FREEDOM OF INFORMATION OFFICE

UNIVERSITY OF MICHIGAN

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April 6, 2006

Edward H. Hammond
Director
The Sunshine Project
P.O. Box 41987
Austin, TX 78704

Re: HAM 0061-06

Dear Mr. Hammond:

I am writing in regard to your Freedom of Information Act request directed to Michael Hanna dated March 15, 2006, which was received on March 16.

You requested "the minutes of all meetings of the University of Michigan Institutional Biosafety Committee (IBC) since 1 May 2003."

Your request is granted in part. Enclosed find responsive documents. Some material has been withheld pursuant to Section 13 (1) (u) of the Michigan Freedom of Information Act, which exempts from disclosure "records of a public body's security measures . . . to the extent that the records relate to the ongoing security of the public body." Additionally, some records have been withheld pursuant to Section 13 (1) (m) of the Act, which allows the University to refrain from disclosing certain communications and notes of an advisory nature.

You also asked that the University answer a question contained within your letter. As a courtesy, the Institutional Biosafety Committee has provided the answer to your question, which is enclosed.

Please note that within 180 days from the date of this letter, you have the right to appeal the denial of information to the President of the University or seek judicial review in the circuit court to try to compel disclosure. If you elect to appeal and the President upholds the denial, you may still seek judicial review within the 180-day period.

An appeal to the President must be submitted in writing to: President's Office, c/o Gary Krenz, The University of Michigan, 2080 Fleming Administration Building, 503 Thompson Street, Ann Arbor, MI 48109-1340. The statement must (1) identify the request and the final determination by the FOIA officer that is being appealed, (2)

specifically state the word "appeal," and (3) identify the reason or reasons why the final determination should be reversed.

If you seek judicial review in the Michigan circuit court and prevail, you will be awarded reasonable attorney's fees, costs and disbursements incurred in maintaining the action. If you prevail in part, you may still be awarded complete or partial reimbursement for those expenses. In addition to actual and compensatory damages, you will be awarded punitive damages in the amount of $500 if the court finds that the University was arbitrary and capricious in its denial.

A copy of Section 10 of the Michigan FOIA is attached for your information.

Sincerely,

Patricia J. Sellinger
Freedom of Information Act Coordinator

Enclosures

Freedom of Information Act Right to Appeal

15.240. Options by requesting person; appeal; orders; venue; de novo proceeding; burden of proof; private view of public record; contempt; assignment of action or appeal for hearing, trial, or argument; attorneys' fees, costs, and disbursements; assessment of award; damages.

Sec. 10. (1) If a public body makes a final determination to deny all or a portion of a request, the requesting person may do 1 of the following at his or her option:

(a) Submit to the head of the public body a written appeal that specifically states the word "appeal" and identifies the reason or reasons for reversal of the denial.

(b) Commence an action in the circuit court to compel the public body's disclosure of the public records within 180 days after a public body's final determination to deny a request.

(2) Within 10 days after receiving a written appeal pursuant to subsection (1) (a), the head of a public body shall do 1 of the following:

(a) Reverse the disclosure denial.

(b) Issue a written notice to the requesting person upholding the disclosure denial.

(c) Reverse the disclosure denial in part and issue a written notice to the requesting person upholding the disclosure denial in part.

(d) Under unusual circumstances, issue a notice extending for not more than 10 business days the period during which the head of the public body shall respond to the written appeal. The head of a public body shall not issue more than 1 notice of extension for a particular written appeal.

(3) A board or commission that is the head of the public body is not considered to have received a written appeal under subsection (2) until the first regularly scheduled meeting of that board or commission following submission of the written appeal under subsection (1) (a). If the head of the public body fails to respond to a written appeal pursuant to subsection (2), or if the head of the public body upholds all or a portion of the disclosure denial that is the subject of the written appeal, the requesting person may seek judicial review of the nondisclosure by commencing an action in circuit court under subsection (1) (b).

(4) In an action commenced under subsection (1) (b), a court that determines a public record is not exempt from disclosure shall order the public body to cease withholding or to produce all or a portion of a public record wrongfully withheld, regardless of the location of the public record. The circuit court for the county in which the complainant resides or has his or her principal place of business, or the circuit court for the county in which the public record or an office of the public body is located has venue over the action. The court shall determine the matter de novo and the burden is on the public body to sustain its denial. The court, on its own motion, may view the public record in controversy in private before reaching a decision. Failure to comply with an order of the court may be punished as contempt of court.

(5) An action commenced under this section and an appeal from an action commenced under this section shall be assigned for hearing and trial or for argument at the earliest practicable date and expedited in every way.

(6) If a person asserting the right to inspect, copy, or receive a copy of all or a portion of a public record prevails in an action commenced under this section, the court shall award reasonable attorneys' fees, costs, and disbursements. If the person or public body prevails in part, the court may, in its discretion, award all or an appropriate portion of reasonable attorneys' fees, costs, and disbursements. The award shall be assessed against the public body liable for damages under subsection (7).

(7) If the circuit court determines in an action commenced under this section that the public body has arbitrarily and capriciously violated this act by refusal or delay in disclosing or providing copies of a pubic record, the court shall award, in addition to any actual or compensatory damages, punitive damages in the amount of $500.00 to the person seeking the right to inspect or receive a copy of a public record. The damages shall not be assessed against an individual, but shall be assessed against the next succeeding public body that is not an individual and that kept or maintained the public record as part of its public function.

History: 1976, Act 442, Eff. Apr. 13, 1977;--Am 1978, Act 329, Imd. Eff. July 11, 1978;--Am 1996, Act 553, Eff. Mar. 31, 1997.

the sunshine project

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15 March 2006

Michael Hanna
University of Michigan
4080 Fleming Bldg.
Ann Arbor MI 48109-1340

By fax: (734) 763-0085

Dear Michael Hanna

Pursuant to the National Institutes of Health Guidelines on Research Involving Recombinant DNA Molecules (NIH Guidelines), Section IV-B-2-a-(7),[186] the Sunshine Project hereby requests the Minutes of all meetings of the University of Michigan Institutional Biosafety Committee (IBC) since 1 May 2003.

Please send the minutes to the address above. The NIH Guidelines require that minutes be made available "upon request". I request that you send your reply by Friday, 28 April 2006.

This letter is sent to you because IBC registration records of the National Institutes of Health Office of Biotechnology Activities indicate that you are responsible for the University of Michigan IBC.

This letter is sent to you as part of a national survey of compliance with the NIH Guidelines.

When you respond, I would appreciate your answer to the following question (please circle one):

> The University of Michigan IBC HAS / (HAS NOT) implemented written policies for the identification, review, and oversight of research involving any of the seven categories of experiments of concern identified by the National Academies of Science in its report *Biotechnology Research in an Age of Terrorism* (the "Fink Committee" report).

Two UMIBC 4/5/06

Please feel free to attach any additional explanatory materials that you feel are appropriate. Thank you very much for your attention to this request.

Sincerely,

Edward H. Hammond
Director

[186] *Section IV-B-2-a-(7). Upon request, the institution shall make available to the public all Institutional Biosafety Committee meeting minutes...*

Institutional Biosafety Committee Meeting
Friday, July 11, 2003
3:00-5:00 p.m., 4006 Fleming

Committee members present: Jan Berry, Brad Carlson, Michael Hanna, Phil Hanna, Michael Imperiale (chair), Carl Marrs, Judy Nowack, Howard Rush, John Schiefelbein, Jackie Hoats-Shields (committee coordinator)
Absent: Fred Askari, Cary Engleberg, Rebecca Head
Guest: Janet Follo, OSEH

(Committee members present: 9. Quorum: 7.)

1. Updates from the Chair

a. ***Containment of lentivirus vectors.*** Michael Imperiale said that a colleague at University of Virginia had recommended BL2+ containment for all lentivirus vector work because of the risk of integration. In a later communication, she said instead that BL2+ may be more containment than is needed. Dr. Imperiale said his own opinion is that BL2 containment is probably adequate in most cases based upon the risk of integration.

b. ***Mentoring of investigators.*** Dr. Imperiale said that based upon the content of various registrations submitted to the committee, he is concerned that some investigators are not receiving basic mentoring on how to work with recombinant DNA. This seems to be the case for various investigators proposing basic science recombinant DNA work, as well as for some who propose human gene transfer work. Dr. Imperiale has already discussed the need for mentoring at the departmental level with one Medical School department chair. In another approach, each registration on the IBC the website now contains a message from Dr. Imperiale emphasizing the need for investigators to carefully consider the registration questions. The registration forms assume a certain amount of basic knowledge about recombinant DNA work.

Committee members discussed whether a training session should be considered, such as a half-hour talk that could be presented at lab meetings or in departmental faculty meetings. One question is whether such training would be required or voluntary. It was noted that the recently launched PEERRS program may be a place where this type of training could happen in an online setting. It is possible for PEERRS to include a link to a short PowerPoint presentation. The IBC could begin to accumulate ideas about how such a training module could be designed and what it could contain.

c. ***Annual gene therapy meeting.*** Dr. Imperiale said that the annual meeting of this group was last month. He said there was discussion of Picornavirus vectors but otherwise little else new was covered.

2. **Human gene transfer proposal.** ***Paul Michael Grossman,*** *A Phase II, Multi-Center, Double-Blind, Placebo-Controlled, Trial of VLTS-589 in Subjects with Intermittent Claudication Secondary to Peripheral Arterial Disease, sponsored by Valentis (IBC no. 1543-003).*

   Dr. Imperiale asked if there were any concerns about this proposal for a Phase II trial using the same gene transfer product that Sanjay Rajagopalan is currently using in a Phase I trial that was approved in January. No concerns were raised about the proposal. It was noted, however, that the scientific abstract does not explain well what is to be done in the project. In addition, some documentation must still be supplied to complete the IBC file administratively, such as updated financial conflict of interest disclosures.

   Jan Berry: Motion to approve (once disclosures are obtained) with a suggestion about the scientific abstract.
   Phil Hanna: Seconds motion.
   Vote: All in favor.

3. **Serious adverse events**
   There were no concerns raised about the serious adverse events enclosed in the packet.

4. **Select and select-like agents – Michael Hanna, Biosafety Officer, OSEH**
   Dr. Imperiale reminded the committee about the confidentiality of the information to be presented by Michael Hanna.

