UNIVERSITY OF WASHINGTON
Office of Public Records and Open Public Meetings
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Campus Mail: Box 354997
Prepared for release on:
Friday, April 14, 2006

Edward H. Hammond
The Sunshine Project
PO Box 41987
Austin, TX 78704

Dear Mr. Hammond:

The following is provided in response to public records request #06-10176 in which you request photocopies of the minutes for all meetings of the IBC since May 1, 2003.

The responsive items are enclosed. The meeting minutes from the January 13, 2006 meeting have not been approved and as such are exempt per the following public disclosure law provision:

RCW 42.17.310(1)(i)

(i) Preliminary drafts, notes, recommendations, and intra-agency memorandums in which opinions are expressed or policies formulated or recommended except that a specific record shall not be exempt when publicly cited by an agency in connection with any agency action.

Once these meeting minutes have been approved by the committee, they will be available to you. Please make a request at a later date for this item.

Sincerely,

Josy A. Rush
Public Records Officer

Office Number: (206) 543-9180
Email: pubrec@u.washington.edu

Date: Fri, 2 Sep 2005 13:55:38 -0700 (PDT)
From: P. Azeltine <azeltine@u.washington.edu>
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Cc: Karen VanDusen <kav@u.washington.edu>,
Susan Alexander <susanka@u.washington.edu>,
Pat Azeltine <azeltine@u.washington.edu>, jwponder@u.washington.edu,
martines@u.washington.edu, Joann Kauffman <jlkauff@u.washington.edu>,
Sharon Murphy <murphys@u.washington.edu>
Subject: IBC Meeting for September 9, 2005 - CANCELLED

Dear IBC Members:

On behalf of Dave Emery, Chair, of the IBC this is notification that next week's
IBC convened meeting for Friday, September 9th from 1-3 pm
has been cancelled.

There is currently no research protocols or other agenda items needing review or
discussion. We will be rescheduling this meeting for sometime in the month of
October.

Thank you.

Pat Azeltine
Administrative Assistant to the IBC
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Final

University of Washington
Institutional Biosafety Committee

Ad-Hoc Committee Meeting
Wednesday, July 20, 2005
1:00 – 3:00 pm
SCC 354
Meeting Minutes

Members Present:
Michael Agy, Washington National Primate Research Center
David W. Emery (IBC Chair), Medicine / Medical Genetics
Mary Lampe, Laboratory Medicine
Stephen Libby, Laboratory Medicine
David Russell, Hematology
Paul Swenson, Seattle-King County Dept. of Public Health
Donald Wang, ZymoGenetics
Bruce Whitney, Environmental Health and Safety (BSO)
James Woods, Environmental & Occupational Health Sciences

Members Absent:
William Atkins, Medicinal Chemistry
Ashley Fleischman, ASUW Student Representative
Elaine Jong, HH Primary Care Ctr/UW Campus Health Svcs
Pamela Morris, Comparative Medicine
Carol Sibley, Genome Sciences
Estella Whimbey, Healthcare Epidemiology and Infection Control

Guests:
Susan Alexander, Environmental Health and Safety
Patricia Azeltine, Environmental Health and Safety

Handouts:
Powerpoint Presentation
IBO Reports

1. **CALL TO ORDER**
   1a. Chair David Emery called the meeting to order at 1:06 p.m.

2. **APPROVAL OF MINUTES from April 25, 2005 Meeting**
   2a. The minutes from the April meeting were unanimously approved as submitted to the membership.

3. **ADMINISTRATIVE/INFORMATION UPDATES**
   3a.
   Responding to community concerns over the recently proposed regional biocontainment laboratory, the University of Washington is planning for two additional public members to the membership roster. The goal is to identify candidates from the public sector who are knowledgeable about biological issues either in a general sense or with specific expertise that they could bring to the committee.

   This increase in committee membership is in addition to the current need for an IBC member from the University with expertise in plant genetics. The Dean's Office is actively recruiting for candidates

and suggestions from current committee members should be directed to David Emery, IBC Chair, or Karen VanDusen, Director, Environmental Health & Safety.

3b.
Susan Alexander, Manager, Occupational Health & Safety, provided a powerpoint presentation on several pertinent issues:

a. The recently established Research & Biological Safety (RBS) Office in EH&S
b. Compliance questions involving SAGE
c. Ongoing review and revision of the Research Project Hazard and Assessment form (RPHA)

4. SPECIFIC RESEARCH PROPOSALS

4a. Biosafety Officer Reports

There was no Biosafety Officer from Deanna Frost at the April 25th meeting of the IBC due to her recent resignation. In the interim, Susan Alexander compiled a report based on Deanna Frost's documentation covering the period September 18, 2004 through April 1, 2005. Bruce Whitney, as sole Biosafety Officer, has been approving both select agent and non-select agent projects. His report contains approvals covering the period of April 25, 2005 through July 8, 2005.

Bruce began by noting that his report contains a footnote that the only BL-3 approvals listed in the report are for renewals since the IBC administrative policy is that the BSO can only approve up to BSL-2. Bruce asked the committee's assistance in helping to clarify already existing but broadly stated policies in the EH&S Biosafety Manual regarding research involving cloning or inserting oncogenes into cells with vectors. What would the committee advise as to the appropriate biocontainment level? Should these protocols be presented to the full committee with specific criteria?

David Emery, Chair, acknowledged that the cloning of genes has been a recurrent safety issue. The most current information is available on the internet where a list can be found of genes that have been associated with human cancer such as the Sanger website.

Questions about biocontainment levels for research protocols involving genes on this list is a more complicated issue due to the number of different delivery methods. For example, plasmid genes are delivered by electroporation and the risk to the investigator does not increase because the chances of the gene entering their blood cells is imperceptibly small. A wild type virus known to infect humans and can integrate into the genome of the blood cells is already at a high level of biosafety containment. There is the gray area of replication defective viruses that can at some rate infect humans but don't actively divide and will not spread. Some of these viruses will integrate into the genome and are maintained after cell division while others are not maintained. A subcommittee will be formed to address these concerns and to develop an abbreviated list addressing the properties of delivery systems and their corresponding risk level.

David Emery had the following comments in regards to Deanna Frost's report:

Robert Richard's protocol (Gene Therapy for HIV Infection) was approved appropriately. The research involves growing small amounts of wild-type HIV. The material will be handled with BSL-3 practices within a BSL-2 facility. This was deemed appropriate for several other investigators at the UW at a previously convened meeting of the IBC based on the NIH standards. Dr. Richards has completed the process of developing a lab safety manual and training requirements. He is the first of several researchers with similar proposals who has completed this necessary step for IBC approval. Dr. Richard's lab safety manual has been reviewed and approved by Environmental Health & Safety. Committee members can obtain a copy of this manual for review from Bruce Whitney.

Deanna Frost's report also contains several approved proposals listed as BSL-3 and in each case these are re-approvals of previously approved protocols with one exception which is in error. Principal investigator, Nancy Haigwood's research proposal (Role of Neutralizing Antibodies in

Transmission of SHIV) has not been approved and is, in fact, the same protocol that appears on Bruce's more recent report under principal investigator, David Anderson.

4b. Principal Investigator: Oliver Press

Research Title: "A Phase I Study to Evaluate the Safety of Cellular Immunotherapy Using Genetically Modified Autologous CD-20 Specific CD8+ T-cell Clones for Patients with Relapsed CD-20+ Indolent or Mantle Cell Lymphomas"

Subcommittee Review and Recommendations
Dr. Press has submitted several significant changes to his clinical gene transfer trial. This trial involves the plasmid transfection of patient blood cells, the growth of these cells in culture for an extended period, and the reinfusion of these cells back into the patient. The project was last reviewed in the spring of 2004. The protocol was deemed very low risk, due in large part to the use of plasmid as the means of gene delivery and the delivery of the plasmid ex vivo. The changes, in essence, involves the modification of the enrollment criteria to include patients with other forms of lymphoma for which the therapy is relevant, modifications of the adjuvant chemotherapy consistent with these new forms of lymphoma, the addition of a second consent process, and the replacement of Dr. Press with Dr. Eric Chen as principal investigator. The changes in patient population and the principal investigator would not increase risk. These changes have been approved by the FHCRC IRB. David Emery, Chair, reviewed the changes and recommended approval.

A vote was called to approve/disapprove the protocol with its' significant changes and the results were as follows:

APPROVE: 9
DISAPPROVE: 0

5. ISSUES FROM THE FLOOR

5a. There were no issues from the floor.

Meeting Adjourned at 2:05 pm.

Meeting Minutes by Patricia Azeltine

Date: Thu, 5 May 2005 13:23:57 -0700 (PDT)
From: P. Azeltine <azeltine@u.washington.edu>
To: Institutional Biosafety Committee <ashf@u.washington.edu>,
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martines@u.washington.edu, Joann Kauffman <jlkauff@u.washington.edu>,
Sharon Murphy <murphys@u.washington.edu>
Subject: May 13th IBC Meeting - CANCELLED

Dear IBC members:

On behalf of Dave Emery, Chair, next week's May 13th meeting has been CANCELLED
.
There are currently no specific research protocols requiring
review.

The meeting shall be rescheduled for late June or early July. There are several proposed administrative items as well as possible research proposals requiring review. This will result in a full agenda for our
next meeting.

We will be notifiying you as soon as possible in regards to the date and time.

Thank you.

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45.3.1
21.2.5

FINAL

University of Washington
Institutional Biosafety Committee

Ad-Hoc Committee Meeting
Monday, April 25, 2005
1:00 – 3:00 pm
SCC 303
Meeting Minutes

Members Present:	Michael Agy, Washington National Primate Research Center David Emery (IBC Chair), Medicine / Medical Genetics Ashley Fleischman, ASUW Student Representative Elaine Jong, HH Primary Care Ctr / UW Campus Health Svcs Stephen Libby, Laboratory Medicine David Russell, Hematology Carol Sibley, Genome Sciences Paul Swenson, Seattle-King County Dept. of Public Health Donald Wang, ZymoGenetics Estella Whimbey, Healthcare Epidemiology and Infection Control Bruce Whitney, Environmental Health and Safety (BSO)
Members Absent:	William Atkins, Medicinal Chemistry Mary Lampe, Laboratory Medicine Pamela Morris, Comparative Medicine James Woods, Environmental & Occupational Health Sciences
Guests:	Susan Alexander, Environmental Health and Safety Patricia Azeltine, Environmental Health and Safety JoAnn Kauffman, Environmental Health and Safety
Handouts:	Membership Roster Powerpoint Presentation

1. **CALL TO ORDER**
   1a. Chair David Emery called the meeting to order at 1:08 p.m. Ashleigh Fleischman, ASUW representative was introduced as the newest member of the committee.

2. **APPROVAL OF MINUTES from December 14, 2004 Meeting**
   2a. The minutes from the December meeting were unanimously approved as submitted to the membership.

