

FREDERICK NATIONAL LABORATORY FOR CANCER RESEARCH (FNLCR)
INSTITUTIONAL BIOSAFETY COMMITTEE
MINUTES

JUNE 19, 2012

CALL TO ORDER / ANNOUNCEMENTS

The FNLCR Institutional Biosafety Committee was convened at 12:05 p.m. in Building 549 Executive Board Room with the following members in attendance:

Voting (Quorum = 9)

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| <input checked="" type="checkbox"/> Michael Baseler (left at 1:30 pm) | <input checked="" type="checkbox"/> Sarah Hooper (arrived at 12:30pm) |
| <input checked="" type="checkbox"/> Theresa Bell | <input checked="" type="checkbox"/> Bhargavi Kondragunta |
| <input type="checkbox"/> Rev. David Betzner (regrets) | <input checked="" type="checkbox"/> Serguei Kozlov |
| <input checked="" type="checkbox"/> Stephen Creekmore | <input checked="" type="checkbox"/> Dan McVicar (Chair) |
| <input type="checkbox"/> Bruce Crise (regrets) | <input checked="" type="checkbox"/> Randall Morin (arrived at 12:30pm) |
| <input type="checkbox"/> Eric Freed (regrets) | <input checked="" type="checkbox"/> Shalini Oberdoerffer |
| <input type="checkbox"/> Melinda Hollingshead (regrets) | <input checked="" type="checkbox"/> Raja Sriperumbudur |
| <input checked="" type="checkbox"/> Stephen Hughes | <input checked="" type="checkbox"/> Lucien Winegar |

Non-Voting

- Walter Hubert
- Kim DiGiandomenico

Other

Capt. Darrell Laroche, contracting officer's technical representative for EHS (left at 1:30 pm)
Lionel Feigenbaum, Director Laboratory Animal Science Program (left at 12:50 pm)
Kathleen Noer, Manager Flow Cytometry Core (left at 12:50 pm)
Bruce Tobias, Manager Occupational Safety and Environmental Health

Dr. Bhargavi Kondragunta from the VPP technology development group accepted her appointment to the committee. The members introduced themselves and welcomed her to the group.

APPROVAL OF MINUTES FROM MAY 15, 2012 MEETING

The minutes from the May 15, 2012 meeting were approved as written. A motion and second were made. (For: 10; Against: 0; Abstain: 0)

ACCIDENT REVIEWS

There were two NIH/OBA Reportable events and one exposure between the June and July IBC meetings. The first reportable event involved plasmid DNA that included a portion of the HIV genome. A filled needle and syringe was flicked to remove air bubbles and the tip of the needle scraped across the individual's finger. The incident occurred on a holiday and was not immediately reported. NIH-OBA was notified as soon as all pertinent information was received regarding the incident. The employee was retrained in safe sharps handling and OSHA hazard communication requirements.

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The second event included a technician from the small animal imaging program. The technician injected a human breast cancer cell line that contained luciferin into an animal and upon retracting the needle, the technician believed to have been stuck. There was no blood, no open area and was not reported until 24 hours after the potential exposure occurred. Again, OBA was notified, since rDNA was involved; however upon further investigation, it is not clear if the individual had actually been stuck.

Lastly, on the Bethesda campus, a clinician had direct contact with a patient who was later determined to have tuberculosis (TB). The patient had recently been diagnosed with HIV and there were no indications that the patient had a known TB infection. At the time of the IBC meeting, EHS and OHS were still conducting their investigation, as it was not clear if the clinician had had an exposure.