Judy Nowack showed the committee a draft of a new PAF-R form which includes a special section on select agents. Judy described that a PAF-R is a form which initiates the process for the vice president for research to approve the University entering into a contract which contains a non-standard restriction such as a publication delay or a restriction on foreign nationals. Select agents work involves restrictions like others on the PAF-R because an early decision must be made in each case by deans and department chairs regarding the feasibility of the work. The Senate Assembly Research Policies Committee annually reviews the University's implementation of this process, and a summary report goes to the Regents annually from the vice president for research.

5. **OSEH updates – Michael Hanna**

a. Lab inspection process for VAMC. Michael Hanna reported on changes in the inspection process for laboratories of UM investigators at the VAMC. He said that because labs there must contractually comply with VA policies and because the VAMC has its own biosafety officer, UM OSEH will no longer be performing biosafety cabinet certifications or site visits there. Mr. Hanna said that UM OSEH is satisfied with the quality of biosafety operations at the VAMC. Committee members asked and Mr. Hanna clarified that the VAMC does not have its own IBC. UM investigators with laboratories there will still be required to register their recombinant DNA work with the UM IBC. The IBC would still send registration and inspection request materials to OSEH and these would be forwarded to the VAMC biosafety officer. The committee discussed the matter briefly and agreed that it would be beneficial and educational to invite the VAMC biosafety officer to the next meeting to hear about their processes.

b. New OSEH inspection reports. Michael Hanna and Janet Follo described the new inspection report system now in place at OSEH. OSEH personnel carry PDAs which can access a database of information about labs on campus. Through these devices a two-page report is created after a lab inspection. The report includes a list of items reviewed with corrective actions noted. Upon completing the corrective actions, investigators are required to fax a signed and dated copy of the list to both OSEH and the IBC.

6. **IBC acknowledgement of registrations, certifications, and materials transfers**

Jan Berry: Motion to accept the listed registrations, certifications, and information on materials transfers.

Carl Marrs: Seconds motion.

Discussion: A committee member asked a question about what situations require a formal Materials Transfer; it was replied that a formal Materials Transfer is needed when there are proprietary issues with the item being transferred. The IBC receives a copy of the Materials Transfer Form if the investigator has checked "yes" about the work involving recombinant DNA. The investigator also proposes on the MTF the biosafety level to be used. A check is done by the IBC on whether the investigator is already registered for the proposed biosafety level; if not, a communication goes out requesting registration.
Vote: All in favor.

7. **IBC approval of minutes from the March 18, 2003 meeting**
   Phil Hanna: Motion to approve.
   Judy Nowack: Seconds motion.
   Vote: All in favor.

8. **Matters arising:**
   a. Committee members noted the recent success of UM researcher Yehoash Raphael's gene transfer work growing new auditory hair cells in guinea pigs.
   b. Howard Rush said that Lesley Colby, Clinical Assistant Professor of Laboratory Animal Medicine and a guest at the last IBC meeting, is going to be handling biohazard issues at ULAM.

These notes approved at the October 15, 2003 IBC meeting.

Institutional Biosafety Committee Meeting
Wednesday, October 15, 2003
2:30-4:30 p.m., 4006 Fleming

IBC members present: Jan Berry, Brad Carlson, Cary Engleberg, Mike Hanna, Phil Hanna, Rebecca Head, Mike Imperiale (chair), Carl Marrs, Judy Nowack, John Schiefelbein
Staff: Jacqueline Hoats-Shields
Guests: Janet Follo, OSEH; John Mather, ORCR
IBC members absent: Fred Askari, Howard Rush

(Committee members present: 10. Quorum: 7.)

1. Updates from the Chair – Michael Imperiale

a. The National Research Council is about to publish a report entitled "Biotechnology Research in an Age of Terrorism: Confronting the Dual Use Dilemma" which recommends that Institutional Biosafety Committees play a role in determining whether research is potentially dangerous. The report outlines seven areas of concern against which IBCs would assess proposed research. There is also a provision for publication review. Whether the recommendations of the report are put into action will be determined by the Department of Health and Human Services and Congress. Pre-publication copies of the report are available at http://www4.nationalacademies.org/news.nsf/isbn/0309089778?OpenDocument.

b. Dr. Imperiale noted an article included in the agenda regarding a clinical trial at New York Presbyterian Hospital using gene transfer with an adeno-associated virus vector delivering the glutamic acid decarboxylase (GAD) gene to treat Parkinson's disease. He pointed out that the trial is controversial because they have skipped the non-human primate model and gone straight to human research.

2. Updates from OVPR – Judy Nowack

The Office of Research Compliance Review (ORCR)
Dr. John Mather was introduced to the committee. He has joined the UM as director of the new Office of Research Compliance Review (ORCR), which is part of the Office of the Vice President for Research and will be located in the North Ingalls Building. Judy Nowack explained that the ORCR grew out of a multi-element initiative begun a year ago to look at all compliance committees that relate to research with human subjects. Outcomes of the initiative include the PEERRS program, improvements in the IRBs themselves, and investments in the support of clinical research along with an increase in the capacities of project coordinators. The initiative called for a provision for review and the ORCR will address this with the ability to look at any of these subsystems for compliance with regulations. The ORCR

will also take over management of the PEERRS program. Dr. Mather, who is a pediatric otolaryngologist by training, comes to the UM from the Veterans Administration system where he headed the office of research compliance and assurance as well as inspected the quality of patient care. He has also worked in the National Institutes of Health and the Department of Defense.

3. Human Gene Transfer Reporting

a. IRB status of active HGT trials

The committee was provided with a spreadsheet showing the IRB status of currently active human gene transfer clinical trials.

b. Annual reports and terminations

1. A general question was raised about whether a potential subject is considered to be in the withdrawn category if they didn't meet screening criteria. The answer is no, if they do not meet the screening criteria they are not counted.
2. There was a request to add more descriptive information about the serious adverse events listed in the IBC SAE database tables which are provided as background.
3. A question was raised in reference to a table on page 000008 of the GenVec annual report (Rajagopalan IBC no. 1314-003) regarding at what point is a causal relationship to the agent considered when the events such as respiratory effects are so often listed as "possibly related." There was discussion among committee members about how an investigator might determine relatedness. There was agreement that the question should be put to the investigator regarding how he interprets the data. *Post-script: through e-mail communication with the principal investigator it was clarified that the table in question contained data pertaining to a related trial of the same drug to treat coronary artery disease instead of peripheral arterial disease which the UM trial is studying.*
5. The annual report for Dr. Grossman's Berlex trial (IBC no. 1543-001) was passed out for the committee's information. The title of this trial is: A Multicenter, Randomized, Double Blind, Placebo Controlled Study to Evaluate the Efficacy, and Safety of Ad5FGF-4 in Patients with Stable Angina (Protocol 304386).

c. Serious Adverse Events

1. *Follow-up on Merkel cell tumor issue (external SAE), Grossman IBC no. 1543-002.* Michael Imperiale summarized the history of this SAE. Based upon the expert report provided and the fact that Merkel cell tumors are not generally receptive to FGF Dr. Imperiale said it seemed convincing that the tumor growth would not be related gene transfer. Cary Engleberg said he agreed with that assessment. Another committee member had written that he felt it is reasonable to classify a malignancy as possibly related. The IRBMED opinion is that the growth of the tumor should be considered possibly related. The committee briefly discussed the matter. If FGF did not

cause tumor, it could be questioned whether it made it capable of growing faster. Dr. Engleberg stated there is little reason to believe FGF facilitated tumor growth because the progress of the tumor is what it would have been without the FGF.

2. There were no concerns raised about the other serious adverse events in the packet.
3. Two external SAE reports were received October 10, too late for inclusion in the agenda, and were handed out. Both are on the Genzyme trial (Rajagopalan 1314-004, 005, 006). One is an above-knee amputation and the other is for "confusion," both in the same patient, both considered by the investigator to be unlikely related.

4. Biosafety Officer Report – Michael Hanna, OSEH

a.

b. Select agents. Mr. Hanna reported that there have been no changes in status of select agents at the University list since his last report in July.

c. VAMC inspections. At the July IBC meeting it was noted that the Veterans Administration Medical Center (VAMC) biosafety officer would be performing lab inspections for UM investigators with labs at the VAMC. In the meantime it has been decided that Janet Follo of UM OSEH will accompany the VAMC biosafety officer on these inspections to attend to UM-specific requirements for these seven recombinant DNA labs.

d. FAA/DoT inspection. Mr. Hanna said a recent, routine Federal Aviation Administration/Department of Transportation not-for-cause inspection focused on shipment through Detroit Metropolitan Airport of a biological item from the lab of a UM investigator. The item was chosen at random from a set of other biologics from other senders also being shipped out of the airport. As is routine, the inspectors talked with the person from the lab who packed the item and she was asked to demonstrate how she packed it for shipment. Janet Follo has recently revised OSEH's training document for shipping and receiving biologics and it will be sent to the committee for information. In discussion committee members noted it key is to make sure there is a designated person in the lab for handling shipping and it should be someone intimately involved with the research or an experienced lab technician.

e. **Vector Core training sessions.** Janet Follo said she recently directed the staff of a newly approved lab who did not have experience with their vector to Tom Lanigan of the Vector Core. Mr. Lanigan put together a 20 minute training presentation and the staff who saw it reported to Ms. Follo that it was excellent. She said Mr. Lanigan would be interested in doing such training on a monthly basis. Mike Imperiale noted that the Vector Core finds it important to provide training because of the chance that agents could be mishandled when removed from the Core. The question was raised as to whether the IBC would consider such training as recommended or required, and whether the IBC could promote it. Dr. Imperiale said the IBC could ask Blake Roessler, Director of the Vector Core, if the IBC could put a parenthetical comment beside the "experience" question on the registration form suggesting individuals go to Vector Core with questions. Committee members also agreed that Tom Lanigan should be thanked by the IBC for providing this training.

5. IBC acknowledgement of recombinant DNA registrations, certifications, and materials transfers

Jan Berry: Motion to accept the listed registrations, certifications, and information on materials transfers.

Rebecca Head: Seconded motion.