3. **ADMINISTRATIVE/INFORMATION UPDATES**
   3a. Deanna Frost (Institutional Biosafety Officer) submitted her resignation effective April 1, 2005. Environmental Health & Safety is actively recruiting for her replacement.
   3b. The proposed construction of a regional biocontainment laboratory at the University of Washington has generated immense interest both on and off campus. The U.W. has applied for a federal grant to construct this building in support of a Regional Center of Excellence for

biodefense and emerging infectious disease research. The review process for this building is proceeding in accordance with the regulations set by the NIH (the funding agency) and by the University Siting Committee. The issue has not formally come before the IBC because it is currently a UW application for the construction grant. Should the project receive funding it will then come up for review before the committee. The IBC is fully engaged in reviewing the research, given some preliminary recommendations and will continue to be involved in on-going review.
If contacted by the public or the press, IBC members have every right to discuss this issue and to feel free to do so. Interested parties may also be referred to Theresa Doherty, Assistant Vice President for Regional Affairs, Office of Regional Affairs and Tina Mankowski, Director, HS/UW Medicine News and Community Relations.

3c. The University of Washington Infectious/Biomedical Waste Management Plan has been under development and the committee has already reviewed two draft versions. This final draft was reviewed in depth by two IBC members: Pam Morris and Don Wang. Dr. Morris could not be present at today's meeting but has conveyed to chair, David Emery that she approves the plan. Dr. Wang also recommends approval. There was no further discussion by the committee, the vote was taken and the plan was approved unanimously.

4. SPECIFIC RESEARCH PROPOSALS

4a. Principal Investigator: David A. Saperstein
Research Title: An Open-Label, Phase 1, Single Administration, Dose-Escalation Study of AdGVPEDF.11D in Neovascular Age-Related Macular Degeneration (AMD), IBC reference number 1425-593

Brief Summary: This is a re-review of a clinical gene transfer. The study involves the injection of a replication-defective adenovirus vector for human pigment epithelium-derived factor (PEDF) into the eyes of patients with age-related macular degeneration (an eye disease). This project was originally approved by the IBC in June 2003. However, the trial was subsequently suspended by the PI, and in our September 2004 meeting it was decided that this project should be reviewed prior to re-initiation. In addition, Dr. Saperstein has requested to extend the study to include patients with less severe AMD.

Subcommittee Report and Recommendations: The revised application was reviewed by IBC members David W. Russell and David W. Emery. Dr. Russell's re-review summary states that he has read the revised Saperstein/GenVec protocol submitted for IBC review. This protocol is a revision of an already approved protocol for treatment of age-related macular degeneration (AMD) with an adenovirus vector expressing Pigment-Epithelium-Derived Factor (PEDF) to inhibit angiogenesis. No major adverse events were noted in the original protocol. The revision extends this study to patients with less severe AMD. Dr. Russell recommends approval by the IBC of the revised protocol and Dr. Emery concurs with this recommendation.

The vote for the approval of this application was done electronically and the results of that vote are as follows:

15 APPROVE
1 ABSTAIN

4b. Principal Investigator: A. Dusty Miller
Research Title: Transduction of the Upper Airway Epithelium in Patients with Cystic Fibrosis by an AAV2 Vector that Encodes Human Alkaline Phosphatase

Brief Summary: This project involves the administration of a recombinant vector based on human adeno-associated virus, serotype 2 (AAV2) designed to express a reporter gene (human alkalin phospatase), into the upper airway (nasal) tissue in patients with cystic fibrosis. The goal of this trial is to establish the efficacy and safety of this vector in support of future trials in a which a similar vector designed to express normal human CFTR, the gene that is defective in patients with cystic fibrosis patients. The results of this trial will also be used in support of future trials comparing the

safety and efficacy of a similar vector based on AAV serotype 6. Recombinant vectors based on AAV are generally considered very safe and are approved for use at BSL-1. There are no outstanding safety issues with the proposal.

Subcommittee Report and Recommendations: The subcommittee consisted of Mary Lampe (IBC member) and William Osborne (ad hoc reviewer). Mary Lampe stated in her review that the vector has been shown to be safe. The AP gene is a normal human protein and should not stimulate an immune response. The study procedures carry a risk but patients are adequately notified in advance and have consented to participate in the study. Safety measures are extensive and patients will be monitored for life. Safety data will be reviewed and the study will proceed only if the initial dose levels are found to be safe. William Osborne, in his summary review stated that he had no concerns regarding the biosafety of this protocol to patients and staff. Dr. Osborne is in agreement with the deliberations of the NIH Recombinant DNA Advisory Committee and the review by the Data and Safety Monitoring Board. Both members of the subcommittee recommend approval of the protocol.

Mary Lampe could not be present at today's meeting but conveyed her approval of the proposal to chair, David Emery. There were two questions raised as to whether it had been reviewed elsewhere (yes, such as the RAC) and whether the Human Subjects Office had looked at it? (Yes, and will so again when the IBC gives final approval.) A vote of the committee was called (two members having recused themselves) with the following results:

9	APPROVE
2	ABSTAIN

The A. Dusty Miller protocol was approved by the committee.

4c. Biosafety Officer Reports

Dave Emery reiterated that research proposals that include human gene transfer or environmental releases, biosafety level 3 research or select agent research is reviewed and voted on by the committee. For all other research including biosafety level 1 and 2, the committee has set standards by which the biosafety officers provide administrative approval on behalf of the IBC and then notify the IBC with written reports. These reports are reviewed at the next meeting and a committee member can bring up any questions or issues.

Deanna Frost, Biosafety Officer, was responsible for the majority of these administrative reviews but has, as previously mentioned, recently resigned. The report consisting of approximately 74 biosafety level 1 and 2 protocols that Deanna has approved is not ready at this time. Environmental Health & Safety is working on completing this report and it will be available at the next committee meeting.

Bruce Whitney, Biosafety Officer, is predominantly responsible for research involving select agents and exempted select agents and toxins. There were two approvals since the last committee meeting of 12/14/04. One approval is for principal investigator, Michael Katze, for a biosafety level 2 protocol involving a mouse strain of influenza. The second approval was for a biosafety level 2 protocol involving human cell lines containing EBV with Melissa Austin as principal investigator.

5. IBC MEMBER TRAINING – David Emery

5a. Dr. Emery provided training on the function, responsibilities, and operating guidelines of the IBC committee as required by the NIH.

6. ISSUES FROM THE FLOOR

6a. There were no issues from the floor.

Meeting Adjourned at 2:00 pm.
Meeting Minutes by Patricia Azeltine

Date: Thu, 13 Jan 2005 15:01:06 -0800 (PST)
From: P. Azeltine <azeltine@u.washington.edu>
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martines@u.washington.edu
Subject: IBC MEETING - CANCELLED

Dear IBC Committee Members:

On behalf of Dave Emery, Chair, tomorrow's IBC meeting has been CANCELLED.

The one business item on the agenda was review and approval of the UW Infectious/Biomedical Waste Management Plan. New comments were received this week and may require changes to the plan which will need to be brought before the IBC and the Infectious Waste Committee. In addition there were no research proposals to review. In light of this, tomorrow's meeting will be rescheduled and we will take that opportunity to expand the training segment.

We appreciate your patience in this matter and will be notifying you as soon as possible in regards to the new date and time.

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FINAL

University of Washington
Institutional Biosafety Committee

Ad-Hoc Committee Meeting
Tuesday, December 14, 2004
12:00-2:00 pm
SCC 303
Meeting Minutes

Members Present:
Michael Agy, Washington National Primate Research Center
William Atkins, Medicinal Chemistry
David Emery (IBC Chair), Medicine / Medical Genetics
Deanna Frost (IBO), Environmental Health and Safety
Elaine Jong, HH Primary Care Ctr / UW Campus Health Svcs
Mary Lampe, Laboratory Medicine
Stephen Libby, Laboratory Medicine
Pamela Morris, Comparative Medicine
David Russell, Hematology
Carol Sibley, Genome Sciences
Paul Swenson, Seattle-King County Dept. of Public Health
Donald Wang, ZymoGenetics
Bruce Whitney, Environmental Health and Safety (BSO)

Members Absent:
Ashleigh Fleischman, ASUW Student Representative
Estella Whimbey, Healthcare Epidemiology and Infection Control
James Woods, Environmental & Occupational Health Sciences

Guests:
Susan Alexander, Environmental Health and Safety
Patricia Azeltine, Environmental Health and Safety
Ann Collier, UW AIDS Clinic / Harborview Medical Center
JoAnn Kauffman, Environmental Health and Safety
John Thompson, Division of Oncology / Fred Hutchinson Cancer Research Ctr
Karen VanDusen, Environmental Health and Safety

By Teleconference Call:
Mark Murray, President & CEO, Protiva Biotherapeutics
Ian MacLachlan, Chief Scientific Officer, Protiva Biotherapeutics

1. **CALL TO ORDER**
   - 1a. Chair David Emery called the meeting to order at 12:03 p.m.
   - 2b. IBC members and guests present in the room identified themselves. A call to Protiva was placed by Deanna Frost. Mark Murray and Ian MacLachlan of Protiva Biotherapeutics were present via speaker phone.

2. SPECIFIC RESEARCH PROPOSAL

2a. Principal Investigator: John A. Thompson
Research Title: A Phase I Study to Evaluate the Safety and Pharmacokinetics of Pro-1, A Liposome-Encapsulated Thymadine Kinase Gene Formulation, In Patients with Stage IV Melanoma

Brief Summary: This trial is sponsored by Protiva Biotherapeutics and involves the systemic delivery of a plasmid/liposome complex to patients with advanced stage (stage IV) melanoma. The plasmid contains a gene for thymadine kinase that renders transfected cells susceptible to killing by subsequent oral administration of the prodrug Valtrex (valacyclovir hydrochloride). The liposome allows the plasmid complex to be delivered systemically and, in theory, to selectively traffic to the sites of tumor. Preclinical studies in immunodeficient mice transplanted with human melanoma cells demonstrate a modest degree of efficacy. However, these studies also demonstrated systemic, long-term persistence of vector plasmid, and short-term systemic pathology (apoptosis/necrosis of hematologic, pulmonary, renal and gastrointestinal tissues).

Dr. Thompson began his presentation at 12:05. Mark Murray and Ian MacLachlan were present via speaker phone to help answer any specific questions regarding the protocol. This is a clinical trial that has been underway for two years involving Dr. Thompson, the Department of Oncology and Protiva. Dr. Thompson finished at 12:25 where a question and answer session about the protocol took place between IBC members, Dr. Thompson and Protiva.

3. SUBCOMMITTEE REPORT AND RECOMMENDATIONS

3a. There were two IBC committee members who reviewed the protocol: Dr. Dave Emery and Dr. David Russell.

Dr. Emery felt the review was complicated by several factors:

1. Response to recommendations of the RAC.
2. The occurrence of serious adverse events in the clinical trials.
3. Reinitiation of the protocol trials without IBC review/approval.

Dr. Russell's concerns included:

1. The animal models were not convincing as to anticipated effects in humans.
2. The single case of a steroid being used to limit toxicity was not adequate proof.
3. The preclinical data did not demonstrate that there was any expected efficacy when steroids are included.
4. The Consent Form mentions some of the serious adverse events but does not suggest that these side effects were serious.
5. Although the TK gene being delivered in this study may have little or nothing to do with the toxicity of the treatment, it is still a gene therapy study, and as such will receive an exceptional level of scrutiny if serious adverse events occur resulting in liability by the University.
6. How much risk is acceptable in a terminal cancer patient and the issue of risk benefit is not typically the domain of the IBC.

At 1:16, Dr. Thompson was asked to leave the room and Protiva's teleconference call was placed on mute so that a vote by committee members could take place.

