The University Of Chicago
.Risk Management, Audit and Safety.
Safety and Environmental Affairs
5555 South Ellis Avenue, Chicago, Illinois 60637

Steven Beaudoin
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August 3, 2006

Edward Hammond
The Sunshine Project
P.O. Box 41987
Austin, Texas 78704

Dear Mr. Hammond :

We are responding to your request for minutes of the University of Chicago Institutional Biosafety Committee for the last three years. Copies of the minutes from June 2003 through May 2006 are enclosed.

Please note that future requests should be sent directly to the IBC at the following address to ensure a timely response :

Chair
Institutional Biosafety Committee
The University of Chicago
5841 S. Maryland Avenue, MC 1108
Chicago, Illinois 60637

We regret the delay in responding to your request.

Sincerely,

Steven Beaudoin

The University of Chicago

Institutional Biosafety Committee

5841 S. Maryland Avenue
AMB S-152 ♦ MC 1108
Chicago, IL 60637

Minutes of June 6, 2003
1:00 PM – [redacted]

In attendance:

Voting Members

Kenneth Thompson
Richard Hiipakka
Malcolm Casadaban
George Daskal
Helena Mauceri
Rima McLeod
Louis Philipson
Gopal Thinakaran
Craig Wardrip

Ex-Officio Members

Steve Beaudoin
Michael Holzhueter
David Pitrak
Markus Schaufele
Steve Seps

Staff

Pamela Postlethwait
Bill Pugh

Absent:

Voting Members	Ex-Officio Members	Staff
Clara Gartner	Russ Herron	
James Mastrianni	Manfred Ruddat	None
Mary Ellen Sheridan		
Walter Stadler		

I. Minutes:

A. The minutes of the April 4, 2003 meeting were unanimously approved (8-0) with a minor correction to attendance.

II. Protocol Review:

The following protocols were reviewed at the meeting, with the disposition noted:

PR# Category/Investigator/***Disposition***

776 New/Wang, Chyung-Ru/***Deferred*** (8-0)
Recent studies have shown that lipid and glycolipid antigens from cell wall of mycobacterium can be presented by human class Ib molecules to cytotoxic T cells. However, the antigen-

processing pathway for these unique bacterial antigens and the function of the microbial-specific MHC class Ib-restricted T cells remains unclear. The investigator proposes to infect MHC class Ib deficient mice and MHC class Ib transgenic mice with *Mycobacterium tuberculosis* to study the impact of MHC class Ib-restricted response in acquired resistance to this pathogen. The laboratory will also derive class Ib-restricted T cell lines from infected mice and will study the lipid antigen requirement for presentation by class Ib molecules. Committee review of the protocol centered on the facility requirements for the propagation and manipulation of cultures of *M. tuberculosis* and the associated animal studies. The Committee noted that Biosafety Level 3 (BSL3) practices and containment are necessary for work with this agent and the proposed location of work does not meet these requirements. The Committee determined that the protocol could not be approved until suitable facilities were available.

Reason(s) for Deferral:

1. The Biosafety in Microbiological and Biomedical Laboratories manual indicate that for laboratory activities involving the propagation and manipulation of cultures of *Mycobacterium tuberculosis*, Biosafety Level 3 practices, containment equipment, and facilities are required. Since the proposed location of work does not meet the required biosafety level requirements, the IBC cannot vote for approval at this time. Once suitable BL3 laboratory facilities can be found, please amend the protocol accordingly and the full committee will reconsider the proposal.

812 New/Hoover, Robert S./***Approved*** (8-0)

To study the regulation of rat thiazide-sensitive sodium chloride cotransporter (rTSC), the investigator will utilize a commercially available adenovirus system to introduce GFP-tagged rat TSC DNA into HEK293 cells. Cells expressing the cotransporter will be used to study function and surface expression. During review of the protocol, the Committee noted this system is widely used and had no additional comments.

813 New/Thompson, Kenneth/***Pending Conditions & Recommendation*** (8-0)

The investigator proposes to test the antiviral activity of plant extracts using various clinical and laboratory strains of respiratory viruses. During review of the protocol, it was noted that mouse coronavirus would be utilized in the study. Committee members expressed concern regarding the use of mouse coronavirus since this particular virus is a hazard to the integrity of the animal barrier facilities. Following discussion, the Committee's recommendation would be for the investigator to use another coronavirus instead of mouse coronavirus.

Pending Conditions:

1. The investigator needs to provide a letter from the Institutional Review Board (IRB) for the use of human cell lines.
2. In Section VII, question 14, the investigator needs to designate an individual to provide oversight in their absence.

Recommendation:

1. The Committee strongly recommends that another coronavirus rather than the mouse coronavirus be used in the studies since the use of mouse coronavirus poses a threat to the integrity of the animal barrier facilities.

814 New/Madara, James/***Approved w/Stipulations*** (9-0)

The investigator proposes to use the Sterne strain of *Bacillus anthracis* and T84 cell cultures to investigate the mechanism of spore invasion of epithelial monolayers and to identify genes that promote spore invasion. During discussion of the protocol, the Committee noted that the investigator was using an exempt strain of *B. anthracis* and all work would be done in cell culture, however, the work would be carried out in a laboratory where multiple RG2/BL2 were

being utilized. Committee members agreed that the investigator should segregate the waste stream.

Stipulations:

1. In Section VII, question 7, under item a, the investigator needs to remove "as hazardous waste" and replace with "in designated waste containers". Also, the requested change needs to be incorporated in the Biosafety Manual under the Decontamination/Disposal section.
2. The investigator is requested to segregate the waste stream by disposing of the different pathogens into different designated waste containers.

815 New/Sperling, Anne/***Pending Conditions & Comment*** (8-0)

The study proposes to investigate the immune response to *Yersinia pestis* KIM D27 by identifying targets of the humoral immune response during acute plague infection in mice using enzyme-linked immunosorbent assays (ELISA) and by monitoring the development of T cell response following vaccination in mice by T cell proliferation assays. The study is being done in collaboration with Dr. Olaf Schneewind, therefore tissue and serum will be provided by the Schneewind laboratory. Committee discussion of the protocol centered on the transport of potentially infectious material between laboratories.

Pending Conditions:

1. In Section VII, question 9, under item 3b and 3c, the investigator needs to change "hyperchlorite" to "hypochlorite".
2. In Section IV, Research Summary, the investigator indicates that samples will be moved from [redacted] to [redacted]. A standard operating procedure (SOP) detailing the route of transport between [redacted] and [redacted] as well as transport from the [redacted] to [redacted] and the method for transporting the materials (i.e. packaging) needs to be provided. The SOP will need to be reviewed and approved by Infection Control.

Comment:

1. The IACUC ACUP [redacted] approval is pending IBC approval. The IBC will notify IACUC once the above pending conditions have been addressed and the protocol is approved.

816 New/Sperling, Anne

Protocol review and discussion was deferred until the next regularly scheduled IBC meeting.

817 New/Schneewind, Olaf

Protocol review and discussion was deferred until the next regularly scheduled IBC meeting.

819 New/Weiss, Roy E./***Approved*** (9-0)

The investigator is setting up a core facility to produce lymphoblastoid cell lines using the Epstein-Barr Virus for investigators doing genetic studies. The protocol was very well described and the Committee had no additional comments.

820 New/Macdonald, Robert L./***Approved*** (8-0)

Vasospasm is arterial constriction that develops days after a rupture of an intracranial aneurysm that produces subarachnoid hemorrhage. There are no treatments currently available to prevent vasospasm. Since vasoconstriction underlies vasospasm and vasoconstriction depends on increased intracellular calcium, a treatment that prevents increased intracellular calcium may prevent vasospasm. The investigator hypothesizes that transfection of smooth muscle cells of the basilar artery with a calcium binding protein will prevent increased intracellular calcium in the cells and prevent vasospasm. The studies will utilize an adenoviral vector containing the calcium binding protein. The procedures were thoroughly described and the Committee had no additional comments.

825 New/Chang, Eugene/***Pending Conditions*** (8-0)
The investigator proposes to use *Salmonella typhimurium*, which invades intestinal epithelial cells and enteropathogenic *E. coli*, which adheres to intestinal epithelial to investigate whether induction of small molecular weight heat shock proteins will mitigate the actions and pathogenicity of these bacterial pathogens. While the Committee noted that the protocol was very thorough, information regarding the treatment for exposures to pathogens was not very detailed. The Committee agreed to request a treatment plan for exposures.

Pending Conditions:

1. The investigator needs to provide a standard operating procedure (SOP) for *Salmonella typhimurium* and Enteropathogenic *E. coli* exposures. In the SOP, the following needs to be included: 1.) treatment for ingestion, eye splashes, mucosal exposures, and needle sticks (if applicable); 2.) to whom staff should report (PI, Occupational Medicine during regular hours and ER during off hours); 3.) susceptibility of pathogens to antibiotics; 4.) antibiotic treatment including antibiotic, dose, frequency, and duration; 5.) alternative antibiotics for individuals with allergies. The SOP will be reviewed by the University of Chicago Office of Occupational Medicine (UCOM) and the Infectious Disease section.