REVIEW OF PROTOCOLS

NEW REGISTRATIONS

John Gilly 12-55: Receipt, Storage, and Distribution of a Investigational Influenza Vaccine This is a receipt, storage and distribution registry. The Vaccine Clinical Materials Program (VCMP) Vaccine Pilot Plant (VPP) intends to receive, store, and distribute an investigational influenza vaccine to support the Vaccine Research Center (VRC). The VCMP will distribute this vaccine product in the manufacturer's packaging without modification to various designated clinical sites as instructed by the VRC to support a Phase I influenza vaccine trial in children. Aside from changing the response from N/A to NO under the Dual Use questionnaire, the committee had no additional concerns. Theresa Bell moved to approve the registry. Mike Baseler seconded the motion. For: 12; Against: 0; Abstain: 0

Melinda Hollingshead 12-57: DCTP Repository: storage of biological samples and natural product materials This registry is for the storage of material at the DCTD Repository; there is no manipulation of materials except to transfer vials into and out of freezers; the Repository provides long-term cryostorage for tumor fragments (passaged not fresh), tumor cell lines and natural product collections and extracts – these materials are not manipulated in the PI's research lab for research purposes. Currently there are 927,609 vials/bottles containing natural product raw materials/extracts and 200,000 vials of tumor cells/fragments in cryostorage. During IBC discussion, the committee was concerned about the cargo (genes) in the lentiviral vectors described in Part B. They requested further information from the PI regarding if the list of cargo in the registry was an accurate list of cargo in the lentivectors and also requested additional information regarding how the samples are tracked (cradle to grave) in the long-term storage repository (i.e. what happens if a freezer goes down and samples thaw/leak. Will staff know how to handle the materials? Do the handlers know what is in the materials being stored (ie. lentivectors/ human materials, etc.?). Dan McVicar moved to approve the registry pending clarifications. Theresa Bell seconded the motion. For: 12; Against: 0; Abstain: 0

RENEWALS

Stephen Hou 12-24 (06-08): Mouse models to investigate cancer stem cell regulation For this renewal, the group plans to study the mouse homologue of bmm known as ATGL, to understand its role in adult cancer stem cell regulation in mice. They will conduct this study in two types of mouse cancer models: Chronic myeloid leukemia (CML) and intestinal cancer. Viral vectors will be employed to conduct this research. The pre-review had several iterations prior to the registry going to full committee. The reviewers are more comfortable that the PI understands the safety concerns with the research and that they are using potentially mobilizable cargo once the materials are placed

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into animals. Serguei Kozlov motioned to approve the registry with the revision of sharps use to include dissection tools (as described in the SOP). Lucien Winegar seconded the motion. For: 11; Against: 0; Abstain: 0

Ligia Pinto 12-33 (P181200MBA01): Cellular Immunity Studies using Human Mononuclear Cells originated from Blood or Bone Marrow Tabled to July meeting – reviewers not present

Ligia Pinto 12-34 (06-101): HPV Antibody Assays for serum, saliva and cervical secretions The objective of this renewal is to evaluate the activity of serum and cervical antibodies to neutralize HPV in vitro and to evaluate anti-HPV titers and avidity in biological samples (serum, saliva, cervical secretions). These assays (neutralization, ELISA, Avidity) will be used to determine anti-HPV antibody activity in biologic samples (serum, saliva, and cervical secretions) from individuals vaccinated with an HPV-16/18 L1 VLP vaccine or in patients from natural studies of HPV infection. L1 VLP and L1+L2 PsV will be prepared for this assay. The committee had minimal concerns regarding the handling of the HPV VLPs; however, felt that more detail needed to be provided for the human samples – especially those known to be HIV positive. Steve Hughes moved to defer the registry pending more information regarding the ‘cradel-to-grave’ handling of the human materials. Shalini Oberdoerffer seconded the motion. For: 11; Against: 0; Abstain: 0

Ligia Pinto 12-35 (06-24): HPV Immunology Lab: Effects of soluble factors produced by PBMC on HPV The objective of this IBC renewal is to study the in vitro effect of supernatants from PBMC cultures stimulated with an HPV vaccine on human papillomavirus (HPV) gene expression using cell lines obtained that contain human papillomavirus. Committee concerns stemmed more around the use of the cholera toxin needed in the tissue culture media rather than the HPV vaccine; although the registry and SOP addressed safety concerns the pre-reviewers had. The committee strongly recommended for the lab to attempt to obtain the toxin already reconstituted by the supplier. Serguei Kozlov moved to approve the registry with the aforementioned recommendation. Theresa Bell seconded the motion. For: 11; Against: 0; Abstain: 0