Dr. Emery proposes: The IBC will approve this protocol contingent on rewriting the human subject's informed consent to more accurately reflect the hazard. Dr. Emery asks that Dr. Jong and Dr. Russell be the arbitrators of the satisfactory wording of the consent form. That was the proposal coming from the Chair and it needed no seconds.

The vote took place conditional upon the rewording of the informed consent and was as follows:
YES: 9
NO: 4

The proposal was approved. At 1:18 after the vote was taken, Protiva was reengaged on the telephone. The Institutional Biosafety Officer Deanna Frost) will send notification to the OBA stating the IBC's decision (a non-unanimous vote to approve the protocol) but with modifications to the consent form. Dr. Russell and Dr. Jong will coordinate with Dr. Thompson about the consent form changes.

4. APPROVAL OF MINUTES

4a. Minutes from the September 17, 2004 IBC meeting were unanimously approved as submitted.

5. ADMINISTRATIVE/INFORMATION UPDATES

5a. Membership Updates – There are two new members to the IBC: Elaine Jong, Director of the University Hall Health Primary Care Center and also Medical Director of Campus Health Services. IBC also has a new student representative, Ashleigh Fleischman, who was unable to attend the meeting today.

6. SPECIFIC RESEARCH PROPOSAL:

6a. Principal Investigator: Ann C. Collier
Research Title: A Phase I/II Clinical Trial to Evaluate the Safety and Immunogenicity of the HIV-1 DNA Vaccine in HIV-1 Infected Subjects Treated During Acute Infection

Brief Summary: This clinical gene transfer protocol is similar to the protocol of Dr. Collier approved at the July 13, 2004 convened meeting of the UW IBC, except that it uses plasmid DNA rather than a recombinant adenovirus as the delivery vehicle. This trial is also part of a multi-center trial that has already enrolled subjects at other sites without any agent-related serious adverse events. It involves a phase I/II clinical trial sponsored by the Division of AIDS / National Institute of Allergy and Infectious Diseases (NIAID, NIH) and is designed to assess an anti-HIV vaccine based on recombinant plasmids. The vaccine, produced by NIAID, consists of 4 plasmids encoding the proteins Gag, Pol, and Nef from HIV-1 clade B, and Env from HIV clade A, B, and C. In order to reduce the potential for functional activity, coding sequences contain inactivating mutations. The trial entails injecting the vaccine into the deltoid muscles of HIV-positive subjects, and studying these patients for various immune responses on and off antiretroviral therapy. Pre-clinical and clinical studies with healthy subjects indicate that the vector is both safe and capable of eliciting a significant cellular immune response. The vaccine itself represents essentially no infectious agent risk because it is based on plasmid DNA, and thus can be handled at BSL-1. There is no apparent acute risk to the patient, and good pre-clinical and clinical data to justify the trial. Current data suggests that the long-term oncogenic potential of injected plasmid DNA is extremely low.

Discussion on this protocol began at 1:22. This was reviewed by a subcommittee comprised of David Russell and Dave Emery. There was a consensus recommendation for approval. Chair moved for approval and opened it for discussion. There being no discussion a vote was called and the vote was a unanimous approval.

7. ISSUES FROM THE FLOOR

7a. Carol Sibley asked what if the issue of risk benefit analysis should come up again? And if so what should the members be prepared to do? Dave Emery felt that this particular meeting (in regards to the Thompson protocol and the issues it raised) were very illustrative of what the IBC will be challenged with in the future. The IBC will need to look at how it will assess proposed projects beyond biohazards to research personnel and the community.

Dr. Emery stated he would work on a proposal before the next convened meeting. He felt that excellent issues were raised in the meeting and he understood the committee members' concerns.

It was suggested the members of some of the other review committees (who have approved protocols now before the IBC) could possibly attend the IBC review. Elaine Jong suggested the Bioethics Committee could help with some of these types of difficult decisions and how the IBC should approach these issues. Or perhaps develop a mutual relationship with that committee and rely upon their advice when reviewing such protocols.

Meeting Adjourned at 1:29 pm.

Meeting Minutes by Patricia Azeltine

FINAL

University of Washington
Institutional Biosafety Committee

Friday, September 17, 2004
1:00-3:00 pm
SCC 354
Meeting Minutes

Members Present:
Michael Agy, Washington National Primate Research Center
William Atkins, Medicinal Chemistry
David Emery (IBC Chair), Medicine / Medical Genetics
Deanna Frost (IBO), Environmental Health and Safety
Stephen Libby, Laboratory Medicine
Carol Sibley, Genome Sciences
Donald Wang, ZymoGenetics
Bruce Whitney, Environmental Health and Safety (BSO)
James Woods, Environmental & Occupational Health Sciences

Members Absent:
Mary Lampe, Laboratory Medicine
Pamela Morris, Comparative Medicine
David Russell, Hematology
Paul Swenson, Seattle-King County Dept. of Public Health
Estella Whimbey, Healthcare Epidemiology and Infection Control

Guests:
Susan Alexander, Environmental Health and Safety
JoAnn Kauffman, Environmental Health and Safety
John Kemner, WWAMI RCE

1. **CALL TO ORDER**
   1a. Chair David Emery called the meeting to order at 1:03 p.m.

2. **APPROVAL OF MINUTES**
   2a. Minutes from the July 13, 2004 IBC meeting were unanimously approved as submitted.

3. **ADMINISTRATIVE/INFORMATION UPDATES**
   3a. **Membership**
   The new ASUW Student IBC representative is being recruited. Chair David Emery introduced Bruce Whitney, Biosafety Officer, as a new IBC member serving as the primary contact for work with Select Agents, Exempted Select Agents, and research requiring biosecurity. Bruce is also a member of the Institutional Animal Care and Use Committee.

   3b. **Meeting Schedule**
   The proposed 2005 meeting schedule for regularly convened IBC meetings is as follows:
   Friday, January 14, 2005
   Friday, May 13, 2005
   Friday, September 9, 2005

   Members are asked to check calendars and if conflicts are evident, report them to Susan Alexander from EH&S.

   3c. **IBC Training**
   The Chair stated that training for IBC members is planned for the next two convened meetings. The training, required by NIH Guidelines, will include a general overview of the roles and

responsibilities and operating procedures of the IBC. The committee will be formalizing these procedures as part of this process.

3d. **Infectious Waste Plan Update:** Update by JoAnn Kauffman

The UW's Infectious Waste Management Plan, prepared on behalf of the UW IBC and the UW Infectious Waste Committee, has been revised and is under final review. At prior meetings, the IBC had the opportunity to review and comment on the revised plan. From this review, the IBC identified an issued related to nonhuman primate waste disposal, which required additional evaluation and resolution. JoAnn Kauffman represented a small group, tasked by both committees to address this issue. She reported the group met several times and will be meeting with Seattle King-County Public Health Dept. Results will be incorporated into one last draft prior to finalization and approval.

The Chair indicated a subcommittee of the IBC would be delegated review and final approval of the plan incorporating these last changes. Those wishing to volunteer for this subcommittee should contact Dave Emery.

3e. **UW Biosafety Manual Changes:**
Susan Alexander distributed a section of the Biosafety Manual as it currently appears and a proposed draft. The draft reflects changes resulting from the IBC's decision at the January 2004 meeting to change containment for research with HIV infected samples, in compliance with NIH regulations.

Deanna Frost expressed concern that facilities is assigning lab space for other projects when there has not been a BSL determination made for the specific protocol.

Deanna also asked that the Biosafety manual be revised to clarify responsibilities of the PI regarding assurance that work in laboratories is conducted at the specified biosafety level; and that the PI has the prerogative to work at a higher level of containment than required.

It was decided that further review was necessary and this would be addressed in a future meeting.

4. SPECIFIC RESEARCH PROPOSALS

The Chair reviewed with the committee, the process for IBC review and approval of research. The University's Biosafety Officers, on behalf of the IBC, have executive approval authority for BSL-1, BSL-2 research. The IBC uses subcommittees for initial review and recommendations back to the full committee for consideration and approval by vote for these types of research:

- Research involving RG-3 (risk group-3) organisms
- Activities requiring BSL-3
- Adding things that NIH Guidelines specifically indicates raises the risk
- Human gene therapy, or
- Release to the environment.

4a. BIOSAFETY OFFICER REPORT BY DEANNA FROST:

<u>Actions/Determinations by the IBSO (D. Frost) on behalf of the IBC</u> - w/handout:

A general review of the projects approved by the IBSO was provided. The committee was informed that the report now contains the biosafety level determination. Biosafety levels in parenthesis indicates the agent is not actually being administered.

Two investigators with BSL-3 laboratories, Drs. CheChung Tsai and Shiulok Hu, had commented upon the lowered containment for the HIV work. The lowered containment determination caused concern that was addressed as follows:

- the determination pertained to carefully doing work in a biosafety level 2 facility with biosafety level 3 practices.
- In any biosafety level 3 laboratory, all experiments must be done using biosafety level 3 practices – per NIH Guidelines and the BMBL.

Any comments on this report should be addressed to Deanna Frost, with a copy to the Chair.

Report on the Status of Open UW Registered Human Gene Transfer – D. Frost w/handout:

Mary L. Disis	A phase I study of a plasmid based vaccine encoding the HER-2/neu overexpressing tumors. A Phase I Trial to Evaluate the Safety and Immunogenicity of a DNA Plasmid Based Vaccine Encoding the HER-2/neu Intracellular Domain in Patients with Stable, Advanced Stage HER-2/neu (HER2) Overexpressing Breast and Ovarian Cancer. IRB renewal protocol #1 - 8/13/04-2/12/05; protocol #2 has not been approved yet. Reviewed and administratively approved by Drs. Emery and Frost.
IBC Decision:	**1-year renewal granted.**

John A. Thompson	Phase II Study of High-Dose Allovectin-7 in Patients with Advanced Metastatic Melanoma (VCL-1005-208; version 5.00 received summary on 1/29/03). An updated Investigators' Brochure was received. Enrollment is closed; no longer administering; long-term follow continues. FDA requires 15 year follow-up. The IRB renewal date on handout should be corrected to 6/16/04-6/15/05. Adverse events occurred, but not at this (UW) institution.
IBC Decision:	**Establish a new category of IBC review, entitled, "long-term follow-up", after discussion of the necessity for further review if there would no longer be study administration.**

Oliver Press	Immunotherapy using Genetically Modified Autologous CD-20 specific CD8+ T-Cell Clones for Patients with Relapsed CD-20+ Indolent Lymphomas (FHCRC protocol #1503 / UWCRC protocol 1191) Protocol revisions submitted to IRB, OBA. IRB renewal 8/24/2004 – 1/13/2005. No significant changes to protocol. No adverse events. Recommend renewal.
IBC Decision:	**Renewal decision will be address at next convened meeting.**

David A. Saperstein	An Open Label, Phase I, Single Administration, Dose-Escalation Study of ADgvPEDF.1D in Neovascular Age-related Macular Degeneration (AMD). Enrollment for this does is closed. IRB renewal 7/28/04-7/27/05. 3 adverse events at UW.
IBC Decision:	**Chair is requesting subcommittee review with recommendations to be presented to the full committee at the next IBC convened meeting.**

4a. BIOSAFETY OFFICER REPORT BY BRUCE WHITNEY: w/handouts

General information was provided on the Select Agent and Exempted Select Agent Program. Any work involving Select Agents must be registered with the CDC and the UW's Responsible Official. Work with exempted select agents requires approval and registration by the UW's Responsible Official and compliance with the University's Exempt Select Agent and Toxin Program. Exempted select agents include exempted quantities of listed select agent toxins, attenuated strains, and products. To apply for the Select Agent Program or the Exempted Select Agent and Toxin Program, contact Bruce Whitney or the University's RO/ARO. Requirements for these programs must be met prior to obtaining, using or storing these materials.

