



**NCI-FREDERICK
INSTITUTIONAL BIOSAFETY COMMITTEE**

Minutes – Meeting July 20, 2004
NCI-Frederick

The NCI-Frederick Institutional Biosafety Committee was convened at 12:00 p.m. in the Building 549 Executive Boardroom with the following members in attendance:

Dr. Randall Morin, Chair	Dr. Henry Hearn
Mr. Joseph Kozlovac, Secretary	Ms. Carol Ingraham Tobias
Dr. Bruce Crise	Dr. Stephen Creekmore
Dr. Melinda Hollingshead	Dr. Jeanne Herring
Dr. Steve Hughes	Dr. Donald Court
Mr. Lucien Winegar, Esq	Dr. David Garfinkel
Dr. Paul Nisson (ex Officio)	

Members not in attendance: Dr. Michael Baseler,

Others in attendance: Ms. Cara Lamberson, Mr. Tom Danver, Dr. Lionel Feigenbaum and Mr. Scott Jendrek

INTRODUCTION

Dr. Morin called the meeting to order. Dr. Morin introduced Dr. Paul Nisson as the ex-Officio replacing Ms. Cheryl Parrott as the representative from the NCI-Frederick Deputy Director's Office. Ms. Tobias provided a review to the committee of recent employee accidents and potential occupational exposures. Mr. Winegar brought up the question due to all the Sunshine Project Biosafety Bites if the general public asks members of the committee questions about the IBC how should we answer. Dr. Hollingshead explained the NCI-Frederick Policy. Mr. Kozlovac and Dr. Morin stated that are meetings are open and the minutes are available to anyone interested in reviewing them. Mr. Kozlovac stated that if we had a request for meeting minutes that discussed either confidential information or proprietary information that it would be possible to provide requestors redacted copies of the minutes according to the guidance from OBA.

REVIEW OF PROTOCOLS

Mr. Kozlovac suggested to the committee that since representatives from programs with registrations to be discussed were present that we break from the proposed agenda to discuss those registrations first.

Dr. Bruce Crise introduced a recombinant DNA registration document entitled, *Production of Transgenic Mice with Lentiviral Vectors*. Dr. Crise informed the committee that the constructs were used to infect the embryos and the embryos were then implanted into mice for gestation. The vector system is the Invitrogen Lentiviral expression system. Dr. Crise asked Dr. Feigenbaum to review the implantation process. Dr. Feigenbaum provided an overview of the process, which is conducted under a microscope. The process involves the use of a mechanical pump and glass pipette. Dr. Crise stated that the sharps were a concern however this viral vector system has been reviewed by the IBC extensively and that viral replication was not a concern. Dr. Hughes concurred that it is well documented that the envelope is deleted. Dr. Hughes suggested that the registration to be amended so that the IBC could provide approval for SiRNA that did not express proteins. Dr. Crise agreed that SiRNA inserts would not be a problem but any other insert should be approved by the IBC through an amendment. Dr. Morin asked about the NIH Classification listed on question #4. Mr. Kozlovac stated that the classification provided by the PI was incorrect and that the correct classification that was corrected on the EHS file copy is III.D.4. Dr. Hollingshead asked about the possibility of vector shedding post implantation. Dr. Feigenbaum stated that he was not sure about the length of time shedding could occur. Dr. Hughes suggested that animal handlers be made aware of a 72-hour window post implantation where the risk is greatest, although the actual risk with this vector is small. Dr. Hollingshead stated that a risk to consider is cage changing operations where bedding is dumped since there was a potential for aerosolization. Dr. Hollingshead suggested that during the first 72 hours after implantation that the animals be housed in disposable cages. Dr. Feigenbaum agreed with this approach, he also pointed out that the implanted animals were housed in microisolator cages until the birth of the pups occurred.

CONDITIONALLY APPROVED Amend registration for approval of SiRNAs. SiRNA expressed RNA is related to a gene that the PI wishes to knockout and does not cause expression of new genes but rather turns genes off. Shutting off murine genes will not be a significant hazard to humans as compared to expressing genes of interest. Add a statement to the Standard Operating Procedure that implanted animals will be housed in disposable cages for the first 72 hours after implantation and that they will be housed in microisolator cages until birth of the pups.