646 AD05/Rosner, Marsha/***Approved*** (7-0)
The investigator submitted an amendment requesting permission to use Mouse Stem Cell Virus (MSCV) to examine the roles of various signaling proteins. During review of the amendment, Committee members noted that the investigator routinely uses retroviruses, both ecotropic and amphotropic, to introduce genes of interest into cell lines. The Committee had no additional comments.

707 AD01/Schneewind, Olaf/***Approved w/Comment*** (9-0)
The investigator submitted an amendment requesting permission to add additional staff to the protocol and to perform studies in mice. The original protocol proposed to investigate the role of sortase genes in surface protein anchoring and pathogenesis of *Bacillus anthracis* Ames strain utilizing a guinea pig model. The Committee approved the addition of mice and staff but noted that the stipulations of the original protocol still apply.

Comment:

1. The investigator is advised that the amendment for the addition of staff and mice to this protocol is approved, however, the stipulations of the protocol listed below must be fully addressed prior to the initiation of any work.
    a. Outside consultant(s) acceptable to the Institutional Biosafety Committee (IBC), the Animal Resource Center (ARC), the Institutional Animal Care and Use Committee (IACUC), and the Offices of Safety and Environmental Affairs with expertise in dealing with this agent and animal species in a laboratory setting, human health concerns, and special BL3 facility concerns will be retained to help develop the appropriate standard operating procedures (SOPs), including SOPs relating to security, storage, handling, and disposal of this agent, and to review all aspects of the research program and facilities for use of this agent.
    b. Standard operating procedures (SOPs) must be approved by the IBC, ARC, IACUC, Occupational Medicine, Infection Control, the Medical Center Safety Office and the Offices of Safety and Environmental Affairs. To the extent that the approved SOPs conflict with procedures in the Protocol, the SOPs take precedence and will be followed.
    c. CDC application for use of this agent must be approved.

d. The investigator is not to begin work with the agent or animals under this protocol until all stipulations have been addressed to the satisfaction of the IBC and all other appropriate approvals have been obtained.

752 AD01/Schneewind, Olaf/***Approved w/Stipulation*** (9-0)
The original protocol proposed to investigate the type III secretion pathway of *Yersinia pestis* KIM 5. When the protocol was submitted and approved by the Committee, *Y. pestis* KIM 5 had been listed as a select agent by the Centers for Disease Control and required registration with the CDC. The investigator submitted an amendment to request permission to use *Y. pestis* KIM D27 that is the same strain as KIM 5 but from a different laboratory. Also, since the CDC has exempted KIM D27 from CDC registration, the investigator modified the protocol for additional review. The Committee noted that the investigator had developed a treatment plan for *Y. pestis* exposures and the protocol was approved without further comments from the Committee.
Stipulation:

1. The investigator is advised that Pgm$^-$ mutants of *Yersinia pestis* have been excluded by the Centers for Disease Control (CDC) as a select agent, therefore all stipulations requiring CDC registration and approval of *Yersinia pestis* KIM D27 have been removed. However, PCR and/or Southern blot analysis will be required to ensure that "Pgm$^-$" derivatives have undergone this deletion rather than a mutation in the hemin storage genes (hms), which also causes loss of Congo Red (CR) binding, which is the most common characteristic used to evaluate the pigmentation phenotype.

III. Old Business: None

IV. New Business:

A. Subcommittee Review Process – Deferred until the next regularly scheduled IBC meeting.

V. Updates: None

The University of Chicago

Institutional Biosafety Committee

5841 S. Maryland Avenue
AMB S-152 ♦ MC 1108
Chicago, IL 60637

Corrected Minutes of June 20, 2003
3:00 PM – [redacted]

In attendance:

Voting Members		Ex-Officio Members
Kenneth Thompson	James Mastrianni (left prior to vote)	Steve Beaudoin
Richard Hiipakka	Louis Philipson	
Malcolm Casadaban	Mary Ellen Sheridan	
Helena Mauceri	Craig Wardrip	
Rima McLoed	Gopal Thinakaran	

Guest	Staff
Claude Bake, Hospital Safety	Bill Pugh

Absent:

Voting Members	Ex-Officio Members	Staff
Walter Stadler	Manfred Ruddat	Pamela Postlethwait
George Daskal	Russ Herron	
Clara Gartner	Michael Holzhueter	
	Steve Seps	
	Markus Schaufele	
	David Pitrak	

I. Protocol Review:
The following protocols were reviewed at the meeting, with the disposition noted:

PR# Category/Investigator/***Disposition***

708Ad 03 Amendment/Schneewind, Olaf/***Pending-Conditions*** (7-1)
This amendment requests to add the subcutaneous infection of A/J mice with spore preparations of *Bacillus anthracis* strain Sterne. After an injection of 0.1ml of spore suspension in PBS (dilution of spores 1 x 10^4 or 1 x 10^6 cfu) in the flank, the mice will be observed in 8-hour intervals for acute lethal disease development

for a maximum of 7 days. All injected animals will eventually be euthanized, either after the development of acute lethal disease or after the 7 days. After sacrifice, the liver, spleen, lung and heart will be removed. All tissue samples will be placed in sterile plastic bags, weighed and homogenized. The bacilli will then be removed from the tissue suspension and counted by dilution and colony formation on BHI agar. The number of bacilli in the four organ systems will be recorded, along with the time to development of acute disease for each animal. While this protocol is currently listed as a BL2 protocol, the existing approved animal work with rabbits is only ABSL1, so this amendment changes the maximum ABSL from 1 to 2.

The committee members initially questioned the need to review and vote on this amendment at this point in time, since it was just submitted on June 11th. It was explained that during review of an NIH grant, one of the reviewers recommended that a few pilot studies be performed. The amendment covers the initial pilot study and the anticipated future studies.

The committee also discussed at great length the possibility that the Sterne strain of anthrax is more virulent for some individuals than previously indicated since this particular mouse strain exhibits such great susceptibility to this "non-virulent" agent. After a great deal of discussion, the committee determined that since this was the strain that was used during vaccinations, many people have been exposed to this agent during the vaccination process, and that the CDC considers this to be a BL2 agent, this is properly classified as BL2. One member did disagree with the majority and felt that since there is a mouse strain that is highly susceptible, there could be individuals with the same degree of susceptibility. This member had concerns about the pathogenicity if large amounts of this material was either ingested or inhaled. Also, this member questioned the possibility of lateral gene transfer that would result in the Sterne strain becoming more virulent. This member wanted the investigator to provide referenced data to address these issues. Since this member did not receive support for these viewpoints and thus, it was determined by the committee to not ask these questions of the investigator, this member voted against the motion to approve of this amendment with the conditions as noted below.

Some members asked about the possibility that the Sterne strain could be mixed up with the Ames strain. It was noted by other members of the committee that since the two different strains would not be used in the same facilities this was not a possibility. In its discussion of the virulence of the A/J mouse strain to the Sterne strain, the committee did question if this particular strain also shed the spores. Since the shedding of spores would impact the decontamination procedures of the caging materials and increase the likelihood of an exposure while handling the animals, the committee did decide to require clarification on that issue. Following extensive discussion of this amendment, the committee voted 7-1 to approve the amendment pending satisfactory answers to the following questions:

Conditions:

1. Since this amendment involves work in a new location, please indicate this on the amendment submission form. Also, please indicate (Supplement B, Section VI, question 2) that the animal work will be performed in the [redacted].
2. Since this work does involve recombinant DNA, please answer "Yes" to question 1, Section III and all pertinent questions that follow.
3. In some locations in the protocol, it is stated that waste material will be "heated" to 250°. Please indicate uniformly throughout the protocol that the materials will be autoclaved at that temperature.
4. In Section VII, question 9 of the IBC submission form, please indicate who will assume responsibility for the ongoing day-to-day oversight and supervision of the laboratory operations in your absence.
5. Please indicate where the anthrax bacilli spores will be prepared and the details of how the material will be transported. Please indicate how they will be packaged and the route of transport.
6. Please provide complete details on how and where the animals will be handled when the spores are being delivered. Details should include, but not be limited to, a description of the type of biosafety cabinet, how the animals will be handled and injected, the cleaning of the hood following the injections.
7. Please describe completely the necropsy procedure and where it will be performed.
8. The committee expressed concern that since the A/J mouse is susceptible to the Sterne strain that they could possibly shed the spores. How can you assure the committee that this is not a possibility? Is there any data or publications regarding A/J mice infected with the Sterne strain and shedding spores? If there is any suspicion that spores can be shed by this strain of mice, please indicate that the cage materials will be autoclaved in the same manner as the carcasses.