Discussion on materials transfers: A committee member asked how closely it is monitored whether the agents being transferred are directly covered by an existing registration. What is checked when these forms come through is whether the investigator is registered for the containment level proposed; if not, they are asked to register the work. Also, if there is a clear discrepancy between the type of item being transferred and the level of containment proposed (i.e., adenovirus proposed at BL1 containment) or the type of registration on file (i.e., adenovirus vs. retrovirus), then they are asked to register the work associated with the transfer and possibly have their lab inspected. The Materials Transfer list provided to the committee with each agenda is an opportunity for committee members to question the containment level used for the item (the containment level shown is that proposed by the investigator).

Vote: All in favor

6. IBC approval of minutes from the July 11, 2003 meeting

Rebecca Head: Motion to approve.

Carl Marrs: Seconded motion.

Vote: All in favor

There were no matters arising.

Meeting adjourned at 3:40 p.m.

These notes were approved at the January 30, 2004 IBC meeting.

Institutional Biosafety Committee Meeting
Friday, January 30, 2004
3:00-5:00 p.m., 4006 Fleming

IBC members present: Fred Askari, Jan Berry, Cary Engleberg, Mike Hanna, Phil Hanna, Mike Imperiale (chair), Carl Marrs, Howard Rush, John Scheifelbein
Staff: Jacqueline Hoats-Shields
Guests: Lesley Colby (ULAM), Janet Follo (OSEH), Kate Wiklanski (UCUCA)
IBC members absent: Brad Carlson, Rebecca Head, Judy Nowack

(Committee members present: 9. Quorum: 7.)

1. **Updates from the Chair – Michael Imperiale**
   a. *Peripheral arterial disease trial update (IBC no. 1314-003, Rajagopalan).* Based upon the most recent annual report received (reviewed at the October IBC meeting) there appeared to be a high occurrence of serious adverse events in one arm of the trial. The investigator was asked about it and it turned out that arm of the trial was looking at coronary arterial disease whereas our arm of the trial was examining peripheral arterial disease (PAD). The PAD arm does not have a high occurrence of SAEs.

   b. Michael Imperiale said he recently attended a microbiology chairs meeting and Ron Atlas, former president of the American Society for Microbiology, gave a talk on the work of the Committee on Research Standards and Practices to Prevent the Destructive Application of Biotechnology, of which he was a member. The committee authored the National Research Council report "Biotechnology Research in an Age of Terrorism: Confronting the Dual Use Dilemma," a.k.a. the "Fink report" for committee chair Gerald Fink. (The IBC received the Executive Summary of this report in October.)

   Dr. Imperiale said that from Dr. Atlas' remarks it appears regulatory changes are expected in the near future requiring a new review role for IBCs. Ron Atlas said the Fink committee attempted to propose a process that would use existing structures and leave oversight to the scientific community itself, modeled on the system of self-governance used for recombinant DNA. Thus one of the seven recommendations of the committee is for IBCs to review potential dual-use research. In addition, the committee proposed seven categories of research that comprise the "experiments of concern" requiring review. These experiments would:

   1. Demonstrate how to render a vaccine ineffective,
   2. Confer resistance to therapeutically useful antibiotics or antiviral agents,
   3. Enhance the virulence of a pathogen or render a nonpathogen virulent,
   4. Increase transmissibility of a pathogen,
   5. Alter the host range of a pathogen,
   6. Enable the evasion of diagnostic/detection modalities,

7. Enable the weaponization of a biological agent or toxin.

In his talk, Ron Atlas said it will be up to the scientific community and IBCs to define the standards for review of this type of work, and to standardize themselves and become more rigorous. He proposed the simple addition of questions to registration forms as a good way to begin.

IBC members briefly discussed the implications of the NRC report and noted that the scope of this committee would need to be expanded beyond recombinant DNA to catch projects like those listed above – immunosuppression studies, for example. Dr. Imperiale said his impression is that it may be necessary to implement changes to our process soon. A copy of the complete NRC report will be sent to committee members.

2. Animal containment

a. Containment for housing animals injected with virus

Guest: Lesley Colby, DVM, Clinical Assistant Professor, Laboratory Animal Medicine

Dr. Imperiale said that over the last couple months Lesley Colby, Howard Rush, and he have been exchanging messages with each other and colleagues at other institutions to determine the appropriate containment levels for housing animals injected with different kinds of recombinant viruses. Dr. Colby said she would like to have an algorithm of animal containment levels by virus that she could provide to investigators who are using these agents in animals. It was noted that when it can be determined safe there are practical benefits to lowering the containment for housing injected animals.

The committee discussed containment levels for housing animals injected with specific viruses and the following ideas were proposed:

Adeno-associated virus: BL1 should be fine because the virus cannot mobilize;

Adenovirus: BL1 housing fine, but if administered intravenously the animals should be kept at BL2 for 48 hours;

Retrovirus/lentivirus: depends on the tropism; may need to be case-by-case.

The IBC will work on written guidelines that can be provided to UCUCA and ULAM.

It was also noted that the December 2003 issue of the journal *Current Gene Therapy* (vol. 3, issue 6) has articles applicable to this topic. This journal is available through interlibrary loan.

b. Creation of undesirable traits in transgenic animals

The committee discussed the likelihood of undesirable traits being developed in transgenic animals, using the example of human polio virus in transgenic mice. In order to help ascertain whether genes used in a project may pose a threat, a

revision was proposed to the transgenic animal question on the IBC registrations. The question would read: "Based on the known function of your gene product, or what you suspect its function to be, is it possible that its expression from the transgene will allow the animal to be infected with a pathogen to which it normally would not be susceptible?"

c. Transgenic Animal Model Core blanket approval

It was noted that the Transgenic Animal Model Core is preparing a registration for the IBC in order to receive a blanket approval like that held by the Vector Core and the Sequencing Core. The approval would be for work at BL1, with the requirement that if anyone wishes to make transgenics using an RG2 or higher agent that the IBC would be notified in advance so the appropriate review could take place. The TAMC will also be asked to notify the IBC if they encounter a project that may produce animals susceptible to infectious agents they would otherwise resist.

3. Discussion of a select agent/rDNA registration

There followed a discussion about what the policy should be on the submission method for registrations that involve select agents. It was decided that submissions involving select agents should not go through the online, e-mail registration review system, and should instead be submitted by hand delivery followed by a face-to-face committee discussion possibly with the investigator proposing the work. It was decided that a notice to this effect will be posted on the IBC website. A brief discussion ensued about how much detail is needed for a written record of the review of such proposals.

4. Human gene transfer reporting - Serious adverse events

a. **Grossman, IBC no. 1543-002, Aventis, IND no. 8058**, External SAE, Macular degeneration with retinal hemorrhage and neovascularization, "reasonable possibility (of association) with the study treatment," per investigator in Aventis memo, 10/15/03.

A brief discussion ensued about the timing of the myocardial infarct and the macular degeneration.

b. **Rajagopalan, IBC no. 1314-004, 005, 006, Genzyme, IND no. 8432,** External SAE, Right foot ischemia, right second toe amputation, not related per investigator.

There were no concerns raised about this SAE.

c. **Rajagopalan, IBC no. 1314-004, 005, 006, Genzyme, IND no. 8432,** External SAE, Stent implanted (coronary artery).

There were no concerns raised about this SAE.

d. **Rajagopalan, IBC no. 1314-008, Valentis, IND no. 9524,** Local SAE, creatinine level elevated 2 times upper limit of normal; hospitalization for pre-hydration, renal angiogram, stenting of renal arteries; serious, unexpected, not related per investigator.

There were no concerns raised about this SAE.

e. **Grossman, IBC no. 1543-003, Valentis, IND no. 9524,** External SAE, Patient death, sudden; on study day 21, patient did not feel well; on study day 22 patient awoke with coughing spell (reported by spouse) and died later during night (unwitnessed). Unlikely related per (external) investigator. Autopsy results pending.

It was commented that without autopsy results, it is not possible to rule out that the death could be related to the study product. Dr. Grossman will be contacted to find out when autopsy results are expected.

5. **Biosafety Officer/Responsible Official Report – Michael Hanna**

a. **Update on select and select-like agents**

No other changes were reported in the status of select and select-like agents.

b. **Viral vector training proposal**

Janet Follo of OSEH gave a brief presentation to the committee outlining the viral vector training course put together by Tom Lanigan of the Vector Core. The actual presentation is 1 hour in length, including a 30-minute presentation and 30 minutes for questions. Detailed handouts are provided to participants. OSEH will be assisting with administration of the program and tracking of participants. Mr. Lanigan's time will be paid for by OSEH. The sessions will be offered quarterly, with openings for 6 people per session. Already there are 20 people known to be interested in taking the course. One unresolved question is whether the course will be mandatory by the IBC.

It was decided that the IBC will change the question about experience level on the registration forms so that it asks for the names, experience level, and contact information for each of the individuals who will be doing the experiment. If they are inexperienced, these individuals will be e-mailed to tell them they should take the course.

The new UCUCA biosafety training program for animal use was discussed. This mandatory program is done as a large introductory lecture followed by smaller hands-on groups.

It was noted that with the regulatory burden likely to increase the University is going to have to put more resources into biosafety training in order for it to be effective. There was discussion of whether PEERRS, which is mandated, could be used for online biosafety training. An idea was proposed for a small group of

IBC members to work on a proposal to the vice president for research regarding biosafety as a responsible conduct issue for investigators.

6. **Recombinant DNA registrations, certifications, and materials transfers**
   a. **Discussion of two submitted registrations still under review**
      1. **Kirk McCrea,** (1624-001), gene from RG2 agent being cloned into RG1 agent.
         This registration has been going through review online, resulting in a split decision between the reviewers (BL2 vs. BL1). The reviewers discussed their reasoning. Dr. Marrs said in his reading of the Guidelines, cloning with genes that are well defined makes BL1 a possibility depending on the types of toxins the genes make. He said the genes used in this experiment should not do anything in E. coli, and he did not believe the work would require BL2 containment. He cited an alternative example (Yop genes) that would require BL2 containment. Following the discussion, Dr. Engleberg said he would agree with BL1 containment. Others present said they would also agree with BL1 containment.

      2. **David Fink,** (1563-001), recombinant HSV1 vector and IL4 gene.
         Dr. Imperiale explained that the vector to be used is engineered with two safety features meaning the virulence factors have been knocked out. As for the genes, the one causing concern is IL4. Dr. Fink is an investigator coming to UM in March from the University of Pittsburgh where they do this kind of work at BL2 in the lab, and they keep their animals at BL1+. Dr. Rush said that from the ULAM viewpoint, there is no difference between BL1+ and BL2. Discussion included the question of whether any of this will be excreted at all. The vector will be injected into peripheral nerves. There is a low chance that it will be in saliva.