Mr. Kozlovac summarized the mock run using riboflavin for the 10L production of *Adenovirus Δ24-RGD*, the BDP held on July 2, 2004, with many IBC members in attendance. This protocol, *Adenovirus Δ24-RGD For Glioblastoma and Ovarian Cancer*, submitted by Dr. Ray Harris and Dr. Denise Ekstrom was discussed in

depth at the June 2004 IBC meeting. Mr. Kozlovac introduced Mr. Scott Jendrek of the BDP who was attending to answer any further questions the IBC had as a result of the mock run. Mr. Kozlovac reviewed a few of process improvements suggested to the BDP by the IBC. Mr. Winegar stated that he was pleased with scientists' welcome of the IBC and their appreciation for all the suggestions that the IBC made regarding process improvement and safety. Dr. Hearn also expressed his pleasure that the mock run went so well and that the IBC was able to provide some valuable input into the process. Dr. Hearn wanted to express his compliments for the process in general and work group that participated. Dr. Hughes expressed his belief that this mock run process should be expanded to other research groups outside the BDP.

APPROVED

Dr. Creekmore revisited a pathogen registration submitted by Dr. James Phang entitled, *Metabolic regulation of apoptosis*. This protocol was tabled to provide the PI an opportunity to resolve some of the issues/questions noted by the IBC, such as the testing status of the human tissue received from the Cooperative Human Tissue Network as well as obtaining staff signatures. Dr. Creekmore asked Mr. Kozlovac to check and ensure that the listed staff have completed their training on Standard Precautions as required by 29 CFR 1910.1030. Dr. Morin asked that question #2 on the pathogen registration be modified to delete instruction #1 asking Federal employees to provide their Social Security #. The current question #2 requests an employees initials Dr. Morin suggested converting this be converted to a signature block.

CONDITIONALLY APPROVED – EHS to check training records to ensure that individuals listed on registration have up to date Standard Precautions training.

Dr. Crise re-introduced discussion on an amendment to P230902JLA01, P150703RHA01, P190701JLA01 and P180303JLA01 submitted by Dr. Gopalan Soman through the Principle Investigators, Dr. Raymond Harris and Dr. Jinhua Lu, of the listed registrations. The amendment requests the addition of labs and staff to the listed registrations for the purpose of assay development related to these viral vector projects. Dr. Crise noted a few continuing concerns regarding how the lab would address cross contamination issues if work on multiple projects were conducted in this area at once. If work with the poliovirus is conducted in the area will all the folks working in the lab that are working on different projects be vaccinated? Ms. Tobias stated that if it was known an individual would be working in these areas that individuals would be clinically evaluated and OHS would offer vaccination if necessary. Dr. Hughes asked if they were working within different BSCs for each agent. Mr. Kozlovac indicated that he did not believe that to be the case. Many members of the IBC expressed that further clarification of the procedures be made. The IBC suggested that Dr.

Soman be invited to the next meeting to discuss the amendment to address some of the committee's concerns.

TABLED – PI to further define and clarify procedures. Secretary to invite Dr. Soman to attend the IBC to address committee concerns.

Dr. Stephen Hughes introduced a Pathogen and rDNA registration submitted by Dr. Jeff Lifson entitled respectively, *Laboratory Analysis of Retrovirus Containing Samples* and *Molecular Tools for Laboratory Analysis of Retrovirus Containing Samples*.

Lifson rDNA Registration Discussion

Dr. Hughes wished to know if the replication competent proviral clones being utilized by the laboratory were derived from laboratory adapted strains or from primary patient isolates. Dr. Hughes noted that the roster of names included on the pathogen registration was not included on the rDNA registration. Dr. Crise suggested that this was an oversight on his part. Dr. Hughes inquired whether all the listed individuals have seen the whole packet and was aware of hazards represented by both registrations. Dr. Crise indicated that this was the case. Mr. Kozlovac suggested that AVP provide a statement to the effect that the listed employees are aware of both registration documents. Dr. Hughes noted that a suggested containment level was not provided and would need to be in order to complete the documentation. It was noted by the committee that Triton X would be used as an inactivating assay prior to the ELISA assays. Mr. Kozlovac asked if the lab had efficacy data for Triton X inactivation of HIV.

