NCI-FREDERICK
INSTITUTIONAL BIOSAFETY COMMITTEE

Minutes
May 27, 2008
NCI-Frederick

The NCI-Frederick Institutional Biosafety Committee was convened at 12:05 p.m. in the Building 426 Conference Room with the following members in attendance:

Ms. Theresa Bell, Secretary
Dr. Stephen Hughes
Dr. Melinda Hollingshead
Dr. David Derse
Mr. Scott Jendrek
Dr. Serguei Kozlov
Dr. Stephen Creekmore
Dr. Michael Baseler
Dr. Eric Freed
Dr. David Garfinkel
Ms. Alberta Peugeot

Members not in attendance: Dr. Henry Hearn, Dr. Bruce Crise, Mr. Lucien Winegar, Ms. Dianna Boissey, Dr. Randall Morin, Dr. Dan McVicar

Others in attendance: Dr. Scott Keimig, Ms. Cara Leitch, Dr. Robert Thomas, Dr. Howard Young, Dr. Giorgio Trinchieri, Ms. Robin Winkler-Pickett

Ms. Bell called the meeting to order. The first order of business was to discuss the NCI-Frederick IBC's requirement to register Knock-out mice.

NEW BUSINESS

08-24 (Sedelnikova) "Ganna-H2AX as a Potential Cancer Biomarker"

- This study involves the injection of nude mice with UT-7 cells.
- All pre-review questions have been answered prior to the IBC meeting.

Dr. Kozlov made a motion to approve, Dr. Hollingshead seconded, and all were in favor.

08-27 (Wakefield) "Efficacy of Single Agent or Combination Therapy using an anti-TGF-beta Antibody in Genetically-Engineered Mouse Models of Breast Cancer"

- BRCA1 and MMTV-Neu mouse strains were constructed by conventional transfection. There is a low chance of MMTV-neu being mobilized. Recombination and mobilization issues have been addressed in Section E6a1 and E6e1.
- Sharps hazards for antibody injection have been addressed by the animal facility manager.
- An IBC member made the general comment that one LTR is not necessarily safer than 2 two LTR's but concurred that the level of risk is minimal.

Ms. Bell made a motion to approve, Dr. Hollingshead seconded, and all were in favor.

08-28 (Tatum/Kalen) "Targeting of the HER2 Antigen"

- The discussion of this registration was deferred since the lead reviewer was not in attendance and has not submitted comments yet for the committee's consideration.

08-30 (Trinchieri/Salcedo) "Role of Inflammation in Carcinogenesis"

- The IBC asked about the ability of the pIC-Cre vector and MLV to mobilize the Cre, and if this is a potential hazard that needs to be addressed. Cre can work on endogenous sequences and MLV-LTR can serve as the driver to pick up mobilizable elements.
-How were the viral elements introduced into the mice? Is there a remote possibility of mobilization?
- It is clear the researcher has sufficiently addressed the containment and BSL-2 containment, practices, and procedures requirements.

Dr. Creekmore made a motion to conditionally approve, pending responses to the above items, Dr. Garfinkel seconded, and all were in favor.

08-31 (Whitby) "ACVP Viral Oncology Section"

- This registration involves testing of epidemiological/clinical samples for multiple viruses (HIV, HTLV, KSHV, EBV, HCV, and HBV).
- The paperwork is very minimal – more information should be included.
- PI must address how sharps and glassware be safely used.
- How will the materials be inactivated through chemical disinfectants (some are enveloped viruses and some have infectious DNA). How will the verification of validating each pathogen's inactivation be accomplished?

- PI should indicate what work will be done in the BSC and what will be done outside the BSC.
- How will centrifugation be done safely?
- The different material must be temporally and physically separated; PI is to address how this will be done.
- PI needs to address which viruses pose a potential aerosol risk and how the generation of aerosols will be avoided.
- What happens after the samples have been manipulated? Who gets what?
- Assuming a worst case scenario, since the composition of the samples is not known, the IBC needs to know what will be done to afford the utmost level of protection and safety.