         Dr. Imperiale made the following recommendation: BL2 for the lab virus work and BL2-N for the animal work, dropping down to BL1-N following the first cage change after 48 hours. The committee agreed the issue about the IL4 gene still needed to be addressed. Dr. Imperiale will e-mail Dr. Fink about this, and the committee can vote on approval over e-mail. *Postscript: On February 4 the committee was forwarded information from Dr. Fink regarding the rationale for using the soluble TNF receptor and IL-4 as transgenes. The committee was asked to consider the information and vote on the following proposed containment level: BL2/BL2-N, dropping down to BL1-N following the first cage change. There were 11 votes in favor and one abstention.*

   b. **IBC acknowledgement of recombinant DNA registrations, certifications, and materials transfers since last meeting**
      Carl Marrs: Motion to approve.
      Jan Berry: Seconded motion.
      Vote: All in favor.

7. **IBC approval of minutes from October 15, 2003 meeting**
   Jan Berry: Motion to approve.
   Carl Marrs: Seconded motion.
   Vote: All in favor.

8. **Matters arising**
   There were no matters arising.

Meeting adjourned, 5:10 p.m.

These notes approved by the IBC on May 14, 2004.

Institutional Biosafety Committee Meeting
Friday, May 14, 2004
3:00-5:00 p.m., 4006 Fleming

IBC members present: Jan Berry, Brad Carlson, Cary Engleberg, Mike Hanna, Phil Hanna, Rebecca Head, Mike Imperiale (chair), Carl Marrs, Judy Nowack, Howard Rush, John Scheifelbein **Staff:** Jacqueline Hoats-Shields
Guests: Kate Wiklanski (UCUCA)
IBC members absent: Fred Askari

(Committee members present: 11. Quorum: 7.)

1. **Updates from the Chair** – Michael Imperiale
   a. *National Science Advisory Board for Biosecurity (NSABB) and local efforts*
   In response to the NRC "dual-use" report and the impending formation of the NSABB, a small group has been formed, going by the name "Biosecurity Interest Group" (BIG), to discuss how to inform and educate faculty about these issues. Efforts so far include Mike Imperiale speaking at various faculty meetings, and a flyer about the "experiments of concern" sent to all investigators in the IBC database. Dr. Imperiale noted that a few calls have been received in response to the flyer. BIG is also working on plans for a panel or symposium in the fall with experts on dual-use research, policy, and security issues.

   b. *MPRIME process for review of human gene transfer submissions*
   The system known as MPRIME being developed for online submission of human subjects research proposals has been renamed "eResearch," and is being tested now by focus groups, including individuals from the IBC. The IBC is considered an ancillary committee in the system, and the IRBs are the primary committees. In the system all ancillary committee approvals required on a proposal will need to be obtained before the proposal may proceed to IRB review.

   c. *Future IBC meeting schedule*
   The IBC will need to be prepared to meet more frequently, perhaps monthly, since under eResearch IBC approval will be needed before the IRB will review a human gene transfer proposal. eResearch is to be rolled out in the fall. The monthly meetings can be set up and then cancelled if there are no proposals to discuss. The committee will still meet four times a year at a minimum. An IBC member asked if it would be possible to shorten the monthly meetings from 2 hours to 1 hour. Ms. Hoats-Shields will be in touch with IBC members about scheduling monthly meetings.

   d. *Re-appointments to the IBC*
   Vice President for Research Fawwaz Ulaby joined the meeting to thank members of the IBC for their service and commitment to the work of the committee. He expressed gratitude to those renewing their appointments for three-year terms, and he emphasized how important the work of the IBC is to the University. The

committee members continuing for another three years as of July 1 are Jan Berry, Brad Carlson, Cary Engleberg, Rebecca Head, and Carl Marrs as Associate Chair.

2. Registrations for discussion

a. *Kathryn Eaton, Heliobacter pylori host and bacterial virulence factors/Expression of murine IL-10 in H. pylori*

Dr. Imperiale described this registration which proposes work with Heliobacter pylori expressing factor 10 and said he has asked two outside people for advice but has not heard back from one of them. One opinion is that those who encountered it would likely already be infected. Committee members considered this and said there would still be a risk to someone already infected.

A question was raised about what will regulate the expression. It was proposed that the investigator could be asked to use a certain regulator and that the promoter be something artificial enough that it would not come on in the human body.

Dr. Marrs motioned that the investigator be asked to find an inducible promoter that would be "off" in humans and that there be a common way for it to be turned on such as something the animals could drink, and if she is not able to find one then the committee will need to revisit the issue. Dr. Rush noted that it is not clear if this is to be in germ-free animals or non-germ free. He said often in germ-free animals such experiments are very controllable, and it is the bench work that is more worrisome.

Regarding Dr. Eaton's proposal, it was agreed that she will be asked to engineer the strain so that expression will only be on when she turns it on.

Committee members agreed that any work with immunomodulators needs attention, and they discussed whether it needs to be case by case or whether this response could be generalized to other such projects through a set of guidelines. Some committee members said this would be difficult because it depends on the pathogen being used, and it is also relevant to look at the organism and its interaction with the human host. Investigators who are cloning an immunomodulatory gene can be asked to indicate what safety measures will be used.

Dr. Imperiale noted that this type of registration underscores the need for an immunologist on the committee, and that he will try to find a person with this expertise.

b.

3. **Human gene transfer reporting**
   a. *Principal Investigator changes*
   Dr. Sanjay Rajagopalan has left UM for a position at Mount Sinai School of Medicine. Dr. P.M. Grossman has assumed PI status for the following trials, formerly led by Dr. Rajagopalan:
   Valentis, A Phase I Multi-Center, Open-Label, Single-Dose Escalation clinical Trial of VLTS-589 for Treatment of Patients with Peripheral Arterial Disease
   Genzyme, A Phase I, Open-Label Single Dose, Roll-Over, Multi-Center Study of Ad2/Hypoxia Inducible Factor (HIF)1a/VP16 Gene Transfer Administered by Intramuscular Injection to Patients with Critical Limb Ischemia Who are Not Candidates for Surgical or Percutaneous Revascularization

   b. *Study closures*
   The IBC has received notice that the following human gene transfer clinical trials have been closed:
   1. Dr. P. M. Grossman, IBC 1543-002, Aventis (closed due to lack of enrollment; no subjects recruited here). Title: A Phase II, Randomized, Double-blind, Placebo-controlled, Parallel Group, Efficacy and Safety Study of Different Doses and Schedules of Administration of NV1FGF in Patients with Severe Peripheral Artery Occlusive Disease

   2. Grossman, IBC 1543-001, Berlex (enrollment and treatment closure; subjects being followed). Title: A Multi-center, Randomized, Double Blind, Placebo Controlled Study to Evaluate the Efficacy, and Safety of Ad5FGF-4 in Patients with Stable Angina (Protocol 304386) (Agent 3). In addition, the Phase II Berlex proposal submitted in January was withdrawn.

   3. Grossman, IBC 1543-005, Valentis Phase I (formerly under Rajagopalan, see above). Title: A Phase I Multi-Center, Open-Label, Single-Dose Escalation clinical Trial of VLTS-589 for Treatment of Patients with Peripheral Arterial Disease

   4. Dr. David C. Smith, IBC 1364-003, Cell Genesys (termination). Title: A Phase I/II Dose Escalation and Efficacy Trial of GVAX Prostate Cancer Vaccine in Patients with Metastatic Hormone-Refractory Prostate Cancer

   c. *Serious adverse events*

1. Grossman, IBC no. 1543-003, Valentis Phase II, Follow-up, external SAE, Pt. 10-010 Discussion: The preliminary autopsy showed likelihood that the death was attributable to underlying illness. The final autopsy will need to be reviewed.

2. Valentis Phase II, Three external SAEs, Pt.10-019:
   - Nausea, vomiting, diarrhea; labored breathing, hiccups, bilateral leg soreness; thickening of gallbladder wall, hepatomegaly
   - Right hemicolectomy & biopsy of liver. Ascending colon mass lesion/Hodgkin's disease
   - Diagnosis of classic Hodgkin's disease

   Discussion: Regarding Hodgkins disease, the question was raised could the increased vascularization have made the tumor grow? The committee member present who had reviewed this SAE said that may be possible, but he thought it was not likely.

3. Valentis Phase II, Local SAE, Pt. 06-019: Four blocked coronary artery vessels detected; coronary artery bypass performed. There were no concerns raised about this SAE.

4. Grossman, IBC no. 1543-006, Genzyme, External SAE, Pt. 03-012-327: Coarse liver secondary to suspected cirrhosis, Portal hypertension, Esophageal varices, Upper gastrointestinal bleed, Diastolic hypotension. There were no concerns raised about this SAE.

5. Grossman, Valentis Phase II, External SAE distributed at meeting: Pt. 01-002. Coma, death. Autopsy report to be sent around when received. Possibly related.

4. Biosafety Officer/Responsible Official Report – Michael Hanna

a. Update on select and select-like agents

It was reported that there have been no changes in select agent registrations and no new toxin registrations.

b. Update on viral vector training course

Jan Berry said she took this course and thought it was excellent as did the other participants. The downside, she said, is that it is not offered very often and only to small groups partly because of space limitations. She said there are spaces in the Dental School that could be used. Mike Hanna noted that based on overwhelming demand for the course, it has recently been increased to a class size of 30, and the next one will be held in the Life Sciences Institute.

5. IBC acknowledgement of recombinant DNA registrations, certifications, and materials transfers

Jan Berry: Motion to approve.
Carl Marrs: Seconded motion.

Vote: All in favor.

6. **IBC approval of minutes from January 30, 2004 meeting**
One change was recommended in the minutes, in the second paragraph of section 6.a.2. regarding David Fink's registration no. 1563-001, recombinant HSV1 vector and IL4 gene. The phrase "if he can provide evidence by PCR that the virus is not present" will be struck, and replaced with "following the first cage change after 48 hours." Thus, the sentence will read: "Dr. Imperiale made the following recommendation: BL2 for the lab virus work and BL2-N for the animal work, dropping down to BL1-N following the first cage change after 48 hours."