4b. SUBCOMMITTEE REPORT AND RECOMMENDATIONS – EXECUTIVE SESSION

This section is CONFIDENTIAL and EXEMPT from public disclosure pursuant to RCW 42.17.310(l)(ww).

Chair Emery stated the committee was going into executive session for discussion of the next protocol and any public members would be asked to leave. (There were none present). He also stated that the following guests would remain in the room, Susan Alexander and JoAnn Kauffman, both of Environmental Health & Safety at UW.

John Kemner, Assistant Director for the WWAMI RCE project was introduced and was attending today's meeting on behalf of the PI, Sam Miller.

This project involves RG-2 organisms, which the Biosafety Officer has previously reviewed and administratively approved on behalf of the IBC. The Chair asked if any member of the committee saw a concern or wished further discussion. The project remains approved as submitted.

The portion of the project brought before the IBC today, consists of work involving 3 attenuated strains, which NIH lists the primary organism as RG-3 agents. The 3 strains in review are not specifically listed in NIH. As a result, an IBC subcommittee comprised of David Emery, Stephen Libby, and Bruce Whitney reviewed the portion of this project involving these strains and recommends approval as submitted, at BSL-2. The BSO noted that the 3 strains are attenuated and are exempt from the select agent rules. EH&S has on record, the exempted registration documentation for these strains.

IBC proposal by the Chair:
Move for approval of use of these 3 specific strains w/deletions at BSL-2. Motion seconded.

IBC approval would allow Miller (PI) to conduct work like transposon mutagenesis to knock out genes; however as for adding genes from more pathogenic organisms by random cloning or putting in genes that will change virulence is not approved and must go back before the IBC for consideration. Select Agent exemption criteria must continue to be met.

IBC Decision:
Unanimous approval by vote.

BSO Whitney requesting clarification from IBC if other research on campus meets same exact exemption (vaccine strain), would this need to be brought before the IBC?

Chair responded that per the IBC's decision today, these specific strains can be approved by the BSO at the same level.

Executive session terminated and meeting is open to general public.

5. **ISSUES FROM THE FLOOR**

5a. Deanna Frost reported annual BSL-3 inspections due this month.

5b. Deanna Frost indicated there were issues with Lymphocytic choriomeningitis virus (LCMV) research. This is will be evaluated by an IBC subcommittee with recommendations brought back to the full committee.

5c. Deanna Frost reported 2 BSL-3 labs are not in operation as such; one is undergoing construction and the second is in use for BSL-2 research.

5d. The Chair reported that the UW issued a press release on the Katze study. The NHP work has not been submitted to the IBC for consideration.

Meeting Adjourned at 2:40 pm.

University of Washington

Institutional Biosafety Committee

Tuesday, July 13, 2004
2:00-3:00 pm
SCC 354
Meeting Minutes

Members Present:
Michael Agy, Washington National Primate Research Center
William Atkins, Medicinal Chemistry
David Emery (IBC Chair), Medicine / Medical Genetics
Deanna Frost (IBO), Environmental Health and Safety
Mary Lampe, Laboratory Medicine
Pamela Morris, Comparative Medicine
Carol Sibley, Genome Sciences
Paul Swenson, Seattle-King County Dept. of Public Health
Donald Wang, ZymoGenetics
Estella Whimbey, Healthcare Epidemiology and Infection Control

Members Absent:
Stephen Libby, Laboratory Medicine
David Russell, Medicine / Hematology
James Woods, Environmental & Occupational Health Sciences

Guests:
Susan Alexander, Environmental Health and Safety
JoAnn Kauffman, Environmental Health and Safety
Bruce Whitney, Environmental Health and Safety
Karen VanDusen, Environmental Health and Safety
Ann Collier, Medicine, and Allergy and Infectious Diseases

1. **Call to Order**
   1a. Chair David Emery called the meeting to order at 2:04 p.m.

2. **Welcome and Introductions**

3. **Administrative/Information Updates**
   3a. Minutes from the last meeting on May 4, 2004 have been electronically approved via email with a vote of 9-yes; 0-no; 2-abstain; 3-did not vote.
   3b. ASUW Student Member Aaron Ketola is no longer a member of the IBC, due to graduation. His name has been removed from the roster. A new student member will be assigned to the IBC this fall.
   3c. The next scheduled IBC business meeting is September 17, 2004 at 1:00, in SCC room 354.
   3d. Institutional Biosafety Officer Deanna Frost reported that the laboratory facilities for the Boeckh and Collier projects discussed below have been reviewed and meet required safety, operational and containment criteria.

4. Specific Research Proposals

IBC Subcommittee Review

4a. 1) Principal Investigator: Michael Boeckh
Research Title: *"A Phase I Clinical Trial to Evaluate the Safety and Immunogenicity of the Intramuscular Vical CMV Immunotherapeutic Vaccine in Healthy Adult Subjects"*
Subcommittee Members: *David Emery and David Russell. David Russell is out of town. His vote on this proposal was proxy, presented by Chair David Emery.*

Brief Summary: This application involves a corporate-sponsored, phase I clinical safety trial to assess a plasmid-based vaccine for CMV in healthy adult patients. The vaccine, produced by Vical Incorporated, consists of two plasmids expressing separate CMV genes (extra cellular domain of CMV gB and CMV pp65 tegument protein with a putative kinase domain removed) complexed with a liposome-like copolymer. The vaccine is administered by intramuscular injection at 0, 2, and 8 weeks in a dose-escalation format (up to 5 mg). The immune response is monitored over several additional months. Studies in mice and rabbits demonstrated a strong immune response. Studies in mice also suggest that the vaccine plasmid persists at low but detectable levels at the site of injection, and very low levels at other sites (such as bone marrow), for up to 61 days (last time point tested).

Comments

Because this is a plasmid-based gene delivery system, there are no risks associated with vector mobilization and thus no risk of exposure to the public. Neither of the CMV genes constitute a known biohazard. Preclinical studies suggest that a small amount of vector plasmid will integrate into subject's chromosomes, both at the site of administration and at other sites. However, the level of integration is expected to be very low, and the risk from such events, such as the induction of cancer, should be exceedingly small. The investigator's brochure points out that similar plasmid delivery systems have been administered to over 2000 subjects without evidence of mutagenesis or oncogenesis. The draft Informed Consent document clearly states this risk as "This could lead to cancer or unknown side effects".

Initial Subcommittee Recommendation to the convened IBC: Conditional approval upon

1) *Final* IRB approval, with the statement cited above included stating a small risk of cancer or unknown side effects;

2) The location where vaccine is administered is reviewed and approved by responsible Infection Control Team or Institutional Biosafety Officer for compliance with BL-1 standards;
3) The location where vaccine is stored and/or formulated for injection is disclosed (if different than location of administration) and reviewed and approved by responsible Infection Control Team or Institutional Biosafety Officer for compliance with BL-1 standards;
4) Section E4 of the Research Project Hazard Assessment application is amended to indicate applications involve human gene transfer and to provide description of the inserted genes.

IBC Motion:
David Emery moved to approve the subcommittee's recommendation of conditional approval, with the understanding that the issues involving facilities (conditions 2 and 3) have already been satisfied.

IBC Vote.
Unanimous vote of approval of said motion by all IBC members.

4a. 2) Principal Investigator: Ann Collier
Research Title: "A Phase II Double-Blinded, Randomized, Placebo-Controlled Study to Evaluate the Antiretroviral Effect of Immunization with the MRK Ad5 HIV-1 GAG Vaccine in HIV-1 Infected Individuals who Interrupt Antiretroviral Drug Therapy (ACTG5197)"
Subcommittee Members: David Emery, Mary Lampe and David Russell. David Russell is out of town. His vote on this proposal was proxy, presented by Chair David Emery.

Brief Summary: This application involves a corporate-sponsored, phase II clinical trial to assess an anti-HIV vaccine based on a recombinant adenovirus. The vaccine, produced by Merck & Co., Inc., consists of a replication-defective recombinant adenovirus designed to express the HIV-1 gag gene. The trial entails injecting the vaccine (single dose, three separate times) or placebo into the deltoid muscles of study subjects, and studying these patients for various immune responses on and off antiretroviral therapy. Pre-clinical studies in non-human primates indicate that the vector is both safe and capable of eliciting a significant cellular immune response. Ongoing phase I safety trials in over a hundred healthy and HIV-infected individuals indicate the vector is well tolerated at the proposed dose.

Comments:

The gene delivered by the vector, HIV-1 gag, does not represent a unique biohazard, except to note that unintended exposure to the vector could result in a false-positive HIV test (for gag). The adenovirus vector contains more than 2/3 of the virus genome, and for this reason represents a Risk Group 2 agent. Preclinical studies suggest that most of the vector remains near the sites of injection and surrounding lymph nodes, but that a small amount of vector genomes can be found at various sites throughout the body for several weeks post-administration. Preclinical studies also indicated that the vast majority of vector genomes remain extra-chromosomal, with no or very little chromosomal integration. There is no evidence that intact vector particles are shed from the study subjects. Subjects will be monitored for the exceedingly unlikely development of respiratory or urinary symptoms related to the vector, but no such symptoms have been observed to date. The sponsors are not assessing vector lots for the presence of replication-competent virus using the PCR methods currently approved by the UW IBC and EH&S. David Emery and David Russell discussed this issue with the sponsor via teleconference and are satisfied that the functional assay they use is appropriate, with a limit of sensitivity exceeding our current standards by perhaps two logs. In summary, the study represents a very modest safety risk, with the main hazard involving inadvertent exposure of study personnel to the vector during product administration.

Initially a subcommittee member had concerns related to the ethics of the study. She was concerned that it would not be ethical to take participants off their anti-retroviral therapy, especially since some of them will be receiving only the placebo. In reading the information provided, however, those concerns have been answered. The vaccine may be protective and everyone in the study will be monitored for increasing viral titers. All those with rising titers will be notified and ART resumed if desired.

RECOMMENDATION: CONDITIONAL APPROVAL.

Conditions of approval:

1) Final IRB approval, with the understanding that the informed consent document indicate that there was a death associated with this class of vector.

2) The location where the vaccine will be formulated and the location where the vector is administered is reviewed and approved by the responsible Infection Control team and/or Institutional Biosafety Officer for compliance with BL-2 standards.

3) The vector is formulated and administered using BL-2 practices. This includes formulating the vector is a class II biosafety cabinet, and administering the vector using Universal Precautions. In particular, study personnel must wear gloves, aerosol-resistant mask, and eye protection. Such conditions are currently listed

as only "recommended" in the Investigator's Brochure (pg. 6), and "should" in the study protocol (pg. 46).

IBC Motion:
David Emery moved to approve the subcommittee's recommendation of conditional approval, with the understanding that the issues involving facilities (condition 2) has already been satisfied.

IBC Vote.
Unanimous vote of approval of said motion by all IBC members.

5. Chair called for other issues from the floor.
   a. D. Frost, IBSO: future discussion from IBC on expedited review criteria and Recombinant DNA proposals.

The meeting was adjourned at 2:40 p.m.