The University of Chicago

Institutional Biosafety Committee

5841 S. Maryland Avenue
AMB S-152 ♦ MC 1108
Chicago, IL 60637

Minutes of July 31, 2003
1:00 PM – [redacted]

In attendance:

Voting Members		Ex-Officio Members
Richard Hiipakka	Rima McLeod	Russ Herron
Malcolm Casadaban	Louis Philipson	David Pitrak
Clara Gartner	Walter Stadler	Markus Schaufele
James Mastrianni	Gopal Thinakaran	Steve Seps
Helena Mauceri	Craig Wardrip	

Staff

Pamela Postlethwait
Bill Pugh

Absent:

Voting Members	Ex-Officio Members	Staff
Kenneth Thompson	Steve Beaudoin	None
George Daskal	Michael Holzhueter	
Mary Ellen Sheridan	Manfred Ruddat	

I. Minutes:

A. The minutes of the June 6, 2003 meeting were unanimously approved (7-0) with no corrections. The minutes of the June 20, 2003 meeting were unanimously approved (7-0) with the addition of Dr. Casadaban to the attendance list.

II. Protocol Review:

The following protocols were reviewed at the meeting, with the disposition noted:

PR# Category/Investigator/***Disposition***

816 New/Sperling, Anne/***Approved w/Stipulations*** (7-0)
The research objective is to 1) identify surface proteins from Yersinia pestis KIM and CO92 strains that illicit a humoral immune response and 2) identify surface proteins from Yersinia pestis KIM and CO92 strains that illicit a cellular immune response. The work will be done in collaboration with Dr. Olaf Schneewind, who will provide all tissue and serum. Committee members noted that the agent being used in the protocol is on the Centers for Disease Control (CDC) list of Select Agents and would therefore

require registration with the CDC prior to this work commencing. Also, the investigator proposes to perform the experiments at the [redacted] or [redacted], however, neither facility exists at this time. The Committee determined that since the University of Chicago would have oversight, standard operating procedures (SOPs) for the facility would need to be developed and reviewed.

Stipulations:

1. CDC application for use of this agent must be approved.
2. Outside consultant(s) acceptable to the Institutional Biosafety Committee (IBC), the Animal Resource Center (ARC), the Institutional Animal Care and Use Committee (IACUC), and the Offices of Safety and Environmental Affairs with expertise in dealing with this agent and animal species in a laboratory setting, human health concerns, and special BL3 facility concerns may need to be retained to help develop the appropriate standard operating procedures (SOPs), including SOPs relating to security, storage, handling and disposal of this agent, and to review all aspects of the research program and facilities for use of this agent.
3. Standard operating procedures (SOPs) must be approved by the IBC, ARC, IACUC, Occupational Medicine, Infection Control, the Medical Center Safety Office and the Offices of Safety and Environmental Affairs. To the extent that the approved SOPs conflict with procedures in the Protocol, the SOPs take precedence and will be followed.
4. The investigator has indicated that either the [redacted] or the [redacted] will be the location of the proposed work/experiments described in this protocol. After the facility has been constructed and the location of the work is known, the investigator must submit to the IBC all information as is necessary to allow the IBC to make a proper assessment of the adequacy of the facilities for this protocol. This information must include the completed Biosafety Level 3 facility design and operational procedures, and such other information as the IBC may request. The investigator is advised that amendment to the protocol may be necessary to address these issues.
5. The investigator is not to begin work with the agent or animals under this protocol until all stipulations have been addressed to the satisfaction of the IBC and all other appropriate approvals have been obtained.

817 New/Schneewind, Olaf/***Approved w/Stipulations*** (8-0)

The research objective is to 1) identify *Yersinia pestis* surface proteins that serve as protective antigens; 2) quantify the humoral and cellular immune responses of experimental animals to purified *Y. pestis* surface protein; 3) investigate immune mechanisms against *Y. pestis* surface proteins; and 4) investigate the virulence mechanisms of *Y. pestis* surface proteins. Committee members noted that the agent being used in the protocol is on the Centers for Disease Control (CDC) list of Select Agents and would therefore require registration with the CDC prior to this work commencing. Also, the investigator proposes to perform the experiments at the [redacted] or [redacted], however, neither facility exists at this time. The Committee determined that since the University of Chicago would have oversight, standard operating procedures (SOPs) for the facility would need to be developed and reviewed. The Committee also discussed the routes of administration (intravenous and subcutaneous) the investigator would use to introduce the agent into animals.

Approved w/Stipulations:

1. CDC application for use of this agent must be approved.
2. Outside consultant(s) acceptable to the Institutional Biosafety Committee (IBC), the Animal Resource Center (ARC), the Institutional Animal Care and Use Committee (IACUC), and the Offices of Safety and Environmental Affairs with expertise in dealing with this agent and animal species in a laboratory setting, human health concerns, and special BL3 facility concerns may need to be retained to help develop the appropriate standard operating procedures (SOPs), including SOPs relating to security, storage, handling and disposal of this agent, and to review all aspects of the research program and facilities for use of this agent.
3. Standard operating procedures (SOPs) must be approved by the IBC, ARC, IACUC, Occupational Medicine, Infection Control, the Medical Center Safety Office and the Offices of Safety and

Environmental Affairs. To the extent that the approved SOPs conflict with procedures in the Protocol, the SOPs take precedence and will be followed.

4. The investigator has indicated that either the [redacted] or the [redacted] will be the location of the proposed work/experiments described in this protocol. After the facility has been constructed and the location of the work is known, the investigator must submit to the IBC all information as is necessary to allow the IBC to make a proper assessment of the adequacy of the facilities for this protocol. This information must include the completed Biosafety Level 3 facility design and operational procedures, and such other information as the IBC may request. The investigator is advised that amendment to the protocol may be necessary to address these issues.
5. The investigator is not to begin work with the agent or animals under this protocol until all stipulations have been addressed to the satisfaction of the IBC and all other appropriate approvals have been obtained.

826 New/Vezina, Paul/***Pending Condition*** (7-0)

Replication defective Herpes Simplex Virus (HSV) vectors will be used to study the role played by CaMKII in the nucleus accumbens and the ventral tegmental area in the expression of drug self-administration behaviors in a rat model of amphetamine and cocaine abuse. The investigator is proposing to microinject the replication defective HSV vector into the brain of rats in the [redacted] and after 24 hours is requesting permission to remove the animals from the [redacted] to his laboratory for behavioral testing. Current policy at the University requires work with HSV to be done at Biosafety Level 2 (BSL2)/Animal Biosafety Level 2 (ABSL2) and prohibits the removal of animals infected with HSV from the [redacted] since the animals are considered infectious for life. The investigator contends that the virus can be downgraded to BSL1/ABSL1 since the virus is neurotropic, replication defective, revertants to wild-type have never been documented and that other institutions permit the work to be done at ABSL1 24 hours after injection. During review of the protocol, the Committee noted that the investigator is currently doing the behavioral studies in his laboratory since the studies require the use of special chambers that cannot be accommodated in the central facilities. After thorough review of the information provided, Committee members determined there was not sufficient information regarding virus shedding by animals, detection of wild-type virus, infectious nature of agent after 24 hours, to determine if the downgrading of the Biosafety level was appropriate. The Committee agreed that downgrading of the protocol to ABSL1 could not be considered until the investigator provided additional information regarding use of the vector in animals and the specific criteria that other institutions have used to classify the agent as ABSL1 24 hours after injection. The investigator's responses will need to be reviewed by the full committee.

Pending Condition:

1. The Institutional Biosafety Committee requires laboratory and animal work with Herpes Simplex Virus (HSV) at the University to be conducted under Biosafety Level 2 (BSL2) containment. At this time, the Committee cannot consider downgrading the Animal Biosafety Level (ABSL) from ABSL2 to ABSL1 24 hours after injection of vector until additional information/references on animal studies utilizing the proposed agent is submitted. The information should address issues regarding virus shedding by the animals, detection of wild-type virus, development of herpes encephalitis after injection, etc and must be reviewed by the full committee. The investigator is encouraged to contact Dr. Rachael Neve and colleagues to assist in compilation of this information. Specific information from Harvard indicating the reasons for their downgrading is also requested.

828 New/Madara, James/***Pending Condition & Comment*** (8-0)

In order to better understand the nature and consequences of interactions between intestinal epithelial cells and polymorphonuclear leukocytes (neutrophils), epithelial cell responses to *Salmonella typhimurium* will be analyzed. During review of the protocol, the Committee noted that the investigator indicated that a biosafety cabinet will not be utilized for the experimental work, however the Biosafety Manual indicated biosafety cabinets are to be used whenever procedures have the potential for creating aerosols.

Pending Condition:

1. In Section VII, question 2, it is indicated that a biosafety cabinet will not be utilized for the experimental work, yet in the Biosafety Manual, it is indicated that a biosafety cabinet and other appropriate containment devices are to be used whenever laboratory procedures have a good potential for creating aerosols of infectious materials such as centrifuging, vigorous shaking or mixing, etc. What safety precautions will be taken during the initial culturing of the agent (during the vigorous shaking growth period)? In order to minimize the potential for aerosol or splash injury, should not the transfer of bacteria to tissue culture cells take place in the biosafety cabinet?