Carl Marrs: Motion to approve with the above change.
Jan Berry: Seconded motion.
Vote: All in favor.

7. **Matters arising**
There were no matters arising.

8. **For comment: Animal containment document**
It was noted that under animal housing for Pseudorabies virus (PRV), the phrase "after 48 hours" should be removed.

Meeting adjourned at 4:05 p.m.

These minutes approved at 10/8/04 IBC meeting.

Institutional Biosafety Committee Meeting
Friday, October 8, 2004
3:00-5:00 p.m., 4006 Fleming

IBC members present: Jan Berry, Brad Carlson, Michael Hanna, Rebecca Head, Nick Lukacs, Carl Marrs (associate chair), Howard Rush, Jacqueline Hoats-Shields (staff)
Guests: Janet Follo (OSEH), Kate Wiklanski (UCUCA)
IBC members absent: Fred Askari, Cary Engleberg, Phil Hanna, Michael Imperiale, Judy Nowack, John Schiefelbein

(Committee members present: 7. Quorum: 7.)

1. **Updates from the Chair**
   a. Carl Marrs, associate chair of the IBC, explained that he would be leading the meeting today as Michael Imperiale needed to be absent.

   b. Jackie Hoats-Shields gave a brief update regarding the symposium being planned for Monday, February 14, 2005, entitled "Academic Freedom and National Security: Biological Research in the Post-9/11 Era."

   c. Ms. Hoats-Shields reminded the committee that starting in 2005 IBC meetings will be scheduled on a monthly basis in order to accommodate proposals being submitted through the eResearch system. Another attempt to schedule these meetings will occur soon.

   d. Ms. Hoats-Shields said following the committee's decision last spring all work with Baculovirus *when the proteins are only to be expressed in insect cells* has been designated BL1 containment (down from BL2). The method of identifying and notifying investigators was described.

   e. Dr. Marrs gave an update on a serious adverse event in a Hemophilia study using an AAV vector at another institution. There was a brief discussion of the possible disadvantages of using viral vectors.

2. **IBC approval of minutes**
   a. The committee reviewed the minutes of the May 14, 2004 full committee meeting. There were no comments or corrections.
   Jan Berry: Motion to approve the minutes.
   Rebecca Head: Seconded motion.
   Vote: All in favor.

   b. The committee reviewed the minutes of the June 30, 2004 subcommittee meeting. There were no comments or corrections.
   Rebecca Head: Motion to approve the minutes.
   Jan Berry: Seconded motion

Vote: All in favor.

3. **IBC Standard Operating Procedures for Human Gene Transfer**
The IBC was provided with a copy of the current draft of the IBC Standard Operating Procedures for Human Gene Transfer. The group discussed the document briefly and no changes were suggested.
Howard Rush: Motion to accept the document.
Jan Berry: Seconded motion.
Vote: All in favor.

4. **Human gene transfer proposal (withdrawn): P. Michael Grossman,** A Phase II Multicenter, Randomized, Open-label, Dose Ranging, Multiple-dose Trial of VLTS-589 in Subjects with Intermittent Claudication Secondary to Peripheral Arterial Disease (VLTS-589-122), sponsored by Valentis.
Prior to the meeting the committee was informed by the investigator that this proposal is not going to be pursued by the sponsor, so review of the proposal by the IBC was not continued. There was a brief discussion among committee members about what the control would be if they went ahead with an alternative study using the placebo.

5. **Human gene transfer reporting**
The group commented on the notation of possible relation to the study agent for two of the serious adverse events in the packet (Valentis Phase II, patients 10-019 and 01-002). There were no disagreements or additional comments on these findings.

There was discussion of how the role of the IBC in evaluating serious adverse events (SAEs) is unclear. Presently at IBC meetings SAEs are noted and discussed by the IBC without vote. If based upon the information presented the committee feels there is evidence that a particular vector is implicated in a new kind of problem, then the IBC goes back to the IRB to let them know.

IBC members said it may be helpful if the IRB would give the IBC a report on whether they agree that specific SAEs are related or not, including a summary in lay terms. The IBC members present said in most cases they would defer to the IRB on the determination of related or unrelated. If the IRB feels an SAE is related, the IBC would know whether to go back and look more closely at the vector construct.

Postscript: The following language was added to the IBC SOP for Human Gene Transfer to reflect the ideas expressed above: "The IBC may seek input from the IRB regarding their evaluation of the Principal Investigator's determination of relatedness. If there are any concerns raised by IBC members about an SAE or the determination of relatedness these will be communicated to the IRB."

Additional issues about the role of the IBC in review of serious adverse events will be discussed at a future meeting.

6. **Biosafety Officer/Responsible Official Report – Michael Hanna**
   Michael Hanna said there were no changes to report in the status of select agents on campus. He said some Proposal Approval Forms marked as "yes" for such agents have turned out to be incorrectly marked.

7. **IBC acknowledgement of recombinant DNA registrations, certifications, and materials transfers**
   Jan Berry: Motion to approve.
   Rebecca Head: Seconded motion.
   Vote: All in favor.

8. **Matters arising**
   Howard Rush reported that a group is putting together a grant to get funds to build an animal BL3 lab and ULAM is taking lead on writing the grant. The Medical School and the School of Public Health are both involved. One-to-one matching is required on the grant and funds are being sought from around the university. Dr. Rush said this type of laboratory would fill a need at the University.

   Michael Hanna reported on the RAC symposium he attended recently entitled "Safety Considerations in Recombinant DNA Research with Pathogenic Viruses." He said there were reports on avian influenza, SARS, and coronavirus. The RAC has concerns about university research with these agents, and they have begun to come up with safe constructs to allow work with these agents that may reduce containment levels for this type of work possibly making it BL2 and not BL3. Entire program of symposium web accessible:
   (http://www4.od.nih.gov/oba/RAC/Sept2004/safetysymp.htm).

   Carl Marrs mentioned that he thinks the article on genome production enclosed with the agenda, "Seeking Security: Pathogens, Open Access, and Genome Databases," from the National Research Council, seems to be going in the right direction.

These minutes approved at the 2/8/05 IBC meeting.

Institutional Biosafety Committee Meeting
Tuesday, February 8, 2005
2:00-4:00 p.m., 4006 Fleming

IBC members present: Jan Berry, Brad Carlson, Cary Engleberg, Michael Hanna, Phil Hanna, Michael Imperiale (chair), Nick Lukacs, Carl Marrs, Judy Nowack, Howard Rush, John Schiefelbein, Gwen Thompson **IBC staff:** Jacqueline Hoats-Shields, Judy Crecelius **Guests:** Janet Follo (OSEH), Jeannie Kain (IRBMED), Kate Wiklanski (UCUCA)
IBC members absent: Fred Askari

(Committee members present: 12. Quorum: 7.)

1. **Updates from the Chair**
   a. ***Introduction of Gwen Thompson and Judy Crecelius***
   Michael Imperiale introduced new committee member Gwen Thompson who has joined the IBC as a community representative. Ms. Thompson is Senior Policy Analyst at the Altarum Institute, and she is replacing Rebecca Head who resigned in December. Dr. Imperiale also introduced Judy Crecelius of the Office of the Vice President for Research who will be working with the IBC when staff member Jacqueline Hoats-Shields goes on maternity leave in April.

   b. ***Wiesner Symposium***
   The 2005 Wiesner Symposium "Academic Freedom and National Security: Biological Research in the Post-9/11 Era" is occurring next Monday, February 14, 2005, 8:30-12:30 a.m., in the Great Lakes Room at Palmer Commons. Ron Atlas is the keynote speaker and panelists will be from the CDC, the FBI, the House Energy and Commerce Committee, and the National Science Advisory Board for Biosecurity (NSABB) of NIH OBA. The charter of the NSABB was handed out to the IBC for information.

   c. ***IBC monthly meeting schedule***
   Monthly meetings have been set through May and summer meetings will be scheduled soon. This is a result of the eResearch system in which the IBC (an "ancillary committee") must complete its review of a human gene transfer proposal before the IRBMED will review it. If there is no human gene transfer proposal to review, a monthly meeting may be cancelled. At a minimum, the IBC will still meet on a quarterly basis.

   d. ***eResearch and IBC HGT Standard Operating Procedures***
   Michael Imperiale noted that almost all members of the IBC were able to attend the eResearch training session in January. Under the new eResearch system for human subjects research when an investigator submits a proposal involving human gene transfer an e-mail notification will come from the eResearch system to the IBC chair and staff who will then send a link to proposal to the committee. As with our present process, primary reviewers will be identified and the entire committee will be able to review the proposal as well. Michael Imperiale noted that committee members should not individually use the question feature in

eResearch because this locks access to the proposal until there is a response. Instead, committee members should funnel all questions through the IBC chair and staff, just as in the present process. If responses from the investigator are received before a meeting, these will be forwarded around. The major change with the new system is that the IBC and other ancillary committees must approve the proposal before the IRB will review it.

2. **Human Gene Transfer Reporting**

a. Open studies. There are presently only two human gene transfer trials with open IRB files, both under Dr. Grossman: the Berlex study of Ad5FGF-4 (enrollment and treatment closed, IBC no. 1543-001), and the Valentis Phase II (closed to accrual, observational only, IBC no. 1543-003).

b. Serious adverse events.

- There were no concerns expressed about the two serious adverse event reports related to the Valentis Phase II, one of which was a follow-up. Both are from other sites.

- Discussion focused on the three Berlex serious adverse events which are all from different sites. Each one involves the diagnosis of a different type of cancer. Each of the three patients is on the same protocol which is studying adenovirus expressing FGF-4. In each case the principal investigator has said "possibly related" but Berlex has said these are unrelated or it is not possible to determine the relationship to the study agent. Michael Imperiale has already sent Dr. Grossman a set of questions to which the IBC has not yet received a response. Among other things, Dr. Grossman was asked to find out how many total patients have been treated to date on the study and whether there has been any consideration of unblinding these three patients. IBC members agreed it is important to get answers to the questions posed in order to adequately consider these events. Dr. Grossman will be asked again to respond.

3. **Human Gene Transfer Proposal HUM00000101 from P. Michael Grossman**

This proposal has not yet been officially submitted through the eResearch system. It is now expected to be submitted in the third week of February, for discussion at the March 8 IBC meeting. Ancillary committees are, at this time, not able to view proposals in eResearch until they are complete and have been officially submitted to the system.