Minutes submitted by Glenda Haynes

University of Washington

Institutional Biosafety Committee

Tuesday, May 4, 2004
1:00-3:00 pm
SCC 303
Meeting Minutes

Members Present:	Michael Agy, Washington National Primate Research Center David Emery (IBC Chair), Medicine / Medical Genetics Deanna Frost (IBO), Environmental Health and Safety Aaron Ketola, ASUW Student Representative Mary Lampe, Laboratory Medicine and Medicine Stephen Libby, Laboratory Medicine Pamela Morris, Comparative Medicine David Russell, Medicine / Hematology Estella Whimbey, Healthcare Epidemiology and Infection Control James Woods, Environmental & Occupational Health Sciences
Members Absent:	William Atkins, Medicinal Chemistry Carol Sibley, Genome Sciences Paul Swenson, Seattle-King County Dept. of Public Health Donald Wang, ZymoGenetics
Guests:	Susan Alexander, Environmental Health and Safety JoAnn Kauffman, Environmental Health and Safety Bruce Whitney, Environmental Health and Safety Karen VanDusen, Environmental Health and Safety

1. **Call to Order**
   Chair David Emery called the meeting to order at 1:05 p.m.

2. **Welcome & Introductions**
   The Chair welcomed everyone and introduced the newest member of the Institutional Biosafety Committee, Steve Libby. Steve described his previous experience as an IBC Chair and Biosafety Officer at North Carolina State University, and described his microbiology research with Salmonella.

3. **Administrative / Information Updates**
   3a. Minutes from the last meeting on January 16, 2004 were distributed to members via email before the meeting for review. Deanna Frost moved to approve these minutes. James Woods seconded the motion. There was a unanimous vote to approve the January 16, 2004 meeting minutes.

3b. A revised IBC Roster was distributed to the committee – it will be submitted to the Office of Biotechnology to amend our registration as a committee.

3c. Scheduled IBC meeting dates were adjusted to coincide with the "Just in Time" schedule for NIH grants. Two ad hoc meetings will be called in the near future – one to complete the determinations for a small number of clinical trials and another to review the progress of the SA research.

IBC meetings have been scheduled from 1:00-3:00 p.m. on the following dates. The location of each meeting will be emailed to committee members later.

Friday, September 10, 2004
Friday, January 14, 2005
Friday, May 13, 2005
Friday, September 9, 2005

3d. The Infectious Biomedical Waste Management Plan draft has been updated to address comments from the IBC and will go forward to the Infectious Waste Committee for a follow-up review. The Chair thanked the members that had participated in its review and returned their comments to Susan Alexander, Manager of Occupational Health and Safety, EH&S. Susan had the submitted comments incorporated into the current draft (April 8, 2004). The waste stream schematics are still to be considered rough drafts.

The Chair brought attention to page 7 and the separation of waste and carcasses; after the treatment of carcasses is described, the other waste has been omitted.

The inclusion in the ABSL-1 animal carcass category of transgenic animals and experimental animals to which the BSL-1 viral vectors had been administered was discussed and approved. These animals will end up in the regular waste stream (landfill).

The Chair requested that a subcommittee find out if and why only genus Macaca waste requires autoclaving before entering the solid waste stream; Michael Agy will verify the present practice.

3e. Deanna Frost, Institutional Biosafety Officer (IBO), explained the handout titled: *The Actions/Determinations on Behalf of the IBC*. This report now includes information on biosafety cabinet requests or biocontainment rating change requests.

3f. The NIH approved the NIH IBC registration – the committee's new anniversary date is January 5.

3g. The University has a number of facilities that are capable of being operated at BSL-3 but only 16 of 34 are "active". The EH&S (Facility Safety Office) criteria for a BSL-3 –capable" laboratory includes 1) an anteroom; 2) a bag in/ bag out HEPA filtration system; 3) an certified biosafety cabinet (ACTIVE status). The laboratory must meet further

requirements to meet operational BSL-3 criteria. These include a laboratory-specific biosafety manual, training, etc.; availability of decontamination equipment and implementation of BSL-3 practices.

The operating BSL-3 laboratories were recently inspected. Deanna Frost shared a compiled inspection letter that includes the references for the citations and inspection comments. The committee was asked to review the inspection letter and comment on omissions, necessary revisions, etc.

EH&S has drafted two new forms that pertain to the operation of biocontainment laboratories.

- The UW Biohazard Signage has been revised and is available electronically and has 1) instructions for posting at BSL1-3 and ABSL1-3, as well as 2) the sign with the requisite symbol and information lines (room, date posted, biological agents, special entry/exit procedures, PI, Emergency Contact, protocol numbers). Committee discussion included the requirements for communicating the presence of a BSL-2 laboratory with the housekeeping/custodial staff and visitors.
- The UW Laboratory Decommissioning and Clearance Form

Members of the IBC questioned the requirement to post BSL-2 signage. It was confirmed this is required when agents are in use.

Comments on the content and /or the development of these forms and processes should be submitted to Susan Alexander, Manager, Occupational Health & Safety Office at EH&S.

3h. Deanna Frost, IBO, working from the handout titled: *Report to IBC, May 4, 2004; UW REGISTERED, OPEN STUDIES* reported:

- Dr. Gal's study never enrolled and Dr. Gal has left UW; the mentor for the Otolaryngology residency program, Dr. Neal Futran, will close out the site with NIH OBA.
- Two studies recently began enrollment (Disis; Press),
- Status reports were requested from two ongoing studies (Thompson; Saperstein)
- Celestia Higano's protocol has been transferred to the FHCRC; it is going well and a new protocol was developed to follow-up one patient. The lab will request that the sponsor change the OBA registration to reflect that it is being conducted at FHCRC.
- All other studies were closed to accrual or closed (see May 4, 2004 handout).

4. <u>Specific Research Proposals</u>

4a. The IBC discussed and voted on five research proposals outlined in the handout titled *IBC Subcommittee Primary Review Summary - Draft 3/29/04.* Subcommittee members are Michael Agy, David Emery, Mary Lampe and Donald Wang.

The current version of the UW Biosafety Manual indicates that all research with HIV/SIV and similar constructs needs to be carried out at BSL-3 labs. The Chair believes this decision was made many years ago by one of the predecessors of this committee, because at that time modern biosafety cabinets were not available for use in all research projects. The NIH Guidelines assign a Risk Group 3 rating for this type of agent, but stipulate that the research can be done at Biosafety Level 2 containment if appropriate Biosafety Level 3 practices are incorporated into the methodology. During an April 6 discussion of the Preliminary Review Summary between the Chair and Karen VanDusen and other members of EH&S it became clear that the recent revision of the WISHA requirements had implications pertaining to the appropriate biocontainment level for the research laboratory.

JoAnn Kauffman, Interim Biosafety Supervisor / Occupational Health Nurse at EH&S advised the IBC regarding WISHA regulation changes, after consultation with WISHA. She distributed a handout titled: *Additional Requirements for HIV and HBV Research Laboratories and Production Facilities.* This listed the requirements, in addition to the BBP regulations, for work with HIV/HBV in research labs and production facilities.

It had been discovered that HIV/HBV research labs had been incorrectly placed with HIV/HBV production facilities specific facility requirements. WISHA is in the process of correcting the regulation. WISHA informs the University that it will hold us to the corrected version of the BBP regulations for HIV/HBV research labs and production facilities.

Discussion followed on conditional approvals being compliant with WISHA regulations. There was also discussion on lab signage and access issues.

NOTE ON QUORUM: The non-UW-affiliated representatives of the IBC were not present for the convened meeting but Don Wang, Zymogenetics, was a primary reviewer on the IBC subcommittee for the submitted projects below and his votes presented by proxy (via the IBC Chair).

RESEARCH PROPOSAL DETERMINATIONS:

4a. 1) *Principal Investigator:* Bradley Preston
Research: Biochemical Determinants of Retroviral Mutation
Request: BSL2 with BSL3 practices

Original Subcommittee Recommendation: Conditional approval at BL2 with BL3 practices (BL2+) given. Conditional approval is dependent on development of proper working procedures to be codified in a lab safety manual and approved by the Institutional Biosafety Officer, as well as a site inspection by the IBO. Specific attention should be placed on the following: current bloodborne pathogen training (including acceptance and declination of Hep B vaccine); use of sealed rotors for centrifugation; training of all personnel using the facility of proper working procedures regardless of whether or not they are working under this protocol.

Amended Subcommittee Recommendation: Amended such that the lab safety manual is to come back to the committee by way of email, as opposed to the biosafety officer.

IBC Vote: Motion by Dave Emery, seconded by Steve Libby with unanimous approval.

4a. 2) *Principal Investigator:* David Evans
Research: Inoculation of macaques with single-cycle SIV
Request: Production of single-cycle SIV at BSL2 with BSL3 practices

Original Subcommittee Recommendation: For tissue culture: conditional approval at BL2 with BL3 practices (BL2+), especially since wild type SIV apparently cannot replicate in humans. For animal work: conditional approval at BL2 with BL3 practices (BL2+), especially since wild type SIV apparently cannot replicate in humans and viruses used here are attenuated. Conditional approval is dependent on development of proper working procedures to be codified in a lab safety manual and approved by the Institutional Biosafety Officer, as well as a site inspection by the IBO. Specific attention should be placed on the following: current bloodborne pathogen training (including acceptance and declination of Hep B vaccine); eye protection is required.

There was discussion that the protocol did not include the expected rate of reversion of the constructs.

Amended Subcommittee Recommendation: Amended such that the lab safety manual is to come back to the committee by way of email, as opposed to the IBO and that the investigation must be conducted in compliance with WISHA. It's the responsibility of the PI to test vector product for contamination by replication competent RCV virus.

IBC Vote: Motion by Deanna Frost, seconded by Michael Agy with unanimous approval

4a. 3) *Principal Investigator:* Shiu-Lok Hu
Research: Development of an RT-SHIV Model
Request: BSL-3 for laboratory work

Subcommittee Recommendation: For tissue culture: conditional approval at BL3 (as requested). For animal work: conditional approval BL2 with BL3 practices (BL2+), especially since wild type SIV apparently cannot replicate in humans and HIV cannot replicate in monkeys. Conditional approval is dependent on development of proper working procedures to be codified in a lab safety manual and approved by the Institutional Biosafety Officer, as well as a site inspection by the IBO. Specific attention should be placed on the following: verification that DOT and IATA regulations are followed for packaging, shipping, and transport of research materials between UW campus and Western building or other research sites.

IBC Vote: Motion by Dave Emery, seconded by Deanna Frost with unanimous approval.

4a. 4) *Principal Investigator:* David Anderson
Research: In vivo enhancement of SHIV 89.6p pathogenicity in Macaca fascicularis
Request: BSL-3 for laboratory work

Subcommittee Recommendation: For tissue culture: conditional approval at BL3 (as requested). For animal work: conditional approval at BL2 with BL3 practices (BL2+), especially since wild type SIV apparently cannot replicate in humans and HIV cannot replicate in monkeys. Conditional approval is dependent on development of proper working procedures to be codified in a lab safety manual and approved by the IBO, as well as a site inspection by the IBO.

IBC Vote: Motion by Deanna Frost, seconded by David Emery with unanimous approval.

4a. 5) *Principal Investigator:* Chao-Zhong Song
Research: Molecular Mechanisms of Breast Cancer Growth and Metastasis
Request: Recombinant [lentiviral] HIV vectors expressing oncogenes in culture.

