



**NCI-FREDERICK
INSTITUTIONAL BIOSAFETY COMMITTEE**

Minutes
October 19, 2006
NCI-Frederick

The NCI-Frederick Institutional Biosafety Committee was convened at 2:04 p.m. in the Building 549 Conference Room A with the following members in attendance:

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|------------------------------|---------------------------|
| Dr. Randall Morin | |
| Ms. Theresa Duley, Secretary | |
| Dr. Henry Hearn | Dr. Bruce Crise |
| Ms. Alberta Peugeot | Dr. Dan McVicar, |
| Mr. Lucien Winegar | Dr. Melinda Hollingshead, |
| Dr. Stephen Hughes | Dr. Stephen Creekmore |
| Dr. David Garfinkel | Ms. Dianna Boissey |

Members not in attendance: Dr. Jeanne Herring, Dr. Michael Baseler
Others in attendance: Ms. Cara Leitch, Dr. Scott Keimig, Dr. Robert Thomas

INTRODUCTION

Dr. Morin called the meeting to order.

Dr. Morin asked for a final vote on the September 2006 meeting minutes. Dr. Hearn made a motion to approve them as written, Dr. Crise seconded, and all were in favor. Mr. Winegar abstained from the vote since he was not in attendance at the September meeting.

The August 2006 meeting minutes were distributed through email for review just prior to the October meeting. A final vote on the August minutes will be obtained through email.

PROTOCOL REVIEWS

NEW BUSINESS

06-90 (Dr. Trinchieri/Dr. Salcedo):

This study involves knock out mice and no mobilizable vectors, so there is a relatively low level of risk. However it was mentioned that there are some concerns regarding the carcinogens in use. The lead reviewer was instrumental in obtaining additional documentation from the PI, to include an SOP detailing how this work will be performed. There was a request made for a list of employees performing this work, to include their training and experience. The work cannot occur in Building 567, Room 208 as mentioned in the registration, as additional time is necessary to obtain proper approvals to use this space. The new location for this work is in Building 539 and personnel currently working in Building 539 will be used for this study. The animals will be housed in Building 567 and then transported to Building 539 for research studies.

Dr. McVicar made a motion to approve, Dr. Crise seconded and all were in favor.

06-92 and 06-93 (Dr. Monks):

- Confirm that screening will be done on cell lines from other investigators
- For item A4, state that the needle biopsies are covered under Dr. Melinda Hollingshead's protocol, provide the applicable registration numbers and further clarify that needle biopsies will not be performed as part of this registration or by the personnel listed in this registration
- Are the patients from which the samples are obtained prescreened for agents of consequence before they are placed on a cancer therapy protocol?
- D2 on 06-92 should be "yes"

Dr. McVicar made a motion to approve with very minor changes, Dr. Crise seconded and all were in favor.

06-85 (Dr. Klinman):

- A standard operating procedures manual is needed for activities to be performed in vitro and in vivo. The animal facility manager for Building 571, 3rd floor (JanNean Williams) should be contacted to assist with appropriate SOP's for the in vivo portion of this work
- With autoinjection, there is a bacterial growth risk, how is this being addressed?
- Will microisolator cages be used in conjunction with negative pressure ventilated cage racks?
- Clarify that cages will be changed in a BSC, caging and bedding will be autoclaved before being dumped, and will then be sent to the cage washer
- The animal facilities here require a full change of clothes when entering, tyveks or scrubs, hair bonnets, shoe covers and/or facility shoes, eye protection and face mask are to be worn at all times. Because of these differences in facility requirements, separate SOP's and employee risk assessments for in vivo and in vitro work are important. The SOP for animal studies should include what will be done with the animals at the end of the study, to include death or continued

monitoring and what will be extracted from the animal, where the material will be taken, and what will be done with the animal material in vitro.

-Only those individuals with healthy immune systems should be working on this protocol since there are potential issues with Listeria and teratogenicity. Those who are immunocompromised will be at a higher risk should an exposure incident occur. *F. tularensis* and *B. anthracis* (sterne) are only truly attenuated in healthy individuals

-D3b: Where does the use of blood/serum/blood components fit in?