4. **Biosafety Officer/Responsible Official Report – Michael Hanna**

5. **Registrations, certifications and materials transfers**

a. Robert Fuller registration. Mike Imperiale directed the committee's attention to the recently submitted registration from Robert Fuller which is for "select-like" work. There was discussion of the nature of the work and how it presents few safety issues, but perhaps there are some public relations considerations. Michael Hanna said placing the work at BL2 containment allows for a structured reporting system through OSEH. Another opinion expressed was that if all such work is automatically placed at BL2 then it is not clear what is the importance of committee's guidance.

Carl Marrs: Motion to approve the work at BL2 containment and if desired by the investigator an appeal can be addressed at the next meeting.

Jan Berry: Seconds motion.

Discussion: Judy Nowack spoke in support of the alternative view expressed above, saying that we do not want to put in place an unnecessary regulatory burden such as always moving to BL2 for "scary-sounding" agents.

Vote: 7 in favor
3 opposed
2 abstentions

Motion carried.

b. IBC acknowledgement of recombinant DNA registrations, certifications, and materials transfers

Phil Hanna noted that many of the same names keep appearing on the registration lists and he asked whether investigators know they can do one registration to cover multiple projects. It was noted that in many of these cases the investigator is completing a "new construct" form which is shorter than the initial form they filled out. It is also hoped that future implementation of the comprehensive registration form will streamline the process for investigators.

Jan Berry: Motion to approve.

Phil Hanna: Seconds motion.

Vote: All in favor.

6. **Minutes from the 10/8/04 IBC meeting**

Howard Rush: Motion to approve.

Phil Hanna: Seconds motion.

Vote: all in favor

7. **Matters arising**

- Michael Imperiale introduced Jeannie Kain from the IRBMED, who is visiting the IBC to increase coordination between the two committees. In future months the IBC may continue to have guests from the IRBMED depending upon upcoming agenda items.

- Kate Wiklanski said at the end of February the AALAC site visit will take place. This occurs every three years. For the visit UCUCA has prepared a 500 page document on animal care and use at the University. Ms. Wiklanski said the AALAC team may inquire into how the UCUCA and the IBC interact.

- Judy Nowack said that as part of the Human Research Participant Protection Program (HRPPP) the University will be submitting its first trial human subjects accreditation in March to the Association for the Accreditation of Human Research Protection Programs (AAHRPP) for pre-review. After the initial submission the accreditation process will be on a 3-year cycle.

- Howard Rush said the Medical School has submitted a grant to build an animal BL3 facility in the new BSRB.

These minutes approved at the 03/08/05 IBC meeting.

Institutional Biosafety Committee Meeting
Tuesday, March 8, 2005
1:30-2:30 p.m., 4006 Fleming

IBC members present: Jan Berry, Brad Carlson, Cary Engleberg, Michael Hanna, Phil Hanna, Michael Imperiale (chair), Nick Lukacs, Carl Marrs, Judy Nowack, Howard Rush, John Schiefelbein, **IBC staff:** Jacqueline Hoats-Shields, Judy Crecelius
Guests: Janet Follo (OSEH), Jeannie Kain (IRBMED)
IBC members absent: Fred Askari, Gwen Thompson

(Committee members present: 11. Quorum: 7.)

1. **Updates from the Chair – Michael Imperiale**
   a. According to reports recently in the New York *Times* an FDA panel was put together to look at issues related to the French X-SCID trial. Michael Imperiale said the recommendation of the panel is that if all else fails the gene transfer treatment in this study would be an acceptable treatment even considering the risks (several patients had developed leukemia). An impetus for convening the panel was that one patient has died from the leukemia.

   b. Michael Imperiale thanked committee members for their attendance at the Wiesner Symposium last month, "Academic Freedom and National Security: Biological Research in the Post-9/11 Era." Committee members remarked that it was an interesting and worthwhile event. The entire program was taped and is being transcribed.

2. **Human gene transfer reporting**
   a. **Open Studies**. The two presently open studies (with open IRB files) were listed for the committee's information. Both are under Dr. P. M. Grossman. One **[1543-003]** is sponsored by **Valentis**, and entitled "A Phase II, Multi-center, Double-Blind, Placebo-Controlled, Trial of VLTS-589 in Subjects with Intermittent Claudication Secondary to Peripheral Arterial Disease." The other **[1543-001]** is sponsored by **Berlex**, and entitled "A Multicenter, Randomized, Double Blind, Placebo Controlled Study to Evaluate the Efficacy, and Safety of Ad5FGF-4 in Patients with Stable Angina."

   b. **Serious adverse event reporting.**
   Three serious adverse events from other sites on the Berlex trial **[1543-001]** involving the development of various cancers (lung carcinoma, melanoma and brain mass, and a spinal cord tumor) where discussed again after receipt of responses from Dr. Grossman to questions posed by Michael Imperiale. The discussion also included a fourth report of cancer which was distributed at the meeting; this fourth report is of prostate cancer in a 73 year-old male.

   Dr. Grossman's response to Dr. Imperiale's questions included that there were 416 patients in the trial. It was commented that given this the development of 4

cancers may not seem like a lot. Jan Berry made the point that the study is not yet unblinded, however, and knowing the number of patients who actually received the agent and whether these four patients did would make a difference to the interpretation. It was noted that the advanced age of the patients must also be considered.

Cary Engleberg was asked his reaction to the information provided by Dr. Grossman. He said that one important thing to know about these four patients is how long it has been since each was treated. Still, it was remarked, some cancers are slow growing. Dr. Engleberg said that even so, with this age group these cancers are not extraordinary, but still it is a tough call if one considers the earlier point about unblinding down to a smaller group. Carl Marrs said it would have been helpful for the investigators to have predicted at the start how many incidents of cancer would be likely to occur.

The question arose of whether this study has a formal data safety monitoring board. Jeannie Kain said the IRB looks into this and the other questions raised above during its review. It was noted that the study will be unblinded in May. Dr. Engleberg said it may be difficult to determine the relatedness even if we had a threshold/formula as suggested above because these are such garden-variety cancers. Dr. Imperiale said the committee can continue to watch for when a pattern arises and then go back to the investigator.

3. **New human gene transfer proposal from P. M. Grossman (HUM00000101), submitted through eResearch. Proposal title: "A Multi-Center, Randomized, Double-Blind, Dose Ranging, Placebo Controlled, Study Evaluating Defined Doses of Percutaneously Delivered via Boston Scientific Stiletto Endocardial Direct Injection Catheter System pVGI.1 (VEGF2)," sponsor: Corautus Genetics Inc.**

Michael Imperiale said in his review he did not find any major biosafety concerns in this proposal. Carl Marrs concurred, remarking that this plasmid vector has been approved already in several contexts. He said his concern is with the noted oncogenic potential of anything that promotes blood vessel growth, especially in light of the serious adverse events also under discussion today. He said it would be helpful to have it explicitly stated in a protocol ahead of time under what conditions the code will be broken.

Cary Engleberg said he was concerned about the accuracy of the stiletto device and that the issue of incorrect injection is not addressed. He asked what happens if [the study agent] gets injected by mistake into another area (the pericardium, the myocardium or into the ventricle) and a proliferation of blood vessels starts there? It was noted that in the proposal materials they refer to this in animals, that the blood vessels did proliferate, and they detected the DNA in PCR. Dr. Engleberg said the issue of incorrect injection is something Dr. Grossman should be asked about. How accurate is the catheter injection system? They are doing more than just cardiac

catheterization. Another committee member noted this is not a public health safety issue.

There was a brief discussion of who holds the IND as it was initially thought to be the local principal investigator, however, it has been clarified that the IND is held by the sponsor which is the more common arrangement. It was mentioned that the IRB notes who holds the IND and there is no institutional policy prohibiting a principal investigator holding it, and that in such a case the individual is responsible.

Dr. Imperiale asked if there were any other concerns about the proposal, and there were none mentioned.

Carl Marrs: Motion to approve on condition that they add a statement to 23.1-8 of the eResearch submission (potential significant adverse events) regarding the fact that the injection could go into the heart muscle and this could result in blood vessel proliferation.
Jan Berry: Seconds motion.
Discussion: Howard Rush asked whether this means the statement should go into the informed consent. Carl Marrs said no, the informed consent only includes events that have happened. We just want to know they are monitoring for this.
Vote: All in favor.

Postscript: The above proposal was subsequently withdrawn by the Principal Investigator (3/23/05).

4. **Biosafety Officer Report – Michael Hanna**
   a. Ron Maio, Associate Dean for Research Regulatory Affairs in the Medical School, has requested a briefing by OSEH. Michael Hanna passed around a document to be used at the March 25th briefing. If IBC members are interested in receiving a copy of this brief it can be made available.
   b.

5. **IBC acknowledgement of listed registrations and materials transfers**
   Jan Berry: Motion to approve with stipulation Janet Smith provide the information described below. (Stipulation added after discussion.)
   Howard Rush: Seconds motion including stipulation.
   Discussion: Phil Hanna said that one investigator on the list, Janet Smith, works with virus proteins which may require added scrutiny and suggested asking her to list out the proteins to give a broader picture for the registration. It was further suggested she be asked which viruses and genes she will be expressing. On the submitted registration Dr. Smith wrote Risk Group 1. During the review process Dr. Imperiale had asked for her assurance that she would not be expressing any dangerous toxins or virulence factors to which

she replied she had no such plans. She will be asked for additional detail on the viruses/organisms she will be cloning genes from and what specific proteins she is expressing. Discussion continued regarding how much license an investigator has for the development of their work without updating the IBC. Michael Imperiale said every time an investigator makes a new rDNA clone they should let the IBC know.

Vote: All in favor.

6. **IBC approval of minutes from February 8, 2005 meeting**
   Michael Hanna: Motion to approve.
   Judy Nowack: Seconds motion.
   Vote: All in favor.

7. **Matters arising**
   Judy Nowack said that in the coming year the NIH Office of Biotechnology Activities intends to do between five and twenty not-for-cause site visits of institutions conducting recombinant DNA research.

These minutes approved at the June 7, 2005 IBC meeting.