Original Subcommittee Recommendation: Conditional approval at BL-3 be given, especially because these vectors contain known oncogenes (which may cause disease without the presence of complementing viruses) and will be introduced into primary human cells with unknown viral loads. Conditional approval is dependent on identification of an appropriate facility and development of proper working procedures to be codified in a lab safety manual and approved by the Institutional Biosafety Officer (IBO).

The recommendation was amended after discussion of the relative safety of the lentiviral construction, led by David Russell, and the inability of the provirus to recombine.

Amended Subcommittee Recommendation: Conditional approval at BL2 with BL3 practices (BL2+). Conditional approval is dependent on development of proper working procedures to be codified in a lab safety manual and approved by the Institutional Biosafety Officer, as well as a site inspection by the IBO. Specific attention should be placed on the following: current bloodborne pathogen training (including acceptance and declination of Hep B vaccine); use of sealed rotors for centrifugation; training of all personnel using the facility of proper working procedures regardless of whether or not they are working under this protocol.

IBC Vote: Motion by Dave Emery, seconded by David Russell, with approval given by a vote of 1 abstention, 9 yeahs, and 0 neahs.

The meeting was adjourned at 3:00 p.m.

Minutes submitted by Glenda Haynes

University of Washington

Institutional Biosafety Committee

Friday, January 16, 2004
1:00-3:00 pm
HUB 204N

Meeting Minutes

Members Present:	Michael Agy, Washington National Primate Research Center William Atkins, Medicinal Chemistry David Emery, (Chair) Medicine / Medical Genetics Deanna Frost, Environmental Health and Safety, Biosafety Officer Aaron Ketola, ASUW Student Representative Mary Lampe, Laboratory Medicine and Medicine David Russell, Medicine / Hematology Paul Swenson, Seattle-King County Dept. of Public Health Donald Wang, ZymoGenetics James Woods, Environmental & Occupational Health Sciences
Members Absent:	Pamela Morris, Comparative Medicine Carol Sibley, Genome Sciences Estella Whimbey, Healthcare Epidemiology and Infection Control
Guests:	Susan Alexander, Environmental Health and Safety JoAnn Kauffman, Environmental Health and Safety Bruce Whitney, Environmental Health and Safety Dave Anderson, Washington Regional Primate Research Center Melinda Young, Washington National Primate Research Center Laura Campbell, Comparative Medicine Chris Brown, General Clinical Research Center

Call to Order

Chair David Emery called the meeting to order at 1:10 p.m.

1. **Welcome & Introductions**
   Introductions were made among those present. David Emery introduced Bruce Whitney, who recently joined Environmental Health & Safety as a Biosafety Officer. Bruce is the Alternate Responsible Official of the UW Select Agent Program and is one of two who oversee its day-to-day implementation.

2. **Minutes Approved:**
Minutes from the last meeting on August 22, 2003 were distributed to members via email before the meeting for review. Deanna Frost moved to approve the August 22, 2003 minutes. David Emery seconded the motion. There was a unanimous vote to approve the August 22, 2003 minutes.

3. **Proposed meeting schedule:**
It was decided at the last meeting there should be three IBC meetings each year. It was suggested during the discussion that the dates be adjusted to coincide with the "Just in Time" schedule for NIH grants.

ACTION: The originally proposed IBC meeting dates of 4/14/04 and 9/1/04 will be rescheduled to best match the "Just-in-Time" schedule; these will be obtained from Grants & Contracts or the NIH Extramural Office.

4. **Update on process for project reviews:**

A. Research with Hazardous Genes
HANDOUTS:
1. NIH Guidelines for Research Involving Recombinant DNA Molecules—Summary of Review Requirements
2. University of New Hampshire's IBC Listing of Biological Agents and their Assigned Biological Safety Level

Chair David Emery lead the discussion by stating the IBC assures that all UW research with recombinant DNA and infectious agents is carried out in compliance with the NIH Guidelines. The UW IBC project approval process relies heavily on review by the Institutional Biosafety Officer (IBO), using parameters established by the IBC. This allows the IBO, who is Deanna Frost, to approve most applications coming to Environmental Health and Safety on behalf of the IBC.

At the August 22, 2003 meeting, the Chair proposed to expand the detail of the IBC's guidelines, giving more explicit criteria for the determination of the appropriate biosafety level and practices. The original guidance focused on the recombinant viruses used as gene transfer vectors (Viral Vectors for Gene Transfer website) and most of the genes being used were 'markers.' The criteria should be elaborated to broadly address 'hazardous gene activity' with a limited number of categories. Vector constructs encoding toxins, known oncogenes, and the newly recognized 'hazardous gene activities' would rate a higher biocontainment assignment than would be required on the basis of the vector alone. The Principle Investigator could either agree to adopt the higher level of bio-containment, or petition the IBC to consider a lower level. The IBC provided an example of similar, categorical guidance from the University of New Hampshire IBC. In the past these projects have not been reviewed at the IBC level but rather delegated for administrative review by the BSO.

DECISION: Form a subcommittee to develop specific recommendations for the UW version of "IBC Listing of Biological Agents and their Assigned Biological Safety Level" and present for future adoption by the full IBC.

ACTION: Proceed with forming a subcommittee take up this issue. Volunteers contact David Emery to request assignment to this subcommittee.

Suggestions for hazardous gene categories are welcome. Send all suggestions to Deanna Frost or Dave Emery.

B. BL3 Projects

HANDOUT: Report to IBC; January 15, 2004; UW BSL-3 Projects

The handout Deanna Frost (IBO) prepared, describes research projects requiring BSL-3 containment. Chair David Emery asked IBC members if they want to continue to delegate approval of these projects to the IBO, or establish a policy by which the IBC looks directly at these projects. Mary Lampe suggested experts in this area be consulted.

DECISION: Begin reviewing BSL-3 research applications at a subcommittee level. Subcommittee will report back to full IBC.

ACTION: Form a subcommittee and procedures for processing BSL-3 research applications. Volunteers contact David Emery to request assignment to this subcommittee.

C. Clinical Gene Therapy Trials

HANDOUTS:

1. Report to IBC, January 15, 2004; OBA REGISTERED, CLOSED STUDIES – SEATTLE
2. Report to IBC, January 15, 2004; OBA REGISTERED, OPEN STUDIES – SEATTLE
3. Report to IBC, January 15, 2004; UW REGISTERED, CLOSED STUDIES
4. Report to IBC, January 15, 2004; UW REGISTERED, OPEN STUDIES

David Emery reported that the IBC is now in compliance with the NIH Guidelines in that the IBC reviews clinical gene therapy trials at a convened meeting. The IBC is also supposed to review ongoing clinical gene therapy trials on an annual basis. The IBC has not been doing this.

Deanna Frost prepared four handouts pertaining to the gene transfer clinical trials in Seattle, highlighting those at the University of Washington:

- 6 are ongoing
- 2 were withdrawn from UW review
- 3 are closed to accrual – in follow-up
- 1 is entirely preclinical
- 1 UW registered trial is not registered with OBA.
- 1 OBA registered trial is not registered at UW – at SCCA and overseen by Fred Hutchinson Cancer Research Center.

Discussion opened on the annual review. Deanna pointed out that the UW IBC sees two categories of clinical trials: 1) preclinical to clinical transitions, and 2) industry-sponsored clinical trials that are more contractual than grant-like. The IBC responsible for oversight is that where the agent is being administered to the subject as opposed to the IBC where the investigative agent might be made, though there may be another IBC at that location.

Dave Russell commented that the review of the risk-benefit ratio is a gray area, in terms of whether it is ultimately the responsibility of the IBC or the IRB to decide, and how it should be communicated.

DECISION: Start the clinical trial review with the subcommittee process to address the safety of the vector and the risk-benefit ratio. The subcommittee reports to the full IBC. Previously reviewed protocols will be re-reviewed to be sure they are in alignment with new safety concerns, such as those with integrating vectors or adenovirus vectors.

ACTION: Form a subcommittee for clinical gene therapy trials. Volunteers should contact Dave Emery to request assignment to this subcommittee.

If anyone becomes aware of UW investigators who are not registered, please inform the committee through the Chair David Emery or Biosafety Officer Deanna Frost.

D. Non-human primate cells

The current version of the UW Biosafety Manual indicates that all research with non-human primate cells need to be carried out at BSL-3 labs. David Emery believes this decision was made many years ago by one of the predecessors of this committee, because at that time modern biosafety cabinets were not available for use in all research projects. There is no federal regulation or NIH Guideline which mandates a biosafety level higher than BSL-2 for this type of research.

MOTION: David Emery motioned that the UW Biosafety Manual be amended to indicate that research with non-human primate cells can be carried out at BSL-2 level, with the added condition that all open manipulations with these cells be carried out in a class II biosafety cabinet or with other means of reducing exposure to aerosols.

MOTION 2nd by Mike Agy.

PASSED: All committee members were in favor of the motion.

ACTION: Amend the UW Biosafety Manual to indicate that research with non-human primate cells can be carried out at BSL-2, with the added condition that all open manipulations with these cells be carried out in a class II biosafety cabinet or with other means of reducing exposure to aerosols.

E. Xenotransplantation

The current version of the UW Biosafety Manual mentions xenotransplantation research with both human and non-human primate cells in primates can be carried out at BSL-3, and neglects to mention xenotransplantation into non-primate mammals. David Emery believes this decision was made many years ago by one of the predecessors of this committee, because at that time modern biosafety cabinets were not readily available. There is no federal regulation or NIH Guideline which mandates a biosafety level higher than BSL-2 for this type of research.

MOTION: David Emery motioned that the UW Biosafety Manual be amended to indicate xenotransplantation research with both human and non-human primate cells in rodents and primates can be carried out at BSL-2, with the added condition that all open manipulations with the tissues be carried out in a class II biosafety cabinet or with other means of reducing exposure to aerosols.

MOTION 2nd by James Woods

PASSED: All committee members were in favor of the motion.

ACTION: Amend the UW Biosafety Manual to indicate that xenotransplantation research with both human and non-human primate cells can be carried out at BSL-2, with the added condition that all open manipulations with these tissues be carried out in a class II biosafety cabinet or with other means of reducing exposure to aerosols.

5. **Status of BSL3 Facilities on Campus**

HANDOUT: Biosafety Level 3 Inspection Checklist

Deanna Frost reported on an annual inspection of BSL-3 labs. Biosafety cabinets are tested and certified by FSO technicians and taken out of working status if not operating to specifications. UW has many laboratories capable of being operated as BSL-3; currently approximately 18 are operating at that status. This includes labs located at Magnuson Health Sciences, Children's Hospital, Rosen Building, Roosevelt Building and Harborview Medical Center.

ACTION: Send Deanna any comments on the BSL-3 inspection criteria checklist.

6. **Select Agent Program**

Bruce Whitney, Biosafety Officer, updated the committee on the UW Select Agent Program. To date, one lab has provisional approval from the Center for Disease Control (CDC) and one other lab is working through the procedures seeking CDC registration, which is a very long process. Labs leasing UW property but run by an outside agency are to be registered by UW.

A complete and final list of select agents is still being determined, with details worked through as the new program evolves. Questions regarding the difference between toxins and select agents may be directed to Biosafety Officers Bruce Whitney or Deanna Frost.