Ligia Pinto 12-38 (P210801MBA02, P061196MBA03): Holding protocol for recombinant Adenovirus, Vaccinia Virus and EBV in the HPV Immunology laboratory The materials listed in this registry are only being stored and not actively manipulated. Prior to initiation of any work with these materials, the PI will notify the IBC in writing and further review of experiments and practices may be warranted. The committee requested for the PI to add the following statement to her registry (to which she did): *The materials in this storage registry will not be released to another investigator without prior approval by the IBC for that investigator to work with the materials.* Steve Hughes moved to approve the registry with the aforementioned clarification. Dan McVicar seconded the motion. For: 11; Against: 0; Abstain: 0

Giorgio Trinchieri 12-47 (09-04): Conditional ablation of plasmacytoid dendritic cells in a transgenic mouse sensitive to diphtheria toxin The purpose of this renewal registry is to analyze plasmacytoid dendritic (pDC) contribution to immune tolerance and cancer. The group plans to use a genetically engineered mouse line selectively expressing human diphtheria toxin receptor in pDC. The conditional pDC ablation, achieved by injection of diphtheria toxin, will allow discrimination of pDC functions in immune events. There were no significant changes to the protocols since the last submission. The committee requested confirmation that tissues harvested from infected mice are manipulated inside a biosafety cabinet. Theresa Bell motioned to approve the registry with the aforementioned clarification. Randall Morin seconded the motion. For: 12; Against: 0; Abstain: 0 (NOTE: Post IBC meeting, confirmation was

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received that all necropsies are conducted in a BSC. Additionally staff received refresher training and mock observation on 06/28/12).

Amar Klar 12-49 (09-31): Testing predictions of SSIS hypothesis in vivo, and to develop a mouse model to study selective chromatid segregation phenomenon in mitosis This renewal registry is for the production and breeding of GEM mice as well as to investigate the role of Ird in HSCs and MEPs. These experiments will be performed in collaboration with another FNL laboratory, and will be based on FACS-analysis of bone marrow cells isolated from femurs and tibia of Ird mutant and control littermate mice. With the exception of changing the response to the Dual Use questions from N/A to NO, the committee had no additional comment. For: 10; Against: 0; Abstain: 1 (member briefly left room and was not present for the vote)

Zoe Ohler 12-50 (08-65): Induction of experimental carcinogenesis in genetically engineered mouse models (GEMs) to evaluate the efficacy of novel anti-cancer therapeutics Tabled to July meeting – reviewers not present

Ronald Gress 12-51 (06-68) Breeding and holding of various mouse strains Breeding only Notification to committee

Mark Lewandowski 12-52 (06-14): Role of Cell Signaling during Mouse Embryogenesis Breeding only
Notification to committee

Jeff Lifson / Julian Bess 12-53 (P170804JLA): Virus Propagation and Purification The principal activity of the Biological Products Core Laboratory continues to be the propagation and purification/concentration of cell culture derived retroviruses. The specific aim of the group is to produce preparations of adequate concentration and purity for use in research procedures by other laboratories. In some cases, inactivated retrovirus preparations are made. This renewal registry clearly defines the hazards involved with the research and the steps the lab will take to safely work with the materials and avoid exposures or accidental release. Steve Hughes moved to approve the renewal. Dan McVicar seconded the motion. For: 12; Against: 0; Abstain: 0

OUTSTANDING ITEMS

Trinchieri/Noer – IBC 11-66 (formerly 10-60) Flow cytometry core lab: (Final versions of IBC paperwork received on 03/22/12.) IBC requested an operational SOP from the group for use of the current space. The group requested renovations to the area, but until those renovations are completed, the IBC wants to ensure that the lab is operating safely on a day-to-day basis. (SOP was posted to SharePoint). Dan McVicar moved to approve the current operational SOP and affiliated IBC registry/paperwork. Randall Morin seconded the motion. For: 12; Against: 0; Abstain: 0