Institutional Biosafety Committee Meeting
Tuesday, June 7, 2005
1:30-2:30 p.m., 4006 Fleming

IBC members present: Fred Askari, Jan Berry, Brad Carlson, Michael Hanna, Phil Hanna, Michael Imperiale (chair), Nick Lukacs, Carl Marrs, Judy Nowack, Howard Rush, John Schiefelbein, Gwen Thompson, **IBC Staff:** Judy Crecelius, Kathy Huffnagle
Guests: Janet Follo (OSEH), Jeannie Kain (IRBMED)
IBC members absent: Cary Engleberg

(Committee members present: 12 Quorum: 7)

1. **Updates from the Chair**
   a. Mike Imperiale reminded reviewers of the need to speed up the turn around of their proposal reviews.

   b. Federal officials asked the National Academy of Sciences not to publish a paper on bioterrorism, citing security concerns. The paper detailed how terrorists might attack the nation's milk supply with botulinum toxin, and offered suggestions for how to thwart such an attack. Mike Imperiale said that this was the first time the Federal government has asked a journal to remove a paper that had already been accepted for publication.

   c. Mike Imperiale attended a gene therapy meeting, where they announced Introgen Therapeutics (Texas based company) is getting close to getting the first FDA approval for a commercially available gene therapy drug.

2. **Human gene transfer reporting**
   The comment was made that the un-blinding of the patients should take place by May 31, 2005. Jan Berry asked if something occurs in a study that is not coincidental, should the IBC be the one that picks this up? Mike Imperiale answered that actually the sponsor should technically be the one that is overseeing this.

3. **Human gene transfer proposal submission:** New submission from P. Michael Grossman

   Mike Imperiale wanted to disclose to the committee that for the past year he has been signing off on the quality assurance on the cell-based therapy that has been coming out of the patient labs for the GCRC, so he will not vote on the approval of this proposal.

   Mike Imperiale said that the few issues raised about Conflict of Interest have been straightened out.

Judith Nowack addressed the issues surrounding peer / department review. She said there are some departments that have their scientific reviews and merit process. This is allowed, but the IRBs do not have a binding requirement that they need to have a scientific review before a proposal is submitted to them.

Other comments on performance sites-- up to 2 sites may participate, but presently U-M is the only site.

Jan Berry commented on the information given to the patient participants. She thought that the **consent form** needed to explain more clearly what they were going to do. Another issue is the **bio-distribution** question. For the long term it would be beneficial to know where these genes go in the system, because these tissues disappear in several weeks. In discussions it was determined that if the genes did, in fact, go everywhere that wouldn't change the IBC's decision.

Mike Imperiale said that he has letters from the Recombinant Advisory Committee (RAC). Grossman will have to appear before RAC. They will have a public review of this protocol because (1) it is a novel human gene transfer approach, and (2) it is a new transfer, "Ang-3", that no one has used before.

RAC had questions such as migration of transduced cells in the lung, and also justification why there wasn't a longer cancer study than one year. There are also some questions about terminology.

In summary, the points that Grossman should address are:

1) COI
2) Peer review
3) Informed consent – details about stripping of the veins
4) Understanding of secretion (Did he misunderstand the question about secretion?)
5) Bio-distribution

There were further discussions on the "informed consent form". Jan Berry wanted to give the patients some kind of time frame in the consent form, e.g. Is it going to be one or two weeks between the vein stripping and dosing?

Jan Berry also asked whether there were other IRB concerns. J Nowack commented that currently the IRB is considering the appropriate reading levels in the consent form. The IRB is concerned that the reading levels should be low enough for any patient's understanding.

Mike Imperiale removed himself from the room. Judy Nowack called to a vote the Grossman proposal with appropriate answers to the above 5 stipulations.

Carl Marrs: Motion to approve
Phil Hanna: Second
Vote: All in favor (with the 5 stipulations)

NOTE: Carl Marrs will serve as the approving official. (Mike Imperiale is conflicted because he serves on the RAC.)

Mike Imperiale returned to the room after the vote. He then introduced Kathy Huffnagle to the rest of the IBC members. Introductions were made around the table.

4. Biosafety Officer/ Responsible Official Report- Michael Hanna

a. SPH Viral Collection Review report: After several purges by the School of Public Health, OSEH went over for an inspection and found that SPH had destroyed the materials they felt lacked research value. The CDC took everything they wanted. This collection contains clinical samples and

. Carl Marrs concurred with others that it was safer to keep the cryovials frozen in their present state without further identification.

b.

c.

5. Janet Smith, rDNA questions

Janet Smith did not provide enough information on the genes she was cloning. There was a discussion of what level should be used for this proposal. Phil Hanna and Fred Askari felt that there was a level of concern and BL1 was more appropriate than BL1 Exempt.

Mike Hanna: Motion to have Janet Smith's protocol rated as BL1 and leave off the "exempt" terminology.
Phil Hanna: Seconds the motion

Vote: 9 yes, 2 no, 1 abstention

J Nowack asked whether Janet Smith needed more education. Janet Follo agreed to speak to her.

6. IBC acknowledgement of rDNA registrations, certifications, and material transfers

Jan Berry: Motion to approve
Carl Marrs: Seconds the motion
Vote: All in favor

7. IBC regular set monthly meeting time

After consulting everyone's calendars it was determined that the IBC monthly meetings would take place on the 3rd **Friday, 1:15-2:15 p.m. at 4006 Fleming.** As in the past we may choose to cancel monthly meetings if there aren't any pressing matters to discuss.

8. IBC approval of minutes from March 8 meeting
Jan Berry: Motion to approve
Howard Rush: Seconds motions
Vote: All in favor.

9. Matters rising
Mike Imperiale repeated the need to turn around the proposal reviews more quickly.

M. Imperiale announced that three IBC members agreed to serve for another term. They were Judith Nowack, John Schiefelbein, and Michael Imperiale, chair.

10. The meeting was adjourned at 2:30 p.m.

These minutes were approved at the August 19, 2005 IBC meeting.

Institutional Biosafety Committee Meeting
Friday, October 21, 2005
1:15-2:15 p.m., 4006 Fleming

Minutes

IBC members present: Jan Berry, Brad Carlson, Mike Hanna, Mike Imperiale (chair), Nick Lukacs, Carl Marrs, Judy Nowack, Howard Rush **IBC staff:** Jacqueline Hoats-Shields
IBC members absent: Fred Askari, Cary Engleberg, Phil Hanna, John Schiefelbein, Gwen Thompson
Guests: Lois Brako, OVPR; Kate Wiklanski, UCUCA

(Committee members present: 8. Quorum: 7.)

1. **Updates from the Chair**

Introduction of Lois Brako

Michael Imperiale turned the meeting over to Judy Nowack for introduction of new OVPR staff member, Lois Brako, who has come to UM from the University of Wisconsin. Ms. Brako is working closely with Judy Nowack on a full range of issues as Regulatory Affairs Associate. Among her duties at the University of Wisconsin she worked with the IBC as a liaison between the vice president for research and the committee of which she was an ex officio member. Ms. Brako has offered her assistance with the process of creating the new IBC online system.

Reconstruction of the 1918 Flu Virus and Publication

Dr. Imperiale noted the recent articles appearing in *Science* and *Nature* about the reconstruction of the 1918 flu, published on the advice of the National Science Advisory Board for Biosecurity (NSABB) which held a phone conference on the matter. He was not able to take part in the phone call but had reviewed a transcript of it. He said the NSABB felt strongly that the benefits of publication outweighed the risks. Arguments in favor of publication included that most of the information about this flu is already available and publication could possibly lead to new anti-virals and understanding of what makes flu pathogenic. This decision was the first official action of the NSABB. With regard to the Board's other activities, Dr. Imperiale said the working group he is on met last month with the task to define dual use research. They decided that dual-use wasn't going to be limited to just select agents. There will be another meeting of the entire board later this fall.

Meeting with Steve Forrest

Dr. Imperiale said he met last week with vice president for research-elect Steve Forrest to brief him on the work of the IBC.

2. **Human Gene Transfer Reporting**
Michael Imperiale noted the revised consent for Dr. Grossman's proposed MGVS study which the IBC approved in August. It is still going through IRB review. The revised version of the consent includes information about whether these cells could travel elsewhere in the body which one IBC member had previously mentioned would be helpful to include.

There are no SAEs to report at this meeting.

3. **Biosafety Officer/Responsible Official Report**
Michael Hanna said he and two staff are going to several upcoming conferences focusing on biosafety, including the use of animals, from a design standpoint.

Howard Rush said that ULAM has received one grant toward their BSL3 facility and they are seeking another.

Closed portion of meeting begins. Guests are excused.

End of closed portion of meeting. Guests rejoin the meeting.

4. **eResearch and Basic Recombinant DNA**
Michael Imperiale said the MAIS team, which designed eResearch for human subjects, has said they will be able to work on a new system for the IBC/basic recombinant DNA beginning in the first quarter of 2006. This would allow implementation of the revised registration form that the committee came up with a

few years ago. An agenda enclosure lists some of the advantages in moving to the new system.

Registration of exempt work

There are a number of procedural issues for the committee to address in preparation for designing the new registration system. One is regarding the registration of work that is considered exempt from the *NIH Guidelines*. Dr. Imperiale explained that he thinks there will be a marked increase in the IBC's workload in the future due to changes in regulations. With this in mind he said he is proposing the idea that exempt work wouldn't have to come through the committee for review. The committee discussed the idea. The point was made that some registrations come forward proposed as exempt/BL1 but need a higher containment, and without registration we would not be aware of this. It was suggested that one way to address this if we didn't register exempt work would be to have an audit system of some kind.

One reviewer said in his opinion the exempt ones take very little time for review. Another committee member said it seems safer to register everything so that investigators won't be left trying to figure out what is necessary to register or not, and then perhaps choosing incorrectly not to register. It was suggested that there be a way to ask certain questions up front to determine whether work needs to be reviewed or not. One way to do this would be to enhance the check-off section on the PAF. It was noted that the individuals the committee needs to be most concerned about are those who estimate they need a lower biosafety level or incorrectly assume their work is exempt. It was agreed that the question of whether to continue registering exempt work is an issue that requires more discussion at an upcoming meeting.