Comment:

1. Laboratory staff members should be aware of the following recommendations regarding treatment of Salmonella typhimurium and should be incorporated in the SOP:
   a. First aid and treatment of enterocolitis: It is reasonable to treat mild disease with hydration and anti-motility agents. The decision to treat anyone else with gastroenteritis depends on risk factors for serious disease or severe diarrhea. Treatment could include cipro for 3 – 5 days.
   b. Enteric fever and/or bacteremia should be treated for 10 – 14 days.
   c. Prolonged bacteremia will need 4 – 6 weeks of therapy. Four to six weeks should also be given to patients who continue to shed beyond the usual convalescent period, i.e. chronic carriers. Cipro would be the drug of choice.

646 AD06/Rosner, Marsha/***Pending Conditions*** (7-0)

The amendment is requesting permission to use the pLL3.7 LentiLox system, which is a lentiviral vector (HIV derivative), to induce RNA interference in dividing and non-dividing cells in order to observe how the absence of the protein of interest affects cell signaling and cell proliferation. Due to biosafety issues concerning the use of lentivirus, the investigator will be using a four-plasmid system. During review of the amendment, Committee members noted that the lentivirus would be pseudotyped with the VSV G-protein for use in transfecting cell culture as well as injection into mice to evaluate the effects of silencing genes of interest in vivo. Committee members expressed concern regarding the injection of virus into live animals since there was not sufficient information to thoroughly evaluate the use of the agent in animals. While Committee members agreed the appropriate precautions were being taken for the cell culture experiments, it was determined the investigator would need to provide additional information to address issues such as shedding, the infectious nature, detection of leaks in the uterine wall, etc.

Pending Conditions:

1. The Biosafety Manual needs to be updated to include specific information on lentivirus and precautions to take while handling the agent. Also, the signatures at the end of the Biosafety Manual need to be included.
2. On page 4 of the Supplemental Form B, it is indicated that the supernatant of the medium of infected cells will be tested to screen for recombination events that might result in replication competence. How often will this testing be performed – from every culture of infected cells? From a sampling of such cultures? Only once at initial use? Please explain the safety of this if the analysis is not from each culture.
3. Please provide additional information and/or references regarding the use of the lentivirus in a mouse model system to address issues regarding the shedding of the virus, infectious nature of the agent, leaks in the uterine wall, etc.
4. Please be advised that the associated Animal Care and Use Protocol (ACUP [redacted]) will need to be amended and approved by the Institutional Animal Care and Use Committee for the use of lentivirus.

III. Old Business: None

IV. New Business:

A. Subcommittee Review Process. For Risk Group 2/Biosafety Level 2 (RG2/BL2) protocols, the review process consists of an initial review by a committee member followed by full committee review. A veterinarian, plant specialist, or clinician will also perform an initial review if animals, plants or clinical trials are involved. Two members of the committee reviews RG1/BL1 protocol unless the protocol involves animals, plants or clinical trials then a veterinarian, plant specialist, or

clinician performs an additional review. Subcommittee protocols are reviewed and approved without the entire committee seeing or being aware of these protocols. Mr. Pugh recommended a review process be implemented whereby Committee members are apprised of protocols slated for subcommittee review, per criteria approved by IBC, by email for which members would then indicate whether or not they approve of the protocols for subcommittee review. For each protocol, the protocol number, principal investigator, biohazardous agent, and a brief summary of the research would be provided. Protocols would be made available to any member requesting to review the protocol and any member can send a protocol to full committee review. Committee members requesting Full Committee review would need to provide their reasons for that request. After a quorum is obtained allowing subcommittee review, the protocol is sent to two members for review. After the satisfactory resolution of all issues, the protocol is then sent on to the chair for review and final approval. After thorough discussion of the issue, Committee members agreed to implement the new subcommittee review process.

V. **Updates:** None

The University of Chicago

Institutional Biosafety Committee

5841 S. Maryland Avenue
AMB S-152 ♦ MC 1108
Chicago, IL 60637

Minutes of October 3, 2003
1:00 PM – C-140

In attendance:

Voting Members

Kenneth Thompson
Richard Hiipakka
Malcolm Casadaban
George Daskal
James Mastrianni
Helena Mauceri
Louis Philipson
Mary Ellen Sheridan
Gopal Thinakaran
Craig Wardrip

Ex-Officio Members

Russ Herron
Michael Holzhueter
David Pitrak
Manfred Ruddat
Markus Schaufele
Steve Seps

Staff

Pamela Postlethwait

Absent:

Voting Members	Ex-Officio Members	Staff
Clara Gartner	Steve Beaudoin	Bill Pugh
Rima McLeod		
Walter Stadler		

I. Minutes:

A. The minutes of the July 31, 2003 meeting were unanimously approved (7-0) with no corrections.

II. Protocol Review:

The following protocols were reviewed at the meeting, with the disposition noted:

PR# Category/Investigator/***Disposition***

776 Revised Deferral/Wang, Chyung-Ru/***Pending Conditions & Stipulation*** (9-0)
The investigator proposes to infect MHC class Ib deficient mice and MHC class Ib transgenic mice with *Mycobacterium tuberculosis* to study the impact of MHC class Ib-restricted response in acquired resistance to this pathogen. In addition, class Ib-restricted T cell lines will be derived from infected mice to study the lipid antigen requirement for presentation by class Ib molecules. During review at the June 6, 2003 meeting, the Committee noted that Biosafety Level 3 (BSL3) practices and containment were necessary for work with *M. tuberculosis* and determined that the protocol could not be approved until suitable facilities were available. The investigator has since submitted a revised protocol for review. The

investigator has indicated that the culturing and manipulation of the *M. tuberculosis* will take place in a Biosafety Level 3 (BSL 3) facility located in [redacted] and the animal work will take place in [redacted]. The Committee thoroughly discussed the options available to the investigator with regard to the animal research. Committee members noted that the culturing and manipulation of the organism would require BSL3 facilities, however, the animal work, if done in mice or guinea pigs, could be conducted in ABSL2 facilities. Dr. Seps and Dr. Wardrip informed the Committee that the [redacted] could provide a dedicated, isolated room for the investigator to perform the animal research under ABSL2 conditions with ABSL3 practices. The Committee agreed to require the investigator to culture the organism in the BSL3 facility in [redacted], prepare frozen aliquots in bulk, and transport these aliquots to the Biosafety Facility for storage and subsequent animal research. Committee members also discussed the transport of the agent and agreed that laboratory personnel should receive training on how to properly package and transport the agent. The occupational health issues related to working with this agent was discussed and the Committee agreed to defer to the recommendations of the University of Chicago Occupational Medicine (UCOM). The Committee also concurred with Mr. Schaufele's recommendation that all staff members working with the agent be fit tested for the N95 respirator. During review of the experimental procedures, the Committee noted that while the procedures for culturing the organism and injection of the animals were described, the investigator failed to describe what experiments will be performed with cells and tissues harvested from these animals.

Pending Conditions:

1. The corresponding Animal Care and Use protocol must be approved prior to the initiation of this work.
2. In Section IV, Experimental Plan, please clarify and describe the experiments to be performed on tissue harvested from animals infected with *Mycobacterium tuberculosis*. In the description, please specify where the experiments are to be conducted, the route of transport (if applicable), and manipulations to be performed.
3. All staff participants must sign the current version of the protocol to ensure each participant is aware of and familiar with all experimental procedures to be conducted.
4. Prior to the initiation of studies involving *M. tuberculosis*, the principal investigator must confirm in writing all staff members listed on this protocol will complete the following:
    a. A Laboratory Safety Training Course offered by the UC Medical Center Safety Office for the proper packaging and transport of this agent. Please contact the UC Medical Center Safety Office at 5-SAFE to register for the course.
    b. Fit testing for the N95 respirator. This service can be provided by the University of Chicago Occupational Medicine Office (2-6757).
    c. The principal investigator is responsible for ensuring that each staff member listed on the protocol participates in a surveillence program (every 6 months) for *M. tuberculosis* as recommended by the University of Chicago Occupational Medicine (UCOM). For information about M. tuberculosis surveillence, please contact UCOM at 2-6757. Also, per the recommendations of UCOM, please revise Section VII, question 5, to indicate that lab personnel will be required to take skin-testing with PPD and not 'encouraged' and Section VII, question 6, to indicate that UCOM will document compliance.

Stipulation:

1. The *Mycobacterium tuberculosis* organism is to be cultured in the BSL3 laboratory located [redacted] and frozen aliquots prepared in bulk. All of the frozen aliquots are to be transported and stored in the Biosafety Facility within [redacted] in a freezer provided by the investigator for subsequent injection into animals. Please be advised that frozen aliquots of the agent are not permitted to be transported to or stored in the investigator's laboratory located in [redacted]. Please revise the relevant sections of the protocol submission form and the Form B submitted to the IACUC (dated 10/1/2003) to incorporate this information.