Dr. Hughes made a motion to defer approval pending resolution of the above items, Dr. Derse seconded, and all were in favor.

08-32 (Herring) "Receiving and Quarantine and Breeding Activities within R&Q"

- R&Q will receive animals for standard quarantine requirements.
- Animals should not be received into R&Q until approval has been issued. Subcommittee or designated review should be sufficient for approval.
- PI should provide an estimate of the average number of animals that are expected to come into R&Q, and what an acceptable turn-around time for IBC approval would be for R&Q purposes.
- Insert additional questions provided by PI into the R&Q import forms.
- IBC Coordinator and Biosafety Officer will be copied on all import form submittals to ensure IBC coverage as feasible prior to arrival.

Dr. Kozlov made a motion to approve addressing items as noted above, Dr. Hollingshead seconded, and all were in favor.

08-34 (Malyguine) "Validation of the Caspase-3 Macrophage Apoptosis Assay"

- Pseudotuberculosis is a pathogen and the hazards need to be sufficiently addressed.
- How will the cell transport be handled?
- The volumes specified (25-50 mL) does not fit into the specified eppendorf tubes. Clarification is needed if the cells will be pelleted and if this is what will be transported via eppendorf tubes.
- This work is being done in a shared space. Will work be kept separate and the hazards limited to only those authorized to work with this material? How will temporal and physical separation be assured?
- Will this area be treated as a 2* for the duration of the studies or will it revert back to a BSL-2 to conduct other work?

- Bleach is a good disinfectant; however, it should not be used to wipe down the surface of a BSC since it is corrosive. Another disinfectant should be used and validated that it will inactivate pseudo-TB.
- Is the strain antibiotic-resistant?
- Information should be provided to address a worst-case scenario. Post-exposure prophylaxis should be discussed if warranted.
- Spill procedures should include a 20-minute contact time, rather than a 10-minute contact time with a specified EPA-approved disinfectant.
- Is the centrifuge shared and if so, how will it be effectively decontaminated for the next user?
- The PI should specify is the virus will be grown in plastic or glass flasks.
- The PI must describe which parts of the project are in room 11-1A verses 11-27.
- PI to address how dome covers are decontaminated after they are removed from the centrifuge carriers.

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

08-35 (Choyke) "Evaluation of Contrast Agents in Mouse Tumor Models for Angiogenesis"

- The work involving injection of cell lines into mice is straightforward.
- The concern is regarding the use of the contrast agents.
- The tail vein injection procedures need to be described so that the IBC has relative comfort in that the person performing the tail vein injections is doing so in the safest manner possible to avoid self-inoculation.
- How many injections will need to be done and how frequently?
- The APA only distributes regular mice so genetically modified animals are not an issue on this registration. If animals other than those from APA are added to this protocol at anytime, an IBC approval will be required.

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

07-52 (Soman/Poiley-Nelson) "Bioassays and Product Characterization for Viruses, Immunotoxins, Plasmids, and Protein Products of Recombinant Cells in the Bio-Analytical Development section of QC"

- This study involves the use of sabin strain polio, adenovirus, herpes virus, and immunotoxins.
- No immune-compromised individuals will be working with the viruses. Those vaccinated or infected can carry this home and it spreads quite easily. Vaccinations will be verified by OHS, to include how recent the titer was administered and if a high-titer was exhibited. Vaccinations may be re-offered.

- Can the Sabin strain revert to a wild-type and/or possibly cause a neuropathogenic response?
- What is the LD50 of each toxin and the volume of each?
- Are the toxins in a powder or liquid form?
- PI should how the plate with the adhesive cover will be decontaminated.
- How is contamination of the plate reader avoided?
- The IBC requested to meet with QC to observe the procedures since material is run on a plate reader. Ms. Bell will schedule this. IBC members are encouraged to attend.