Jairaj Acharya 12-06 (06-03 and 06-16): Transport studies in mouse embryonic fibroblasts (MEFs) using Vesicular Stomatitis Virus G Protein A and Functional Analysis of Enzymes of Sphingolipid Metabolism Originally deferred back to full committee at the February meeting. The PI significantly revised the registry and addressed the safety concerns of the committee. The committee, however, did want a few additional statements regarding the separation of materials/experiments. Dan McVicar moved to approve the registry with the aforementioned clarifications. Steve Hughes seconded the motion. For: 11; Against: 0; Abstain: 0

Ding Jin 12-17 (09-25): Transcription Regulation in E. coli (K12) and H. pylori Deferred to full committee at March meeting with delay of in vivo research on April 2, 2012. As of the posting date, no

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revised paperwork or new registrations for the in vivo work were received by the IBC Administrator. May 21, 2012, memo sent to supervisor regarding delinquency in completing the IBC paperwork and addressing safety concerns. As of the June meeting, no further updates or correspondence was received. (NOTE: After the convened IBC meeting, the IBC Chairman sent a second notification to the PI's immediate supervisor)

Scott Durum 12-23 (09-06): Effects of cytokine-expressing bacteria on the development, progression and treatment of inflammatory bowel disease and colon cancer (L. lactis) The objective of this study is to determine the effectiveness of *Lactococcus lactis* (*L. lactis*) expressing murine cytokines on the initiation, development, progression and treatment of inflammatory bowel disease and colon cancer. PI provided responses to pre-review questions requested in March, and the provided SOP adequately addressed safety concerns with manipulation and handling of the agent. Dan McVicar moved to approve the registry. Steve Hughes seconded the motion. For: 11; Against: 0; Abstain: 0

Ji Ming Wang 12-30: Use of normal human blood cells for studies of inflammation and cancer in vitro Deferred to full committee at March meeting. PI revised registry and SOP; however the committee did not want to release approval until it was more clear how / if this registry was affiliated with other laboratory research as well as until the PI provided a new registry for the *H. pylori* animal work. As of the June IBC meeting date, a revised SOP was submitted for 12-30 but no additional registration paperwork was received for the *H. pylori* animal work. At the June IBC meeting, the committee discussed concerns regarding the SOP and staff training. The committee requested for everyone involved with the chemotaxis assay and workflow to demonstrate training on the SOP and proficiency of their techniques. Theresa Bell motioned for a sub-committee of IBC members, including herself, to spearhead the aforementioned request. Lucien Winegar seconded the motion. For: 10; Against: 0; Abstain: 0

AMENDMENTS

Thirty amendments were processed and approved between the May and June IBC meetings, while five remained outstanding.

OTHER BUSINESS

- Pathogen challenge room (Building 571:310) – Drs. Lionel Feigenbaum and Raja Sriperumbudur provided the latest updates to the ABSL2 SOP, which included a specific addendum for practices in Bldg 571:310. It was recommended to remove the list of specific agents at the end of the SOP; as this list was not comprehensive and could change monthly. Another suggestion was to add a statement that ‘only these agents as approved by the IBC can be used in room 310.’ One new addition to the SOP was the development of an IBC sub-committee that would be used to evaluate and provide guidance should disciplinary actions be warranted. Dan McVicar provided a brief synopsis of how this committee would function and who would serve on it. Dr. McVicar indicated that more information regarding this sub-committee would be provided at the July IBC meeting.
- For holding and/or storage protocols: Theresa Bell motioned for the committee's concurrence that full committee review was still warranted for holding and/or storage IBC registries, as opposed to only lead review with notification as is done with the breeding protocols. Dan McVicar seconded the motion. For: 10; Against: 0; Abstain: 0

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ADJOURNMENT

The meeting was adjourned at 2:50 pm.

Next meetings:

July 17, 2012

August 21, 2012