827 New/Aifantis, Iannis/***Approved w/Stipulation*** (10-0)
The laboratory seeks to identify how the pre-TCR, a receptor expressed on the surface of immature thymocytes, is able to control the survival, proliferation and differentiation of these cells. The laboratory

will study the role of different domains of the receptor in the induction of proliferation, cell survival and the up-regulation of the expression of anti-apoptotic proteins of the BCL-2 family. The mutated proteins will be expressed using a Moloney Mouse Leukemia Virus (MuMLV) system or transgenic mice. Upon review of the protocol, the Committee had no additional comments. Mr. Schaufele informed the Committee he had inspected the laboratory and had identified a problem with the flooring in the main laboratory. The Committee agreed with his recommendation that the viral work be confined to the culture tissue room.

Stipulation:

1. The UC Medical Center Safety Office has identified a problem with the flooring in the main laboratory [redacted] therefore all culturing and manipulation of the Moloney Murine Leukemia Virus is restricted to the tissue culture room [redacted]

830 New/Schneewind, Olaf/***Pending Conditions*** (10-0)

The research objective is to characterize the genes and signaling pathways that activate type III secretion in *Yersinia pseudotuberculosis*. During discussion of the protocol, the Committee noted that the investigator did not describe the experimental procedures involving animals even though mice are to be utilized. The Committee also discussed the investigator's use of 70% ethanol for decontamination of spills, surfaces, and equipment.

Pending Conditions:

1. In Section IV, please provide a description of the animal procedures to be performed.
2. In Section V, Staff Group, Katie Overheim needs to sign.

831 New/Franzoso, Guido/***Approved w/Comment*** (9-0)

In order to study the mechanisms by which NF-kappaB controls apoptosis, its inhibitor, IkappaB-alpha will be introduced into the cytoplasm of cells using the TAT protein. The Committee discussed the protocol and had no questions for the investigator, although it was noted the biosafety cabinet would require recertification.

Comment:

1. Please be advised that Biosafety Cabinets must be certified annually, therefore your Biosafety Cabinet will need to be re-certified October 28, 2003.

832 New/Franzoso, Guido/***Approved w/Comment*** (9-0)

Using retrovirally transduced cells, the objectives are 1) study the impact of Gadd45B on Fas-induced pathways; 2) determine the mechanisms by which Gadd45B inhibits JNK signaling; and 3) address the roles of Gadd45B and the targeting of the JNK pathway in NF-kB-dependent tumorigenesis. Following review of the protocol, the Committee had no additional questions for the investigator although it was noted that the biosafety cabinet would require recertification.

Comment:

1. Please be advised that Biosafety Cabinets must be certified annually, therefore your Biosafety Cabinet will need to be re-certified October 28, 2003.

833 New/Abraham, Clara/***Approved w/Stipulations*** (9-0)

As a means to understanding the role of CD18 in T cell-mediated responses to infection, the laboratory will study the ability of CD18-deficient T cells to mediate effective responses to *Listeria monocytogenes* infection. During review of the protocol, the Committee discussed the transport of tissue infected with the agent and post-exposure treatment of investigative staff.

Stipulations:

1. The transport of Listeria monocytogenes and any material infected with this agent must be done according to Department of Transportation (DOT) regulations. Therefore, all staff members listed on the protocol must attend the Laboratory Safety Training Course offered by the UC Medical Center Safety Office prior to transport of this agent. Please contact the UC Medical Center Safety Office at 5-SAFE to register for the course.
2. In the event of an exposure to the agent, the staff member must report to the University of Chicago Occupational Medicine office(L-156) for treatment.

III. **Old Business:** None

IV. **New Business:**

A. **Time Frame for Investigators to Respond to IBC Requests.** Currently, the IBC does not place a limitation on the time in which an investigator has to respond to administrative review letters, preliminary review letters, pending condition letters, or requests for annual surveys. As a result, annual surveys and responses to letters are not being submitted on a timely basis. After discussion, the Committee agreed (9-0) an investigator would be given an initial 30 days to respond to a request. If a response were not received within this time period, a reminder notice would be sent informing the investigator that if a response were not received within the next 30 days, then the protocol or amendment would be withdrawn or terminated. The Committee requested a letter be drafted and forwarded to members for review.

B. **University of Chicago Proposal to NIAID for Regional Biocontainment Facility.** Dr. Sheridan informed Committee members that the University of Chicago's proposal for a regional biocontainment facility to be located at Argonne National Laboratory for the study of bioterrorist agents had been funded.

V. **Updates:** None

The University of Chicago

Institutional Biosafety Committee

5841 S. Maryland Avenue
AMB S-152 ♦ MC 1108
Chicago, IL 60637

Minutes of December 10, 2003
10:00 AM in [redacted]

In attendance:

Voting Members

Kenneth Thompson
Richard Hiipakka
Malcolm Casadaban
George Daskal
Clara Gartner (Arrived late)
Helena Mauceri
Louis Philipson
Craig Wardrip

Ex-Officio Members

Russ Herron
David Pitrak
Markus Schaufele

Staff

Pamela Postlethwait
Bill Pugh

Absent:

Voting Members	Ex-Officio Members	Staff
James Mastrianni	Steve Beaudoin	None
Rima McLeod	Michael Holzhueter	
Mary Ellen Sheridan	Manfred Ruddat	
Walter Stadler	Steve Seps	
Gopal Thinakaran		

I. Minutes:

A. The minutes of the October 3, 2003 meeting were unanimously approved (7-0) with no corrections.

II. Protocol Review:

The following protocols were reviewed at the meeting, with the disposition noted:

PR# Category/Investigator/***Disposition***

776 Revised Deferral/Wang, Chyung-Ru/***Approved w/ Stipulation*** (8-0)
The investigator proposes to infect MHC class Ib deficient mice and MHC class Ib transgenic mice with *Mycobacterium tuberculosis* to study the impact of MHC class Ib-restricted response in acquired resistance to this pathogen. In addition, class Ib-restricted T cell lines will be derived from infected mice to study the lipid antigen requirement for presentation by class Ib molecules. During review at the June 6, 2003 meeting, the Committee noted that Biosafety Level 3 (BSL3) practices and containment were necessary for work with *M. tuberculosis* and determined that the protocol could not be approved until

suitable facilities were available. Subsequently, the investigator submitted a revised protocol for review at the October 3, 2003 meeting. During review of the protocol at that meeting, the Committee noted the investigator needed to clarify experiments performed on harvested tissue, ensure research staff is familiar with the experimental procedures to be conducted, must confirm in writing that staff members have completed training in packaging and transport, been fit tested for respirators, and have enrolled in a surveillance program for M. tuberculosis. The investigator's response to the pending condition letter was brought back to the full committee for review. The investigator proposes to conduct T cell cytotoxicity assays at various time points on isolated lymphocytes. Committee members determined the post-mortem processing of tissues would need to be conducted in the [redacted]. In addition, the procedure will result in the production of mixed waste. The Committee discussed disposal of the mixed waste and determined that the *Mycobacterium tuberculosis* would need to be decontaminated with either 50% bleach or autoclaving however, given the waste is radioactive, Radiation Safety would need to make the final determination regarding disposal. Committee members also discussed the cleaning of the hemacytometers.

Stipulations:

1. The *Mycobacterium tuberculosis* organism is to be cultured in the BSL3 laboratory located [redacted] and frozen aliquots prepared in bulk. All of the frozen aliquots are to be transported and stored in the [redacted] in a freezer to be provided by the investigator for subsequent injection into animals. Please be advised that frozen aliquots of the agent are not permitted to be transported to or stored in the investigator's laboratory located [redacted].
2. Prior to initiation of these studies, the investigator must confirm in writing that all participants have completed the training regarding packaging and transport of the agent, have undergone fit testinf for the N95 respirator, and are participating in a surveillience program (every 6 months) for *M. tuberculosis*.
3. The post-mortem processing of tissues must be confined to the animal room within the [redacted] with equipment appropriately being used in the biosafety cabinet.
4. Disposal procedures for radioactive waste containing *Mycobacterium tuberculosis* must be determined by Radiation Safety however, *M. tuberculosis* must be inactivated with either 50% bleach or by autoclaving. Please consult with Radiation Safety regarding disposal of mixed waste.
5. Hemacytometers and additional materials required for batch processing of samples must be decontaminated between samples as follows: soaked in 50% bleach for 10 -15 minutes, washed with deionized water and rinsed with isopropyl alcohol.