Three people at UW have Select Agent Program signature authority:
Karen Van Dusen, Director, EH&S
Susan Alexander, Manager, Occupational Health & Safety Office, EH&S
Bruce Whitney, Biosafety Officer, Occupational Health & Safety Office, EH&S

7. **Report on Projects Approved Since Last IBC Meeting on August 22, 2003**

HANDOUT: Report to IBC, January 15, 2004; Actions/Determinations on behalf of IBC from August 20, 2003 to January 16, 2004.

Deanna Frost reviewed the handout and reported updates on projects she has administratively approved since the last meeting on August 22, 2003.

8. **IBC Administrative Policy Statement (APS)**

David Emery reported some progress on updating the IBC Administrative Policy Statement, to codify the roles and responsibilities of the IBC. An APS draft is not ready for IBC review. Hopefully a draft will be available for the next IBC meeting.

9. **Infectious/Biomedical Waste Management Plan - DRAFT**

HANDOUT: Infectious/Biomedical Waste Management Plan DRAFT – January 2004

Chair David Emery stated that part of the IBC roles and responsibilities are to consider institutional procedures and practices with regards to research involving recombinant DNA and biohazardous agents. Presumably this includes considering what happens to waste generated as part of these research efforts. The Infectious/Biomedical Waste Management Plan is being developed under the direction of Environmental Health & Safety and the Infectious Waste Committee.

The draft plan was distributed to IBC members for later reading and review. Please send your comments to Susan Alexander at Environmental Health & Safety (susanka@u.washington.edu), by February 2, 2004.

Comments and concerns will be handle through e-mails, with IBC approval of the final version at future meeting.

10. Animal Waste Disposal SOP - DRAFT

HANDOUT: Animal Waste Disposal SOP DRAFT – January 2004

On behalf of Pamela Morris, Laura Campbell from Comparative Medicine submitted the Animal Waste Disposal SOP draft for IBC approval. The Department of Comparative Medicine and the IACUC developed this document.

The first animal waste issue discussed was on the issue of disposing transgenic mice and rat carcasses used in research. The NIH Guidelines states the IBC must assure they don't enter the food chain. David Emery interpreted this to mean the human food chain, although this is not specifically stated. These carcasses are currently bagged and trucked to a landfill.

MOTION: David Emery motioned the IBC agree there is no hazard for transgenic mice and rat carcasses to be disposed of in a landfill.

MOTION 2nd by Deanna Frost.

PASSED: All committee members were in favor of the motion.

ACTION: Develop draft proposal regarding mice and rat carcasses treated with viral vectors being taken to the landfill as BSL-1 carcasses.

The second animal waste issue discussed was about what to do with mice that are currently classify as BSL-1 but treated with recombinant viruses or bacteria. This could include recombinant retrovirus vectors that can infect mice but not humans, or recombinant adenovirus vectors which presumably cannot replicate directly in the mice but which may recombine with other types of rodent viruses.

MOTION: David Emery motioned that mice or rat carcasses treated with viral vectors be taken to the landfill as for BSL-1 carcasses.

TABLED: Because several members were no longer present

ACTION: Move the issue regarding the safe disposal of carcasses of mice or rats treated with BSL-1 vectors in the landfill to a subcommittee at a later date.

Send questions or comments on the Animal Waste Disposal SOP draft to Pam Morris (pcm252@u.washington.edu).

11. **Specific Proposals**

Chris Brown, Research Scientist at the UWMC General Clinical Research Center, presented a review proposal to the IBC for the Oliver W. Press facility design and practices for the Gene and Cell Therapy Core Laboratory. This lab is being used for the clinical gene therapy trial approved in 2002, entitled "*A Phase I Study to Evaluate the Safety of Cellular Immunotherapy Using Genetically Modified Autologous CD-20 Specific CD8+ T-Cell Clones for patients with Relapsed CD-20+ Indolent Lymphomas* (FHCRC protocol #1503 / IBC reference #201-371 / NIH OBA reference #491-[2001-7]).

This trial involves the collection of blood from patients with lymphoma, genetically altering T cells from this blood by plasmid transfection so they express a fusion antibody -T cell receptor protein that targets the tumor B cells, and expanding these cells in culture to very high numbers. These cells are then given back to the patient. This of course requires a large amount of tissue culture work. The FDA lifted the clinical hold on this protocol this week.

The issue before the IBC today is if this lab facility has proper procedures in place to make the tissue culture work safe. At the August 2003 meeting, Tony Blau, Associate Professor in Medicine, addressed the IBC about the design of this lab facility. At that time the IBC agreed the facility was appropriate for BL2 work and the four procedure rooms could be considered as functionally separate so the studies in one room would not effect other rooms. The IBC also agreed that specific clinical protocols using these rooms would also be review by the IBC. This is the first case of the specific clinical protocols.

David Emery, David Russell and Deanna Frost reviewed the detailed plan submitted by the GCRC. This plan outlined the flow of personnel and supplies in the facility related to this protocol. Personnel don't enter from the de-gown room. Airflow is always into the lab, from clean to dirty regions. The air change rate is 60 times per hour (once every minute).

MOTION: David Russell motioned that the facility core plan is appropriate for this clinical trial.
MOTION 2nd by Deanna Frost.

PASSED: All committee members were in favor.

Discussion: David Russell recommended the RISK: BENEFIT ratio be re-reviewed, due in part to recent information on the induction of leukemia due to chromosomal insertion by the investigative vector. The relative role of the IBC vs. the IRB was discussed. The Chair acknowledged that IBC's are being encouraged to evaluate the Risk:Benefit to the subject as well as the public health dimension.

MOTION: David Russell motioned that an IBC subcommittee review this proposal via email for further considerations before final approval, regarding the RISK:BENEFIT ratio to the subject.

MOTION 2nd by Deanna Frost.

PASSED: All committee members were in favor of the motion except David Emery.

ACTION: Form a subcommittee for review the Oliver W. Press facility design proposal. Volunteers for this subcommittee, please contact Dave Emery.

12. Issues from the Floor

Change Notification of Approval process to require the infection control and respiratory protection program signoff prior to IBC approval.

Append Biohazard Safety Manual and website to clarify which human clinical trails need to be reviewed by the IBC. Besides viral vectors, this included any administration of:

- Vaccines that are recombinant
- DNA agents
- Organisms that are recombinant
- Cells that are recombinant

Clinical Xenotransplantation is not listed in the Biohazard Safety Manual nor our Website and several members have expressed concern. The OBA office does cover xenotransplantation (and there is an upcoming meeting), but the NIH Guidelines do not explicitly address Xenotransplantation.

Committee members were reminder about upcoming guidance from OBA on Informed Consent issues.

Genetic Modification Clinical Research Information System (GeMCRIS) is a web-accessible database of human gene transfer trials recently developed by NIH and FDA. This is a public information resource and new electronic tool to facilitate the reporting and analysis of adverse event on these trials. For more information on GeMCRIS see the press release concerning this development at **www.nih.gov/news/pr/mar2004/od-26.htm**

The meeting was adjourned at 3:10 p.m.

Minutes submitted by Glenda Haynes

University of Washington

Institutional Biosafety Committee

Friday, August 22, 2003
1:00-3:00 pm
South Campus Center 248/250

Meeting Minutes

Members Present:	Michael Agy, Washington National Primate Research Center William Atkins, Medicinal Chemistry David Emery, Medicine / Medical Genetics Deanna Frost, Environmental Health and Safety Mary Lampe, Laboratory Medicine and Medicine David Russell, Medicine / Hematology Carol Sibley, Genome Sciences Paul Swenson, Seattle-King County Dept. of Public Health Donald Wang, ZymoGenetics Estella Whimbey, Healthcare Epidemiology and Infection Control James Woods, Environmental Health
Members Absent:	Aaron Ketola, ASUW Student Representative Sheila Lukehart, Medicine Pamela Morris, Comparative Medicine
Guests:	JoAnn Kauffman, Environmental Health and Safety Kimberly Braun, Environmental Health and Safety Nancy Whittington, Healthcare Epidemiology and Infection Control Robert Ernst, Medicine Tina Guina, Pediatrics

Call to Order

Chair David Emery called the meeting to order at 1:05 pm.

Welcome & Introductions

Introductions were made among those present. Since the last meeting (12/2/02):

- David Emery replaces Stanley McKnight as the Chair of the IBC
- Sheila Lukehart has been named the new Assistant Dean for Research and Graduate Education at Harborview Medical Center, and will have to resign from the IBC responsibilities.

Minutes Approved:
Minutes from the last meeting on December 2, 2002 were distributed to members via email before the meeting for review.

Dr. Frost moved to approve the December 2, 2002 minutes
Dr. Emery seconded the motion
Unanimous vote to approve December 2, 2002 minutes

Administrative Policy Statement (APS) Status
Dr. Emery distributed attached handout summarizing IBC Roles and Responsibility. He emphasized the need for the IBC to consider containment, agents, and barriers. The APS is under revision. It will be based on the NIH Guidelines for Recombinant DNA Activities summarized in the handout. Interested IBC members were invited to participate in the drafting process. A final draft of the APS will be presented to the IBC for modification and/or final approval.

Viral Vectors for Gene Transfer Guidance
Interested IBC members were invited to participate in the update and further development of the Viral Vectors for Gene Transfer guidance that appears on the EH&S website. Dr. Emery is currently working with Drs. Russell, Sibley, and Frost. A final draft of the proposed guidance document will be presented to the IBC for modification and/or final approval.

Proposed IBC Meeting Schedule
Even though the IBC has traditionally met annually, it will now have to meet more often because of research involving Select Agents, more complex gene transfer, and the fact that roles and responsibilities of the committee have expanded.

Dr. Emery proposed meeting 3 times a year about two weeks before the NIH RO1 grant submission deadline. This would accommodate all projects regardless of whether they are submitted for "Just-in-Time" review.

Proposed dates are:

- January 16, 2004 – for the February 1 NIH RO1 submission deadline
- April 14, 2004 – for the May 1 deadline NIH RO1 submission deadline
- September 17, 2004 – for the October 1 deadline NIH RO1 submission deadline

In response to Dr. Lampe's concerns that two weeks before the deadline may not be enough time, Dr. Emery replied that by the time a protocol comes to the full committee most problems should be worked out. Two weeks in advance also allows the committee members enough time to work on their own grants.

Additional convened meetings may be called as needed.

Program / Facility Review

Proposal (Emery): The responsibility for deciding when and how to maintain serum banks for personnel involved in biohazardous research is delegated to the EH&S Occupational Health Nurse.
To address Dr. Sibley's suggestion Dr. Emery suggested adding a friendly amendment to motion so it would read: The responsibility for deciding when and how to maintain serum banks and determine vaccinations for personnel involved in biohazardous research is delegated to the EH&S Occupational Health Nurse.

Dr. Emery stated that passing this motion would not preclude the Occupational Health Nurse from coming to the IBC for advice and that essentially she is doing this already as part of her Occupational Health Review.

Dr. Whimbey expressed concern for the process by which an occupational health review occurs and that the Occupational Health Nurse makes recommendations singly. Ms. Kauffman indicated that she envisioned presenting Occupational Health recommendations to the IBC for projects that are brought before the committee. The IBC would make the final approval.

Dr. Frost suggested the Occupation Health Nurse routinely submit a report indicating the projects she approved. The attached handout of protocols administrative approved for the IBC since the last meeting was distributed at this time.