-D9a: Are rotors in centrifuge containment style? Are they disinfected before removal from BSC?

-E7a needs to be answered

-E8a: Are forceps and gloves disinfected between transitioning to another cage? Are cage exteriors disinfected prior to removal from BSC?

-Medical surveillance programs will need to be considered with Occupational Health Services prior to initiating work. An informed consent should also be completed by each employee performing this work to ensure they are informed of and understand all pertinent hazards involved with this work.

Dr. Hollingshead made a motion to defer approval until the above issues are resolved and SOP's are in place, Dr. Crise seconded and all were in favor.

RENEWALS

06-70 (Dr. Wiltroat):

-This registration seems to involve multiple viral systems; therefore, necessary safeguards should be in place Describe them.

-Who serves as the laboratory safety officer and lab chief? Responsibility for supervision and audit functions needs to be determined

-Is the virus replication competent? They should be handled as if they are replication competent all of the time

-The assays appear to be difficult and not completely explained, boundaries should be defined as to what will "not" be done, what could be foreseen as going wrong and what are the provisions in place to avoid that?

-Is there a deliberate mixing of materials to be placed into animals? If yes, how will this be done safely?

-Is there a virologist included on this protocol who will oversee this research?

-A3 should read BSL-2

-A3 should also further define disposal beyond autoclaving

-A4a should clearly state that no sharps will be recapped

-There is no answer for B8 for CD40 – it should be "yes" with additional responses for B8a and b.

-CD40 (B6 and B6a) needs to reflect minimal hazards due to use of unscreened cell lines, tell us what the hazards are, and how they will be minimized (how will the risks be controlled)?

- B6c: Further clarify why this answer regarding infectious material is “none”
- Part B for adenovirus, B2c: Please list the strains
- B5d: Explain the likelihood of adeno recombinants in 293 cells?
- B5g and B5i: These responses are blank-please provide more detail
- With the approach described within the registration, replication competence is likely, how will this be addressed?
- Part B for lentivirus: B2C: please list strains
- Further define “genes of interest” in item B3, which genes, which type, how will they be expressed?
- B5g and B5i need to be answered, or provide more details
- Part B for retrovirus: B2c: Please list the strains
- B5 responses (B5e) should indicate the potential for mobilizable elements, please further discuss and explain how potential risks will be mitigated
- B5f1: Please correct “pantrophoic” to “pantropic”
- B6a: Because of the potential for complementation and recombination even though the virus is described as “replication defective”, please further describe the hazards and mitigation measures
- B6c: Clearly explain the differences between infectious and replication competent and for each part B, which is applicable and why.
- D5: How are the biopsy specimens characterized?
- E6a1: What makes these viruses non-infectious? What about replication and infection due to mobilization or recombination with other elements?
- E6: How will there be physical and temporal separation to avoid cross-contamination being that multiple things are being manipulated within the same lab space.
- Individuals with a suppressed immune system should not be permitted to be involved with this work
- SOP's will need to include procedures for spills (large and small volume)

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

06-88 (Dr. Pavlakis):

This study involves DNA and genes, a standard cell culture experiment set-up. DNA vaccines could potentially immunize those individuals working with them in the process of developing these new technologies. Applicable precautions should be taken to address these potential hazards.

- B5d: Confirm that expression vectors with viral promoters are being used and the donor of genetic information should be marked as the promoters (CMV and SV 40 promoters)
- Clarify that no MLV will be used.
- Although this study only involves DNA candidate vaccines, no virus, no well-known oncogenes and no viral proteins, it should not be treated in a cavalier manner. Potential hazards and mitigation measures should be clearly defined.

Dr. Garfinkel made a motion to conditionally approve this registration with revised statements addressing the above noted issues, Dr. McVicar seconded and all were in favor.