826 Revised Deferral/Vezina, Paul/***Approved w/ Stipulation and Comment*** (8-0)
Replication defective Herpes Simplex Virus (HSV) vectors will be used to study the role played by CaMKII in the nucleus accumbens and the ventral tegmental area in the expression of drug self-administration behaviors in a rat model of amphetamine and cocaine abuse. The investigator is proposing to microinject the replication defective HSV vector into the brain of rats in the [redacted] and after 24 hours is requesting permission to remove the animals from the [redacted] to his laboratory for behavioral testing. At the July 31, 2003 meeting, Committee members determined there was not sufficient information regarding virus shedding by animals, detection of wild-type virus, or the infectious nature of agent after 24 hours, to determine if the downgrading of the Biosafety level was appropriate. The Committee agreed that downgrading of the protocol to ABSL1 could not be considered until the investigator provided additional information regarding use of the vector in animals and the specific criteria that other institutions have used to classify the agent as ABSL1 24 hours after injection. The investigator has submitted to the Committee for review additional documentation from individuals who routinely use this viral vector in their studies. Committee members noted that these individuals, while not directly testing for shedding, have not observed any evidence of encephalitis or other CNS dysfunction. In addition, Dr. Rachel Neve, who constructs the virus, has never detected replicating virus. Based on the information provided, the Committee determined that the animals could be removed 24 hours after injection, however prior to use, the viral vector would need to be tested for the presence of wild-type virus.

Stipulation:

1. Prior to injection into animals, all batches of the replication deficient Herpes Simplex Virus (HSV) must be tested for the presence of wild-type virus.

Comment:

1. The Committee has approved the investigator's request to remove animals from the [redacted] for behavioral testing 24 hours after injection of the replication deficient Herpes Simplex Virus. The Committee would like to thank the investigator for his assistance in providing the additional information necessary to make this decision.

835 Renewal/Conzen, Suzanne/***Pending Conditions*** (8-0)

The research laboratory studies the functional regions of SGK-1, a serine/threonine kinase, which contributes to cell cycle progression, apoptosis, and transformation in mammary epithelial cells. The investigator proposes to use replication-defective retrovirus expressing various recombinant DNAs to infect human mammary epithelial cells or rodent cells for analysis of cell cycle, apoptosis and signaling pathways. During review of the protocol, Committee members noted some of the recombinant DNAs were proto-oncogenes and expressed concerned regarding the volume of retrovirus to be produced.

Pending Conditions:

1. In Section III, question 3b, please indicate 'Yes' since proto-oncogenes are being studied. Accordingly, please indicate 'Yes' in question 3c and describe the potential hazards of the proto-oncogenes.
2. In Section VII, question 9, instructions are provided for the procedures to take in case of a spill of less than or greater than one liter. Given the nature of the agent, the Committee has concerns regarding the volume of retrovirus that will be generated at any given time. In order to assure the Committee that the retrovirus and retroviral waste will be limited to a volume that can be easily managed and cleaned in the event of a spill, please indicate the maximum volume of retrovirus that will be generated.

836 New/Steiner, Donald/***Approved*** (8-0)

The research objective is to express hairpin siRNA to abrogate expression of prohormone convertase gene(s) in cell lines of mammalian origin. Replication deficient adenovirus expressing complimentary oligos will be used to infect mammalian cells in order to analyze the biological effects of abrogation of prohormone convertase gene expression on proneuropeptide/prohormone processing. Upon review, the Committee had no additional questions or comments and approved the protocol.

534 AD02/Mastrianni, James/***Approved w/Stipulation*** (8-0)

The laboratory studies neurodegenerative diseases such as prion disease, Alzheimer disease and amyotrophic lateral sclerosis. The protocol is designed to test the transmissible nature of human prions to mice that carry normal prion protein transgenes. In addition, mice that carry one or more Alzheimer's disease-related transgenes are inoculated with prions or brain from older mice from these same lines in order to determine if Alzheimer's pathology has a transmissible nature. Since the mice receiving brain from older mice with Alzheimer's pathology are not exposed to infectious prions, the investigator has submitted an amendment requesting permission to transfer these mice from the [redacted] to a regular barrier facility room. During discussion of the amendment, Committee members noted that the same stereotaxic equipment used to inject prions was also used to inject mice in the Alzheimer's study. Members expressed concern that the equipment might be contaminated with prions even if the equipment is decontaminated. Therefore, the Committee unanimously agreed that any animal that received an injection with this equipment could not be removed from the [redacted].

Stipulation:

1. The Committee has concerns about the removal of animals from the [redacted] that utilized the same stereotaxic instruments when prions were delivered, even if the equipment is decontaminated. Accordingly, the Committee has determined that any animal currently housed within the [redacted] that has received injections from the same equipment used to inject prions into animals must remain within the [redacted]. Animals that have not received injections may be removed from the [redacted] for housing in another facility.

551 AD01/Di Rienzo, Anna/***Approved w/ Comment*** (8-0)
The research laboratory extracts genomic DNA from tissue or lymphoblastoid cell lines for sequencing and studies of sequence variation. The investigator submitted an amendment requesting permission to culture non-human primate lymphoblastoid and fibroblast cell lines for extraction of genomic DNA and RNA. The majority of the non-human primate cell lines will be acquired from commercial sources and are screened for common primate viruses such as herpes and hepatitis. However, some of the cell lines have not been screened for which Committee members noted that these cell lines would need to be treated as if they were positive for these agents and discussed the appropriate handling and disposal procedures. The Committee agreed these cell lines would need to be cultured and waste disposed of according to Biosafety Level 2 practices.

Comment:

1. Please be advised that the handling and disposal of cell culture materials must be done according to Biosafety Level 2 practices. For information regarding Biosafety Level 2 practices, please consult the Biosafety in Microbiological and Biomedical Laboratories handbook available at http://www.cdc.gov/od/ohs/biosfty/bmbl4/bmbl4toc.htm.

634 AD05/Peter, Marcus/***Approved w/Comment*** (8-0)
The laboratory utilizes replication deficient adenoviruses expressing various signaling proteins to infect cultured cells to analyze the influence of the signaling proteins on cell growth, cell death and cell cycle progression. The investigator has submitted an amendment requesting permission to use replication deficient adenovirus expressing Fas receptor and Fas truncation mutants to infect mouse tumor cell lines. These tumor cell lines will be subsequently injected into the flanks of mice and the effect on tumor growth assessed. Committee members discussed the appropriate containment for these experiments. Following discussion, the Committee determined that while the adenoviral experiments require Biosafety Level 2 (BSL2) practices, the injection of mice with tumors cell previously infected with adenovirus can be conducted at Animal Biosafety Level 1 (ABSL1) with BSL2 practices.

Comment:

1. While experiments with replication deficient adenovirus must be conducted using Biosafety Level 2 practices, the Committee has determined that the injection of mice with cells previously infected with replication deficient adenoviral constructs can be conducted under Biosafety Level 1 with Biosafety Level 2 practices.

734 AD01/Singh, Deepti/***Approved*** (8-0)
The primary objective of this clinical study is to determine if a vaccine constructed to immunize against carcinoembryonic antigen (CEA), a tumor antigen found on most colon cancer cells, is safe, has any side effects and can induce an immune response to CEA. The investigator has submitted an amendment to transfer the protocol to Dr. Deepti Singh. Upon review, the Committee had no questions or comments and approved the amendment.

753 AD01/Stadler, Walter/***Approved*** (8-0)
The primary objective of this clinical trial is to assess the biological activity of TG4010 (Modified Virus of Ankara expressing mucin and interleukin-2) by immunologic testing on two different vaccination schedules; to assess the safety of TG4010 administered subcutaneously in this patient population and to provide a preliminary assessment of the relative efficacy of the two different vaccination schedules proposed. The investigator submitted an amendment to clarify changes (mainly editorial) to the clinical protocol. Previously, the US National Institutes of Health classified the MVA as Biosafety Level 1. The MVA has now been classified as Biosafety Level 2. Upon review of the amendment, the Committee had no questions or comments and approved the amendment.

III. Old Business: None

IV. New Business:

A. **Revised Serum Banking/Testing Policy.** The IBC currently has a serum testing/banking policy, however the policy did not address issues such as collection, storage, and handling of samples. A revised policy that addressed these issues was submitted to Committee members for review and discussion. In the revised policy, the University of Chicago Occupational Medicine (UCOM) office would provide oversight for the collection, testing and banking of samples rather than an investigator providing oversight. During review of the policy, it was recommended that the Animal Resource Center Director be consulted in regards to the necessity of testing and banking of sera from animal care personnel. Committee members also recommended that the policy address the issue of historical samples and the fate of these samples if the investigator leaves the University, but noted that these samples should remain under the control of UCOM. The Committee voted to approve the policy with the recommended modification contingent upon the approval of UCOM.