Dr. Whimbey indicated that she would be more comfortable if guidelines were created that indicated which research the EH&S Occupational Health Nurse reviews and which go to the IBC for review. Dr. Emery said it will be worked on and discussed at the next meeting.

Dr. Emery moved to table the motion
Dr. Frost seconded the motion
Unanimous vote to table Occupational Health Program motion

Proposal Reviews:

GCRC Gene and Cell Therapy Core Lab

Proposed Motion (Emery):

The four procedure rooms within the GCRC Gene and Cell Therapy Core Lab can be used for in vitro BL-2 research, and can be treated as independent facilities. Individual studies involving the administration of cells or recombinant products manipulated in these facilitates into patients will be reviewed separately.

C. Anthony Blau, GCRC Associate Program Director gave a presentation about the facility. Cathy Lindgren, the Lab Manager was present to answer questions.

The lab is located in 7-South of UWMC and was opened in October of 2000. They want to work with pre-clinical specimens now and hope to eventually infuse similar cells back into the patient.

The lab design and procedures, especially the ventilation system were discussed to explain why it is believed an outbreak in one room doesn't enter another room:

- 1 room change per minute
- The ventilation system is designed to have <10,000 particles per cubic foot
- Labs A & B are built to BSL-3 standards with HEPA exhaust. The other labs do not have HEPA exhaust
- Sophisticated SOPs for particle monitoring and validating cleanliness of lab.
- Unidirectional traffic control to minimize anti-grade traffic.
- The high-speed cell sorter lasers are on storage side of the room. The cells are manipulated and retained on the clean side of the room.
- UWMC facilities personnel walk through mechanical space every day at 4:00 am and deliver a report to the Lab Manger by 6:00 am.
- The ventilation is constantly monitored and Hospital engineering calls if there is a problem.
- The room is alarmed and there are SOPs for spills, fires, and floods. At Dr. Emery's suggestion, Ms. Lindgren said these SOPs can be modified so that EH&S is also notified if something major occurs.
- This facility meets the BSL-2 requirements of having self-closing doors and handwashing sinks. However, the handwashing sinks are not in the lab, but rather in the exits.
- Rooms C&D share an exhaust, but all rooms have their own HEPA filters. Dr. Emery stated that anything generated in one room gets exhausted before having a chance to escape. There is 24-hour monitoring and backup.

Dr. Whimbey said she would like the hospital to have the opportunity to tour the lab due to its proximity to UWMC. It was suggested that Rob Evans be contacted to arrange the tour.

Dr. Russell expressed concern that a person who, after working in the biological safety cabinet goes out to decontaminate and contaminates the room with fomites in the process. Ms. Lindgren explained that the container the gowns go in is opened with a foot petal and that the only people who go back in from the exit are those that go in to clean at the end of the day. When asked if this was acceptable, Dr. Russell replied, "I guess".

Dr. Emery made the motion
Dr.Sibley seconded the motion.
Unanimous vote to approve GCRC proposal.

<u>WaNPRC Western Building</u>

Proposed Motion (Emery):

The animal BSL-3 facility under design for the Washington National Primate Research Center Western Building can, in principle, be used for animal studies involving BSL-3 agents. This approval is dependent on the satisfactory design, construction, and commissioning of the facility as determined by UW EH&S and defined in the NIH

Guidelines. Individual studies involving specific BSL-3 agents will be reviewed separately.

William Morton, the WaNPRC Director, gave a presentation detailing the proposed remodeling of the Western facility to accommodate research with bioterrorism agents and non-human primates.

Specifics include (see attached copies of overheads):

- This is a BSL-3 facility with HEPA in and out.
- The mechanical space for bag in/ bag out unit is located in the building to reduce exposure during filter changes conducted by personnel in full protective clothing.
- It is a fast paced project; they hope to be conducting research in the space in 6-8 months.
- Procedure rooms will be constructed adjacent to animal housing rooms.
- SOPs are being developed. They will be shared with U.S. Army Medical Research Institute of Infectious Diseases Operations for review before coming to the IBC.
- Individual projects will come to the IBC for review.

Dr. Frost noted that USDA restricted agents require enhanced BSL-3 Ag facilities which entail containment of liquid effluent, respiratory protection, and may result in a USDA inspection. It was suggested the proposal be amended to indicate adherence to these USDA requirements.

Mr. Wang expressed concern and cautioned the University about public acceptance once the community learns what is going on in the facilities. He stressed the need to address community awareness and compliance with the City of Seattle's Department of Design, Construction, and Land Use (DCLU) before proceeding with the project.

Dr. Morton indicated that they would comply with select agent and the other pathogen requirements. Additionally, he said there are no City regulations precluding them from going forward. They will adhere to the Institutional policy that does not allow for BSL-4 laboratories.

When asked if Western was the best location for this kind of research, Dr. Morton indicated Mukilteo as a potential expansion facility. However considering the current time, space, and infrastructure constraints, Western is currently the best option.

Dr. Emery moved to approve the amended motion:

> The animal BSL-3 facility under design for the Washington National Primate Research Center Western Building can, in principle, be used for animal studies involving BSL-3 and **BSL-3Ag** agents. This approval is dependent on the satisfactory design, construction, and commissioning of the facility as determined by UW EH&S and defined in the NIH and **USDA** Guidelines. Individual studies involving specific BSL-3 agents will be reviewed separately, with due consideration for the final criteria to which the facility is built.

Dr. Frost seconded the motion

Unanimous vote to approve the above motion.

Review of specific protocols
Two protocols were reviewed.

Katze – Reviewed by Drs Lampe, Emery and Frost. In vitro characterization of influenza-influenza recombinant viruses: A/Texas/36/91 used as backbone for insertion of genes from A/Brevig Mission/1/18.

The proposed study seeks to infect cell lines with the influenza vector A/Texas/36/91 containing one or more genes from the A/Brevig Mission/1/18 1918 pandemic strain. The recombinant viruses were constructed by a collaborator elsewhere and will be introduced into cell lines in the UW WaNRPRC Western BL-3 facility. The cell cultures will be maintained in the BSL-3 facility until treatment with guanidinium isothyocyanate for RNA extraction. The nucleic acid samples will be removed to a BLS-2 facility where microarrays will be developed and analyzed to study the effect of the recombinant viruses on the host cells.

SOPs have been developed and the work will be carried out in Biological Safety cabinets. Additionally personnel will be offered flu immunizations and antiviral prophylactic, but they are not required.

Dr. Agy circulated the attached handout in which he addressed all five questions Dr. Lampe brought up in her review:

1. What cell lines will be used for these recombinant influenza infections?
2. Is centrifugation required to infect the cell lines with the recombinant influenza?
3. Will the cell cultures produce infectious virus?
4. Can aerosols be created in the incubators holding the infected cell cultures?
5. What precautions will be made for aerosols that might be created in the BL-3 facility?

In response to #5, he also noted that no more than two (2) people will be involved in the BSL-3 at any time and that they will remove their gowns on the inside of the BSL-3 and the Tyvek suit outside the BSL-3. If the Tupperware box filled with plates is dropped between the hood and centrifuge and aerosols are generated, personnel will be trained to stop breathing and leave the room immediately just as they are taught to do when working with HIV and SIV.

Dr. Frost shared information she ascertained from the collaborator, USDA ARS, whose IBC has considered this a BSL-3 Ag agent. The implications are that they will not ship the agent to a facility that does not meet BSL-3 Ag requirements. In further discussions between Dr. Frost and one of the collaborators, who also sits on their IBC, they decided that the UW IBC should determine BSL level for this project, send their decision to the collaborator's IBC for consideration, and they will then decide whether to ship the agent or if they will require a BSL-3 Ag facility is available.

Dr. Emery suggested notifying UWMC since they would see an exposed worker. He noted that the approval is dependent upon personnel Bloodborne Pathogen training. Dr. Frost noted that, as stated, this motion does not require additional respiratory protection.

Dr. Lampe made a motion to recommend approval at BSL-3 containment because her aerosol concerns were addressed.
Dr. Frost seconded the motion.
Dr. Agy recused himself from voting
Unanimous vote to approve Katze proposal.

Miller –Reviewed by Drs Agy, Emery, and Frost. WWAMI RCE

At this time the meeting was closed to the public and those in attendance were reminded that all information distributed is confidential. Additionally, project information was collected at the end of the meeting. The only remaining non-IBC member, Nancy Whittington, elected to stay in the meeting and recognized the secure nature of the information being discussed.

Dr. Miller's research has two foci

1. Bacteriology and manipulation of Yersinia pestis, Francisella tularensis, Burkhoderia psuedomallei.
2. In vivo mouse studies

Bacterial work will be conducted in the specified BSL 2/3 suite and the animal work will be conducted in an ABSL-3 lab. The proposal is to work with these agents under BSL-3 conditions with two exceptions:

- Handling of animal tissues that are tested and found to be free of viable bacteria proposed at BSL-2,
- Genomic library generation from BSL-3 agents in laboratory strains of E. *coli* proposed at BSL-2.

From a clinical standpoint, patients coming in with these agents are treated at a BSL-2. However work with the agent cultures or infection of animals requires BSL-3 containment by CDC/BMBL guidelines.

Dr. Frost and Ms. VanDusen described the other requirements for work with select agents. In addition to IBC review, the lab will be subject to federal inspection and must develop:

- Lab specific Biosafety Manual, as is the case for all BSL-3 work
- Safety plan
- Lab specific security plan
- Disaster plan

Dr. Frost reported that as written, NIH guidelines stipulates that the use of restricted agents necessitated NIH/OBA approval, however, 'restricted agents' have been redefined in the

context of these guidelines to include only small pox, alastrim, and white pox. Consequently, Select Agents will not require this separate NIH/OBA approval. She distributed the attached handout describing this change.

Amid questions concerning specific equipment and practices, it was decided that the application was incomplete. Dr. Emery proposed this protocol be approved at BSL-3 contingent upon the investigators complying with BSL-3 regulations and working with EH&S to do that. If approved in that regard today, the IBC would review the proposal again before the research commences.

Dr. Russell asked about the research proposed at BSL-2 and asked about guidelines for cloning genomes of select agents.

To accommodate the research that would not be conducted at BSL-3 and Dr. Frost's report that the regulations require the work be done at the biosafety level at the organism, BSL-3 in this case, Dr. Emery amended the motion to:

1. Wet lab and mouse lab with wild type bacteria be approved at BSL-3
2. Cloning with fragments into E. coli at be conducted at BSL-3 [should be corrected -dmf]
3. DNA, RNA, and tissues, proteins demonstrated free of bacteria can be conducted at BSL-2.

Approval requires the investigator work out the details with EH&S and the IBC has opportunity to review the details before research commences.

Dr. Lampe's concerns about tissues being handled at BSL-2 were addressed by Dr. Guina who indicated that only clinical samples that are not infected would be handled at BSL-2.

Dr. Emery made the motion
Dr. Frost seconded the motion.
Unanimous vote to approve Miller proposal.

After the vote the following IBC members excused themselves:

- Mary Lampe
- James Woods
- Paul Swenson

Issues from the floor

Karen VanDusen was recognized.

She distributed the attached handout obtained by the Infectious Waste Committee that explains the chain of disposal and incineration of biohazardous waste generated in Health Sciences.

The meeting was adjourned at 3:16 p.m.

Minutes submitted by Kimberly Braun.