector and requires further description.
- B5e1: Again, MLV vectors and lentiviral (HIV) vectors are listed.
- B5e2: Phoenix cell lines described have MLV based helper lines—are these amphotropic or ecotropic?
- What about mouse cells and mouse vectors (again, under B5e), they need to be addressed.
- B5f: They are mobilizable in mice. Further explain.
- B5g: Should be "yes" with explanation in B5g1.
- B5i: should also list MLV
- B6a: How are the cells placed into the mice? And remove "fume hood".
- B6c: Denotes "there will be no infectious virus at this point"—why not, was the material inactivated. Describe why the material is no longer infectious.-
- B8b: This is marked "yes" and "no". Which one?

- B10a: remove “fume hood” and address the risks of aerosols for intranasal inoculums versus injections.
- C7b: What is the toxicity? (Pertussis). Answers should be provided to C7a and b.
- Will immunizations be recommended or required? TDAP?
- C13a: Remove “fume hood”.
- For part E, identify modified material going into animals and the use of chemoattractants.
- E5: Shouldn't this be “yes”? Mice are exposed to vectors?
- E6a and E6a1: This should be “yes” especially if mobilization occurs.
- E6b1 states that mice cells will be infectious but doesn't this contradict E6a? Please clarify.
- E6e should be “yes” due to the presence and inherent hazards of MLV based vectors.
- E6g: This should no longer be “unknown”. Please provide a response.
- E8 should be “yes” due to MLV. E8a-what would cause the vectors to be degraded?
- Safety hazards for animal care staff will also require attention. For example, will microisolator caging be used, will cage changing be performed under dump stations or other containment cabinet to provide worker protection for aerosols and animal excrement? Biosafety Level 2 and Animal Biosafety Level 2 requirements will need to be implemented, clarifying PPE.
- Vir, vect, gene, cell – mixture unclear – Mice involvement unclear
- E8a – unclear need protocol consistency. Define the PTx and why would they degrade?

Dr. Crise made a motion to defer approval, Dr. Hughes seconded and all were in favor.

AMENDMENT

(P020401SLA01) Nagashima

- Proteins are not connected to the pathogenicity of the virus.
- The material is fixed in Bethesda

There were no outstanding issues with this amendment and it was approved prior to the meeting by the designated reviewer.

OUTSTANDING ITEMS

Theresa reviews outstanding items

(06-15/05-57) Tarr

-Ms. Bell will be following up with the VPP to determine their status in filing their most recently considered registration. The committee will be updated as more information is available.

-Ms. Bell reported on the updated status for pending registrations.

Other Business

- The BBP compliance rate is holding at 96%. EHS is in the process of revising procedures to ensure an improved compliance rate with this OSHA requirement. The IBC will be updated as progress is made.
- Mouse strains list – We are discussing the benefit of generating a list of “approved” animals and the value added to the IBC approval process.
- Outstanding items protocol – collect IBC comments and vote to be taken.
- Charter revisions: Need to add in transgenic KO, GMO mice so they are clearly defined as requiring registration with the IBC.
- Supplemental form for mouse imaging facility. A vote on the form will be taken by email. A question was asked: Is Dr. Kalen imaging for NIH mice? – No, just for in-house mice.
- ChABSA fliers for the Scientific Symposium to occur in June were distributed to encourage IBC member attendance.

CONCLUSION

Meeting ended at 1:37 p.m.

Theresa D. Bell, MPH, CBSP
IBC Secretary
Biological Safety Officer, EHS

Ms. Cara Leitch
IBC Coordinator
Sr. Safety Specialist, EHS

APPROVED:

Randall S. Morin, Dr. P.H.
Chairman, NCI-Frederick IBC
Director, EHS

Date

xc: All Committee Members
Dr. Reynolds
Mr. Wheatley
Dr. Arthur
Mr. Bufter
Dr. Keimig