Review of BL3 work

Dr. Imperiale said another issue for discussion is the process of reviewing BL3 recombinant registrations and select agent registrations. He said he is making the strong recommendation that such work be handled by in-person discussion at a committee meeting. The committee discussed what this would mean and how to identify recombinant work that may require BL3 containment. It was agreed that more discussion is needed to define what requires BL3. Another issue brought up is how to handle proposed projects by investigators already registered for some BL3 recombinant work. In these cases the question is whether a whole new registration should be submitted or is some lesser amount of information acceptable. One committee member stated that accepting a project certification for BL3 work (i.e., the PI attesting to their work falling under an existing registration) seems risky since the committee is not seeing any description of the work.

It was agreed that the next meeting, on November 18, would be devoted to discussion of these and other procedural issues and the new online system. Dr.

Imperiale directed the committee's attention to the other supporting documents on this topic in the agenda which will be useful for the discussion next time.

5. **IBC acknowledgement of recombinant DNA registrations, certifications, and materials transfers**
It was noted that a couple registrations still marked as "under review" were included on the list by mistake. Note was made of a BL3 registration from Dr. Ono, who is working with infectious HIV and cloning genes onto it, appearing on the list. This registration was discussed at the last meeting where the group agreed on BL3 containment.
Jan Berry: Motion to approve/acknowledge the lists of registrations, certifications and materials transfers.
Carl Marrs: Seconds motion.
Vote: All in favor.

Retrovirus (Lentivirus) registration from Gary Luker for review
Dr. Imperiale explained that Dr. Luker wants to pseudotype a lentivirus vector with the ebola glycoprotein to do experiments in animals. He is using it as a delivery system for his reporter genes and changing the host range by putting on a different surface marker. Dr. Imperiale said he thinks BL2+ would be fine. Dr. Marrs asked if the containment can be lowered to BL2 after being BL2+ if it is determined later that BL2 would be adequate. Michael Hanna described the differences between the two types of containment. Dr. Imperiale said the committee can ask the investigator to later give us a summary of the results at which time a lowering of the containment level could be considered.
Carl Marrs: Motion to approve at BL2+ containment noting in the letter that it is because of newness factor of the work, and requesting follow up information at which time Dr. Luker can let the committee know if he thinks the containment could be lowered.
Howard Rush: Seconds motion.
Vote: All in favor.

6. **Minutes from the August 19, 2005 IBC meeting**
Carl Marrs: Motion to approve the minutes as written.
(No second recorded.)
Vote: All in favor.

Meeting adjourned at 2:35 p.m.

These minutes were approved at the November 18, 2005 IBC meeting.

Institutional Biosafety Committee Meeting
Friday, August 19, 2005
1:15-2:15 p.m.
4006 Fleming

IBC members present: Brad Carlson, Cary Engleberg, Michael Hanna, Philip Hanna, Michael Imperiale, Carl Marrs, Judy Nowack, John Schiefelbein, Gwen Thompson
IBC members absent: Fred Askari, Jan Berry, Nicholas Lukacs, Howard Rush
Guests present: Janet Follo, OSEH; Jeannie Kain, IRBMED; Ruth Lewis, IRBMED; Kate Wiklanski, UCUCA

1. **Updates from the Chair**

National Science Advisory Board for Biosecurity

Michael Imperiale reported on the first meeting of the National Science Advisory Board for Biosecurity (NSABB) to which he was appointed in the spring. The meeting took place June 30-July 1, 2005. Dr. Imperiale is the only member of the board who is chair of an IBC. He said there are about 20 voting members, and about two-thirds of them are scientists. There are also many non-voting members representing various government agencies. The first meeting which had about 200 members of the public in attendance was primarily a series of talks on various issues, with topics including the difficulty of defining dual-use technology and the implications of being able to synthesize viruses in a day and a bacterium in a week, which may soon be possible. He said that a term frequently used during the meeting was "culture of responsibility." During the meeting five working groups were set up to tackle the five main issues of the Fink report:

- Defining "dual-use" (MI)
- Communication of research results
- Code of conduct for life scientists
- International collaboration
- Synthetic genomes (possible regulation of) (MI)

Dr. Imperiale is participating in the working groups on defining dual-use and on synthetic genomes. While the Board will meet quarterly the working groups will meet more frequently and as soon as mid-September. Dr. Imperiale said he welcomes any comments and ideas regarding the issues above. Agendas and webcasts of NSABB meetings are at biosecurityboard.gov.

Regarding the idea of a culture of responsibility in biological research committee members briefly discussed the availability of such training for graduate students. It was noted that PIBS has bioethics training and perhaps biosecurity could be added. It is also a possibility that this could be a part of PEERRS in the future.

Postscript: At the time of the meeting the bioethics portion of the PIBS program did not include this topic, and Michael Imperiale has agreed to present on it for PIBS in the coming year.

Reviewer assignments
Committee members had been asked prior to the meeting if they would like to be assigned to review a particular registration form on a regular basis. Jackie Hoats-Shields relayed the results. It was mentioned that the e-mail format in which registrations appear for reviewers is very difficult to read. This will be corrected in the new IBC registration system that is soon to be developed. A meeting to discuss the new system is set up for next Tuesday. Dr. Imperiale explained that in the future registrations will be investigator-based covering everything in the lab, instead of project-based as registrations are now.

2. **Human gene transfer reporting**
Regarding the Berlex unblinding information for IBC no. 1543-001, it was noted that there was no trend apparent when considering the development of tumors and comparing those who received placebo to those who received the study agent.

The amendment to the Berlex protocol (IBC no. 1543-001) was accepted without comments.

3. **Human gene transfer protocol review: re-submission with changes, via eResearch: MGVS Phase I in Peripheral Arterial Disease (HUM00000223), P. M. Grossman.** This protocol was initially reviewed at the June 7, 2005 IBC meeting. Michael Imperiale opened the discussion by saying the new consent is very much improved. He said that at the June 7 meeting he was recused from the vote on this proposal because of his role at the Human Applications Lab with their quality assurance review; they are now looking for someone to take over that job. He noted that Carl Marrs was the designated reviewer and opened up the floor for comments.

Carl Marrs said that this iteration of the proposal is very impressive. The informed consent touches all the issues. He noted that the RAC comments mirrored the IBC's earlier comments, and the new submission addresses these points. He said he is impressed by the overall improvement. Cary Engleberg said one thing the proposal cover is the distribution of the infected cells. The group discussed this and it seems the investigators don't have the data on this and do not appear to plan to look for it. It was agreed that there is not a good way to do this; it simply may not be feasible. Michael Imperiale brought up the issue of peer review. This was questioned during the last IBC discussion and with this submission of the proposal they have said that Sanjay Rajagopalan has done a peer review. Judy Nowack suggested the committee could get some documentation from Dr. Rajagopalan about his review and Michael Imperiale said he has requested this by e-mail. Ms. Nowack noted that Dr. Rajagopalan should be asked about any possible conflicts of interest.

The group agreed that there were enough changes with this submission to call for a new vote on it.

Carl Marrs: Motion to approve.

Phil Hanna: Seconds motion.
Judy Nowack: Moves to amend that Michael Imperiale and Carl Marrs can receive the response from Sanjay Rajagopalan and the authority is vested in them to approve via eResearch on behalf of committee once a satisfactory response has been received.
Michael Hanna: Seconds amendment.
Discussion: Phil Hanna clarified that the IBC should not hold them to trying to find out where the cells go.
Vote: All in favor.
Postscript: Sanjay Rajagopalan did turn out to have a conflict in performing the peer review on this proposal, but in the end it was determined that a) peer review is not really required by anyone and b) the review of the IBC, along with that of the RAC, constituted adequate scientific review. The proposal received IBC approval via eResearch on August 30, 2005.

4. **Biosafety Officer/Responsible Official Report**
Michael Hanna reported that

Mr. Hanna said that until this is received the IBC cannot vote on approval. Judy Nowack said it must come to vice president for research after going to the dean and first the department chair. Regarding another faculty member new to the University, a letter is expected soon from the Medical School dean. The IBC will receive a copy.

5. **Registrations, certifications and materials transfers**
Discussion: Phil Hanna brought up an issue with two items on the certification list. The first was the certification of Janet Smith's two projects as "exempt at BL1" (listed on page 19) and the second was David Sherman's BL1 project with Bacillus anthracis genes (also listed on page 19, at the top). Dr. Hanna expressed concern that BL1 and exempt designations remove oversight by OSEH. He said that Dr. Smith's work should not be listed as exempt since a decision to that effect was made during the June 7, 2005 meeting. Judy Nowack said that investigators cannot avoid registration and oversight by the IBC and OSEH even if work is listed as exempt. Janet Follo said that while she conducts BL2 lab inspections other OSEH representatives look at non-BL2 labs for various issues. She and Mike Hanna stated that all labs on campus are looked at and tracked, with attention to action items that need follow-up. Mike Hanna said OSEH also does consultations with researchers about their work and handling of biological materials.

Carl Marrs: Motion to approve/acknowledge the lists of registrations, certifications and materials transfers
Phil Hanna: Seconds motion
Vote: All in favor

Registration from Akira Ono for committee discussion
Michael Imperiale introduced this retrovirus vector registration for committee dicussion (e-mailed to the committee prior to meeting). The principal investigator has proposed BL3 containment. The work involves lipid phosphatases, adding genes; it is a true HIV cloning vector experiment. Dr. Imperiale said the work with non-recombinant HIV could be BL2+. However, he has view that this should be BL3 because of the fact that it is a true cloning experiment. He said that his recommendation is that the committee approve it at BL3 for any work involving HIV carrying a transgene.

Phil Hanna: Motion to approve at BL3
Cary Engleberg: Seconds motion
Vote: All in favor

6. **Minutes from June 7, 2005 IBC meeting**
   Motion: (vote was taken without a motion)
   Vote: All in favor of approval (no changes suggested)

7. **Matters arising**
   Michael Imperiale told the committee that in his opinion the work of the NSABB is going to make a lot more work for this committee, beyond just the review of recombinant DNA.

   Dr. Imperiale pointed out the draft of the IBC Standard Operating Procedures included with the agenda. Committee members should send comments to Jackie.

   Michael Hanna said that a future agenda item for the IBC could be restrictions from the Commerce Department (ITAR restrictions) and how to deal with existing export control regulations. He said he had recently met with DRDA on this matter. Judy Nowack suggested that the issue needs shaping a bit more before bringing to the IBC.

These minutes approved at the 10/21/05 IBC meeting.