06-86, 06-87, and 06-89 (Dr. Pavlakis):

- How will the virus and the genes be kept separate?
- The purpose of the research, how it will be conducted and the paperwork to describe such is unclear and incomplete overall. Cell lines are mentioned as are PBMC's from Rhesus macaques. It is unclear what procedures are being performed with each material and why. First, it is recommended to separate animal work and laboratory in vitro research tasks. For each task and for each different material worked with, the risks should be assessed clearly with applicable risk mitigation measures described, as well as implementation plans for the laboratory operations. Are PBMC's/NHP or Rhesus materials being received in your lab and if so, from where and whom?
- B5h-Yes and NO? This is unclear.
- B5k1: Please tell us more about the aerosol production and how this hazardous condition will be addressed.
- SIV and HIV are mentioned for both mice and macaques. It is unclear what is being done here and it would be best to outline all procedures from start to finish in a step by step process
- More information must be provided on the particular strains for HIV and SIV
- Are clinical sample specimens being used?

Vote was delayed pending review of revised registrations

AMENDMENTS

Amendment to P031005SMA01 (Dr. McNeil):

- A3 needs more description to address the potential pathogens that may be encountered in the cell lines.
- The SOP's in the original submission are sufficient to cover this amendment
- D2 says "yes" but D4 is "no". Clarification needed.
- These lines should be tested with the standard 10-panel screen. MCF 7 is commonly used and most likely has been tested before
- D9 should have "injection" marked

Dr. McVicar made a motion to conditionally approve this registration pending the modifications noted above, Dr. Hollingshead seconded and all were in favor.

Amendment A to IBC 05-02 (Dr. Durum):

- Provide additional details on the Phoenix cell line proposed for use. There are hazard warnings on the product information sheet from the supplier
- If Phoenix is a human cell line and the retrovirus cannot infect human cells then what component of this mix allows infection to occur? Does it pose a risk to other human cells?
- Is recombination of the retrovirus in the host mouse possible? Explain why or why not. If recombination is possible, what risks are present?
- A5a: Blood borne pathogens training is not risk specific, what specific in-lab training is provided?
- Is pMIG a murine retrovirus?
- What specific genes are missing in the virus?
- B5d: If Phoenix is a human cell line then how is the vector not human or amphotrophic?
- Is pMIG both a eukaryotic and a prokaryotic virus?
- A9: The laboratory SOP is needed
- B5m was not answered.
- E6e1 is not clear. Provide clarification.
- E6g was not answered.
- The animal facility staff needs to be informed of the risks if this material is being put into mice
- See Orbigen Manual p. 2 of 13 "Important Note" and please sufficiently address the hazards identified within

Dr. Hollingshead made a motion to conditionally approve the Amendment pending resolution of the items mentioned above, Dr. Crise seconded and all were in favor.

Amendment B to IBC 05-02 (Dr. Durum):

- Since 5FU is involved, how will the animal cages be handled safely?
- A5a: An SOP is needed
- Define the mouse strains according to donors and recipients
- Answer A6

Dr. Hollingshead made a motion to approve provided the above items are sufficiently addressed, Dr. Garfinkel seconded and all were in favor.

Amendment C to IBC 05-02 (Dr. Durum):

The responses to the lead reviewer and committee questions for this amendment had not been received at the time of the meeting. This amendment will be handled outside of the full committee.

Dr. Hollingshead made a motion to approve provided the above items and previously submitted committee questions are sufficiently addressed, Mr. Winegar seconded and all were in favor.

OUTSTANDING ITEMS

06-36 and 06-37 (Dr. Schneider) – PI to address questions.

05-49 and Pathogen (Dr. Chatterjee) – On hold

06-79 (Dr. Whiteley) – PI to address questions

06-39 (Dr. Kopp) – Pending riboflavin run

06-13 (Dr. Munroe) – Pending receipt of SOP

06-51 and 06-38 (Dr. Keller) – PI to address questions

OTHER BUSINESS

The Bloodborne pathogen update reported continued compliance around 94%. Ms. Leitch continues to notify program members of their requirement to complete this annual training.

The Outstanding Items were reviewed to update the committee on their status. Ms. Leitch and Ms. Bell hope to reduce the number of outstanding items significantly prior to the end of 2006. Registrations with an outstanding status for 6 months or longer will be put on HOLD until the registering program actively seeks to complete the registration process.

No other issues were raised to the committee's attention and the meeting was adjourned at 4:15 p.m.

MINUTES RECORDED BY:

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

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

Draft 12/07/06

Mr. Wheatley
Dr. Arthur
Mr. Bufter
Dr. Keimig