V. **Updates:** None

The University of Chicago

Institutional Biosafety Committee

5841 S. Maryland Avenue
AMB S-152 ♦ MC 1108
Chicago, IL 60637

Minutes of February 6, 2004
1:00 PM in [redacted]

In attendance:

Voting Members		Ex-Officio Members
Kenneth Thompson	Clara Gartner	Steve Beaudoin
Richard Hiipakka	Helena Mauceri	Russ Herron
Malcolm Casadaban	Gopal Thinakaran	Michael Holzhueter
George Daskal	Craig Wardrip	David Pitrak
		Markus Schaufele
		Steve Seps

Guest	Staff
Olaf Schneewind	Pamela Postlethwait
	Bill Pugh

Absent:

Voting Members	Ex-Officio Members	Staff
James Mastrianni	Manfred Ruddat	None
Rima McLeod		
Louis Philipson		
Mary Ellen Sheridan		
Walter Stadler		

I. Minutes:

A. The minutes of the December 10, 2003 meeting were unanimously approved (7-0) with no corrections.

II. Protocol Review:
The following protocols were reviewed at the meeting, with the disposition noted:

PR# Category/Investigator/*Disposition*

840 Renewal/Li, Yan Chun/*Pending Conditions* & Comment (8-0)
The research laboratory studies the role of the Vitamin D endocrine system using an adenoviral system to deliver recombinant DNA into mammalian cells for functional analysis studies. During review of the protocol, Committee members noted the investigator needed to specify the genes or types of genes to be studied. In addition, the Committee agreed the investigator needed to indicate how viral preparations would be monitored for replication competency, the appropriate personal protective equipment to use and the appropriate method of decontamination. Since the investigator had indicated future work would include the use of animals, the Committee recommended reminding the investigator that the use of live animals would require amending the protocol to incorporate these procedures prior to initiation of the studies.

Pending Conditions:

1. In Section III, questions 2 & 3, rather than indicating a variety of complementary and genomic DNAs, please specify the genes to be studied in the protocol.
2. In Section III, question 4c, please indicate how you will be monitoring your viral preparations for replication competency.
3. In Section VIII, question 8, please also include the use of safety glasses and mask.
4. In Section VIII, questions 9 & 12, please indicate that a 1:5 bleach solution for 15 minutes will be used for decontamination.
5. In the Biosafety Manual, in response to "What do I do if I am exposed?", please indicate that in addition to reporting the exposure to Dr. Li, the individual will report to the University of Chicago Occupational Medicine (UCOM, L-156, 2-6757) during working hours and the Emergency Room (Mitchell Hospital, 2-6250).

Comment:

1. Please be advised that prior to the initiation of studies with this agent in live animals, the protocol will need to be amended to incorporate all procedures performed in live animals.

708 AD05/Schneewind, Olaf/*Approved* (8-0)
The research laboratory studies the genetic factors required for the secretion of protective antigen (PA), lethal factor (LF), and edema factor (EF) using the Bacillus anthracis Sterne strain. With this amendment, the investigator is requesting permission to expand the experiments to include development of a skin contamination model in hairless mice for Bacillus spores and the testing of various formulations of nisin and other cofactors for the capacity to decontaminate the spore-contaminated skin in a gentle fashion. Upon review of the amendment, the Committee members agreed all issues had been addressed satisfactorily and had no additional comments or questions.

III. Old Business: None

IV. New Business:

A. **Request from the Sunshine Project.** Mr. Pugh informed Committee members that the Sunshine Project had made a request for copies of the minutes from the last two IBC meetings. The Committee was reminded that NIH Guidelines state that IBC meeting minutes shall be made available to the public upon request. Mr. Pugh and Mr. Herron are coordinating efforts to determine the appropriate response.

B. Responses to Stipulations for IBC Protocols 707, 816 & 817. Over the past two years, the IBC has reviewed and approved a small number of protocols (IBC 707, 816, and 817) involving Biosafety Level 3 / Animal Biosafety Level 3 agents that are also defined as select agents. These protocols were approved with a standard set of stipulations composed of the following: a) retention of an outside consultant to review all aspects of the program and to help in the development of standard operating procedures; b) development of standard operating procedures; c) Centers for Disease Control (CDC) approval for use of the agent; and d) the investigator is not to begin work with the agent or animals until all stipulations have been addressed to the satisfaction of the IBC and all other appropriate approvals have been obtained. Progress on the first stipulation has already been made with the hiring of a consulting group, [redacted] and [redacted]. With this latest submission to be reviewed at this current meeting, the principal investigator is attempting to address the remaining stipulations. Committee members were also informed that while the investigator has received an approved registration from the CDC for the use of *Bacillus anthracis* Ames strain, CDC approval for the use of *Yersinia pestis* strains was still pending. As the Responsible Facility Official (RFO), Mr. Steve Beaudoin presented to the Committee the responses to the stipulations. Dr. Olaf Schneewind, the principal investigator, was present to address questions from Committee members, however, he was asked to recuse himself from the meeting during discussion and a vote. During discussion of the materials provided, Committee members noted that several of the standard operating procedures were not complete and some remained yet to be written. In addition, the Committee was made aware of the guideline stated in the Biosafety in Microbiological and Biomedical Laboratories Handbook (BMBL) that the Biosafety Level 3 facility design and operational procedures must be documented. Recognizing that the facility operations must be tested, more SOPs need to be written, all SOPs need to be tested, staff need to be trained and various test scenarios need to be developed and run successfully (i.e., emergency response, cold testing of use of facility, etc.) and that finalization of certain standard operating procedures are dependent upon this, several Committee members recommended that a plan really needs to be developed to adequately describe how this all is to be accomplished. While this written plan, now known as a Commissioning Plan, would need to be approved by the IBC, progress on the commissioning process could still continue. It was recommended that individuals from the Select Agent Working Group and the IBC could participate in the development of this plan. The plan would need to encompass review of the facility, equipment, specified operating procedures, training of personnel and any other aspects related to the safe operation of this facility. Upon completion of the commissioning process, the Committee must then be presented with a report accompanied by all supporting documentation in their final version for review and approval. Following discussion of the above mentioned recommendations, Committee members unanimously agreed (8-0) to this course of action with the addition of the following Stipulation to IBC protocol 707:

> As stated in the 4th Edition of the Biosafety in Microbiological and Biomedical Laboratories Handbook, "The completed Biosafety Level 3 Facility design and operational procedures must be documented. The facility must be tested for verification that the design and operational parameters have been met prior to operation". This is

commonly called 'commissioning' of the facility. Therefore, the IBC requests a plan for the commissioning of the BSL 3 facility be submitted for review and approval. Representatives from the Select Agent Working Group and the IBC will participate in the development of this plan. The plan should encompass review of the facility, equipment, specified operating procedures, training of personnel and any other aspects related to the safe operation of this facility. Upon completion of the commissioning process, the IBC must be presented with a report accompanied by all supporting documentation in their final version.

V. **Updates:** None

The University of Chicago

Institutional Biosafety Committee

5841 S. Maryland Avenue
AMB S-152 ♦ MC 1108
Chicago, IL 60637

Minutes of April 2, 2004 Meeting
1:00 PM in [redacted]

In attendance:

Voting Members

Kenneth Thompson
Richard Hiipakka
Malcolm Casadaban
George Daskal
Clara Gartner
Helena Mauceri
Louis Philipson
Mary Ellen Sheridan
Walter Stadler
Gopal Thinakaran

Ex-Officio Members

David Pitrak
Markus Schaufele
Steve Seps

Staff

Pamela Postlethwait
Bill Pugh

Absent:

Voting Members

James Mastrianni
Rima McLeod

Ex-Officio Members

Steve Beaudoin
Russ Herron
Michael Holzhueter
Manfred Ruddat

Staff

None

Craig Wardrip

I. Minutes:

A. The minutes of the February 6, 2004 meeting were unanimously approved (8-0) with no corrections.

II. Protocol Review:
The following protocols were reviewed at the meeting, with the disposition noted:

PR# Category/Investigator/*Disposition*

838 New/Gajewski, Thomas/*Approved* (10-0)
The study objective is to research a new investigational drug, a fowlpox virus encoding three co-stimulatory molecules, to determine efficacy and safety. The virus will be injected intra-tumorally into accessible lesions in patients with metastatic melanoma to show that the presence of co-stimulatory molecules on the surface of melanoma tumors can be increased, to determine if this change results in an enhanced immune response, and to determine if this treatment results in tumor regression, either locally or systemically. During discussion of the protocol, Committee members noted that the agent being used is a recombinant fowlpox virus that, while capable of infecting mammalian cells, will only replicate in avian cells and as such, the protocol is classified as a Risk Group 1/Biosafety Level 1 protocol. The Committee agreed the investigator had sufficiently addressed all aspects of Appendix M of the NIH Guidelines and voted (10-0) to approve the protocol.