CONDITIONALLY APPROVED – Provide information on the source of proviral clones. Provide a statement that the staff roster is the same for both registration documents and that each staff member has read both registration documents. Provide efficacy information on Triton X inactivation of HIV.

Lifson Pathogen Registration Discussion

Dr. Hughes informed the committee that material produced in this is inactivated and sent to animal facilities utilizing guinea pigs and non-human primates for testing. Dr. Hughes asked the committee what is our responsibility once the material leaves the gate. Dr. Hughes felt that more information on the inactivation method and the procedure for viral inactivation needed to be provided. Dr. Hughes also noted that a number of primate pathogens were also listed on the registration and that a potential for cross contamination existed. Dr. Hughes felt that the researcher should provide a statement that no deliberate attempt to co-culture any of these viral pathogens to generate recombinant viruses would be performed.

CONDITIONALLY APPROVED – Provide information on viral inactivation and lot testing for material being shipped to other research facilities. Provide a statement that no work with guinea pigs or non-human primates is conducted at

NCI-Frederick. Provide a statement that the purposeful co-cultivation of viral pathogens in order to generate a recombinant virus will not be conducted in this laboratory.

Dr. David Garfinkel introduced a renewal rDNA registration and Pathogen registration respectively submitted by Dr. Peter Johnson. Dr. Garfinkel reviewed the rDNA registration first since there were a number of changes including the addition to use lentiviral, retroviral and *E. coli* plasmid expression vectors. Dr. Hollingshead and Dr. Herring asked since there were major changes to rDNA registration should this be considered a new registration? Dr. Hughes wanted to know if all studies will be conducted invitro except for the generation of transgenic or knockout mice, or if the PI plans to insert cells into animals. Dr. Hughes stated that he wanted to know if viruses were going in before or after Dr. Feigenbaum or Dr. Tessarollo are performing their manipulations of the animals. If they inject cells into mice an ACUC amendment will be required. The IBC also felt that a statement needed to be made that laboratory staff will be dealing with cells that are producing virus that is expressing a transgene C/EBP.

TABLED – PI to further clarify and provide additional information requested by the Committee.

Renewal rDNA registration 04-09

Drs. Court introduced a renewal registration submitted by Dr. Toshiyuki Mori entitled, Recombinant engineering of HIV-inactivating protein and application of phage display technology in molecular target research. Dr. Court informed the committee that the work involved regulatory proteins which does not increase the risk of the vector system being utilized. Dr. Hughes stated that question #9 on the form should be clarified. The question reads, *Are plant or animal cells to be exposed to the recombinant?*, Dr. Hughes stated that the question is not clear if it is asking if the cell is exposed to the rDNA or recombinant protein. Mr. Kozlovac stated that the intent was to ask if the cells were exposed to recombinant DNA molecules. Mr. Kozlovac agreed that the question as written was not clear and that EHS would modify the form and let the committee comment on the change prior to finalizing the change to the form.

APPROVED

Amendment to Recombinant DNA Registration #03-22.

Dr. Crise informed the committee that he was assigned as lead reviewer for the amendment to Dr. Narayan Bhat's registration to generate lentiviral vectors. Dr. Crise reviewed the amendment with the committee.

APPROVED

Amendment to Recombinant DNA Registration #03-20

Dr. Hughes informed the committee that he was assigned as lead reviewer for the amendment to Dr. Philipp Kaldis's registration to additional lentiviral vectors from Invitrogen. Dr. Hughes reviewed the amendment with the committee.

APPROVED

Meeting Adjourned: 1:50 p.m.

Respectfully submitted,

Joseph P. Kozlovac, M.S., CBSP, RBP
Executive Secretary, NCI-Frederick
Institutional Biosafety Committee

Approved: _____ Randall S. Morin, Dr. P.H.
Chairman, NCI-Frederick IBC

xc: Each Committee Member
Dr. Wilttrout
Dr. Reynolds
Mr. Eaton
Dr. Arthur
Mr. Bufter