Dr. Hughes made a motion to defer approval, Dr. Baseler seconded, and all were in favor. Dr. Creekmore and Mr. Jendrek abstained from the vote.

RENEWALS

08-33 (Schmidt) "Study of Renal Cancer Susceptibility Genes Retrovirally Restored to Human and Mouse Cell Lines Lacking Expression of these Genes"

- The vendor site is providing misinformation regarding the replication incompetence of VSV-G being purchased.
- There seems to be some misunderstanding of how the lentiviral vector systems work from the statement given in B5g1.
- C5a: The paperwork is incorrect on recombination with endogenous murine viruses.
- Mice with MLV will require microisolator housing all of the time.
- For lentiviral work with mice, no microisolator housing is required.
- Employees must be extremely cautious when injecting potentially hazardous material into the mice.
- What are the hazard mitigations in place to ensure safety?
- Four different rooms are listed in Addendum 2. Which procedures will be done in which rooms?
- A member of the IBC will counsel the PI on working with these materials.

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

08-36 (Sayers) "Modification of Tumor Antigenicity and Cell Death In Vitro and In Vivo"

- PI must address how the use of multiple viruses will be temporally and physically separated.
- A3: Does the phoenix cell line contain MLV? MLV can be mobilized by murine viruses, HIV cannot. This should be addressed along with potential hazards posed.

- Amphotropic lentiviruses (non-replication competent) can mobilize and recombine with endogenous viruses to the animals. PI is to acknowledge this risk and describe how it will be addressed.
- VSVg is gone after the initial round of infection and poses a different set of risks. VSV is not necessarily a decreased risk (p. 5) because different tropisms lead to different risk profiles. The hazards and these concerns must be addressed.
- How will sharps be used safely when working with virus carrying oncogenes that may affect humans?
- If animal material is being transported, how will it be done safely? Are the samples fixed?
- PI need to explain why those immunocompromised with cold and flu symptoms are at an increased risk. Will they be restricted from performing this work and why?
- BSL-2 containment is appropriate, but animal work is the higher risk and bigger concern. What will be done with animal parts (samples) and how will the bedding be handled? What protection will need to be provided to animal care staff?
- Specific Spill SOP is mentioned in the lab SOP. A copy of the SOP should be provided.

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

AMENDMENTS

06-70 (Wiltrout) "Title"

- This amendment involves the use of Diptheria toxin which should require a new IBC registration and full committee review. Questions have been submitted to the PI for consideration and the IBC is currently awaiting a response from the PI.

OPEN ITEMS

- Ms. Bell and Ms. Leitch briefed the IBC on the outstanding items. An IBC registration for Ms. Conde and responses on IBC #06-70 needs to be expedited as soon as possible.

OTHER BUSINESS

- The Bloodborne Pathogen Program is maintaining a compliance rate of 99.5%.
- OHS reported a needlestick injury involving a metastatic human breast cancer cell line to an NCI/NIH employee who was working in building 571. OMS was contacted by OHS to report the incident. EHS will follow up with an accident investigation in accordance with NIH DOHS. It was discussed that the employee injured was frustrated as part of the procedure was not going well. The IBC agreed that when employees become frustrated for whatever reason, the best

recommendation is to walk away from the work and take a break. Frustration and distraction usually lead to further errors and make way for accidents.
- Two other needlesticks occurred. One employee stuck her finger while extracting a needle after performing a tail-vein injection with a catheter system. The other employee stuck herself when she was performing a mandibular bleed on mice in series. This employee was reusing the same needle for each bleed and in the process of laying the needle down, it stuck her thumb. This employee suffered a significant allergic reaction. Both needlestick accidents are under investigation.

The meeting ended at 2:53 p.m.

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Theresa D. Bell, MPH, CBSP	Ms. Cara Leitch
IBC Secretary	IBC Coordinator
Biological Safety Officer, EHS	Sr. Safety Specialist, EHS

APPROVED:

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

xc: Dr. Reynolds
Mr. Wheatley
Dr. Arthur
Mr. Bufter