842 New/Lesniak, Maciej/*Rejected* (10-0)
The research study involves developing new techniques to bypass the blood-brain barrier in order to treat malignant brain tumors. The investigator has developed a retargeted, replication competent adenoviral vector and proposes to assess cell and tissue type specificity of the virus, virus spread in tumor and normal tissue, impact of the virus on normal brain acutely and in the long term and efficacy of the retargeted virus to deliver gene therapy to brain tumors using a mouse model. During review of the protocol, Committee members noted the adenoviral vector to be used would be replication competent and had been engineered to have an altered tropism for alpha v beta3 and alpha v beta5 integrins. Committee members discussed at length and in great detail the hazards associated with using a replication competent adenovirus containing recombinant DNA to the investigative staff and by extension, the general population. Since the investigator wishes to assess specificity and efficacy of the virus, the Committee questioned the need to use a replication competent virus when the same objectives could be more safely achieved using a replication deficient or conditionally-replicative virus. Several Committee members also questioned whether the proposed study as written could be safely conducted under Biosafety Level 2 conditions. Based on the reasons indicated above and the absence of scientific justification for using a replication competent virus, the Committee unanimously agreed (10-0) to reject the protocol as written.
Reasons for Rejection:

1. The Committee has concerns regarding the use of a replication-competent adenovirus engineered to express a recombinant DNA and the probability of dissemination of the agent within and outside of the laboratory under BL2 conditions. While it is recognized that the virus has an altered tropism, the virus is still capable of infecting and replicating in a variety of cell types. In the absence of scientific justification for the use of a replication competent adenovirus expressing a recombinant DNA under BL2 conditions, the Committee has rejected this protocol as written. Please note that any further consideration will require the submission of a new protocol and further information regarding the safe use of a replication competent adenovirus in patients or lab animals. However the Committee strongly recommends the investigator consider the use of a replication defective or conditionally-replicative adenovirus.

844 Renewal/Olopade, Funmi/*Pending Conditions* (10-0)
The research involves the use of human blood, tumor samples and cell lines (commercially available lines and Epstein-Barr Virus transformed lymphoblastoid lines) to study the genetic and epigenetic changes that contribute to breast cancer and leukemia. During review of the protocol, Committee members discussed the use of the Epstein-Barr Virus to infect B-cells and disposal of the cell culture waste. The investigator proposes to discard all cell culture waste into the biohazard waste drums for pickup by

Environmental Services. Several Committee members recommended the solid viral waste should be inactivated by autoclaving and liquid waste be inactivated by bleach prior to disposal in the biohazard bins. The Committee discussed at length whether steps should be taken to inactivate infectious waste prior to disposal in the biohazardous bins. Following the discussion, Committee members determined (10-0) the investigator needed to inactivate all waste contaminated with virus prior to disposal.

Pending Conditions:

1. Since a replication competent virus is being used, the Committee requests that all solid waste that comes in contact with the virus be autoclaved prior to disposal in the red biohazard bins and all viral liquid waste be inactivated by bleach. Please revise the appropriate sections accordingly and submit the revised protocol to AMB S-152 (MC 1108).

817 AD02/Schneewind, Olaf/*Deferred* (9-0)

The research objective is to 1) identify *Yersinia pestis* surface proteins that serve as protective antigens; 2) quantify the humoral and cellular immune responses of experimental animals to purified *Y. pestis* surface protein; 3) investigate immune mechanisms against *Y. pestis* surface proteins; and 4) investigate the virulence mechanisms of *Y. pestis* surface proteins. The investigator has submitted an amendment to request permission to perform intranasal infection in mice and to change the location of work to the [redacted] BSL3 facility and the [redacted] ABSL3 facility. During review of the amendment, it was noted that the investigator is requesting permission to remove infected tissue from the animal facility for transport to the [redacted] BSL3 laboratory. Since the investigator had indicated in previous versions of the protocol all cultural and animal work would be done in the same facility, several Committee members questioned the need for transport of infected tissues. If it is necessary to remove harvested tissue, the Committee agreed the investigator would need to clarify the procedures to be performed on the harvested tissue as well as specify where the experiments will take place, transport routes, packaging and any manipulations to be performed. Committee members also discussed whether the proposed intranasal inoculation would pose any additional hazards or risks to investigative staff as well as animal caretakers. In addition, since several standard operating procedures (SOPs) have yet to be prepared, several Committee members questioned whether is was necessary to review the protocol at this time. Several members recommended the revised protocol contain all the experimental procedures to be performed and all pertinent SOPs in a logical format for final review and approval. Until the issues discussed above could be resolved, the Committee agreed (9-0) to defer the protocol.

Reason(s) for Deferral:

1. In Section IV, Experimental Plan, please explain to the Committee the necessity for the removal and transport of infected tissues from the [redacted] BSL3 laboratory to the [redacted] BSL3 laboratory.
2. In Section IV, Experimental Plan, please describe the procedures to be performed on tissue harvested from animals infected with *Yersinia pestis*. In the description, please specify where the experiments are to be conducted, the route of transport, the packaging of the material and manipulations to be performed.
3. In Section IV, Experimental Plan, please provide to the Committee the justification for using intranasal inoculation and specify any additional hazards/risks that may be associated with this method.
4. In Section V, Staff Group, please have all individuals listed as staff sign the page.

III. Old Business:

A. Response to Stipulations for IBC #826. IBC protocol 826 was approved on December 10, 2003 with the stipulation that prior to injection into animals, all batches of the replication deficient Herpes Simplex Virus (HSV) be tested for the presence of wild-type virus. The investigator submitted, for the Committee's review, test results confirming that the 01/19/2004 batch of HSV vectors was incapable of replication and free of wild-type virus. Upon review of the material, Committee members had no questions or comments but requested the investigator be sent a thank you letter.

B. **Response to Sunshine Project Request.** At the February 6, 2004 meeting, Committee members were informed that the Sunshine Project had made a request for copies of the minutes from the last two IBC meetings. According to the NIH Guidelines, if requested, the IBC minutes must be made available. Mr. Pugh informed the Committee that in response to the request, the Sunshine Project was invited to the University upon which the minutes of the IBC meetings would be made available to them for review. At this point in time, no response has been received from the Sunshine Project.

IV. **New Business:**

A. **Draft BL3/Select Agent Lab Commissioning Plan.** At the February 6, 2004 meeting, Committee members reviewed documentation to address the remaining stipulations for IBC Protocol 707. Progress on the first stipulation has already been made with the hiring of a consulting group, [redacted] and [redacted]. However, during discussion (February meeting) of the materials provided to address the remaining stipulations, the Committee recognized that the facility operations needed to be tested, more standard operating procedures (SOPs) needed to be written, all SOPs needed to be tested, staff needed to be trained and various test scenarios needed to be developed and run successfully (i.e., emergency response, cold testing of use of facility, etc.) and that finalization of certain standard operating procedures were dependent upon this testing. These procedures are commonly referred to as "commissioning of the facility" therefore a plan for the commissioning of Biosafety Level 3 facilities was requested for review and approval. For discussion today, a draft Commissioning Plan has been submitted to the Committee for review and approval. During discussion of the plan, Committee members noted that as part of the process, an outside commissioning agent will be retained to perform the mechanical and physical aspects of the commissioning process, while SOPs involving operation of the facility will be done by [redacted] personnel, laboratory personnel, safety personnel, etc. Dr. Seps presented Dr. Wardrip's comments (which Dr. Wardrip desired to have entered into the minutes) regarding the draft-commissioning plan to the Committee. Dr. Wardrip's comments were as follows: 1) a full-scale emergency practice decontamination should be performed (as if an agent has been spilled) to test the procedures, equipment, and integrity of the containment strategy; 2) testing of the autoclave procedures for carcass decontamination to confirm the time and temperature indicated are appropriate for sterilizing an intact guinea pig carcass; 3) the functional tests of mechanical systems should include all aspects of the HVAC systems; and 4) a determination must be made about the level of decontamination required for the facility (surfaces, equipment, ducts, etc) when switching from one agent to another. There was no discussion with regards to Dr. Wardrip's comments. The Committee voted (9-0) to approve the draft-commissioning plan with the understanding that Dr. Wardrip's comments be taken into consideration.

B. **Proposed Changes to the IBC Review Process.**

1. **Review of Clinical Protocols.** Currently, IBC protocols that involve human subjects are reviewed based upon the biosafety level (BSL) of the protocol. Therefore, if the protocol is BSL1, then the protocol is reviewed through the subcommittee process that entails notification of all members by e-mail and review by two members of the Committee with final review by the Chair. If the protocol is BSL2 or greater, the protocol is initially reviewed by two members (one being a clinician) and once all issues are resolved, the protocol is presented and discussed at a Committee meeting. The Committee members were presented with a proposal that all clinical protocols regardless of biosafety level be reviewed at a Committee meeting. Committee members were in unanimous agreement (9-0) that all clinical be submitted for full committee review.

2. **Assignment of BL1/BL2 Protocols to Reviewers.** Currently, members sign up to review protocols on a monthly basis. A proposal put before the Committee would assign protocols to members as they are received according to the membership roster except for the public members.

The idea would be to equally distribute protocol review among the members so that no one member is overwhelmed with protocols to review. During discussion of the proposal, it was recommended that the number of protocols a reviewer may receive be limited to a maximum of three. Committee members unanimously agreed (9-0) to implementation of the proposal.

C. **Proposed Revisions to the IBC Protocol Submission Form.** Committee members reviewed a draft of the IBC protocol submission form in which questions regarding virus competency (Section III, 4c), procedures for exposure/needlestick (Section VII, 10), decontamination procedures (Section VII, 12) and disposal methods (Section VII, 13) were revised. Committee members voted (9-0) to accept the proposed changes to Section III – 4c, Section VII – 10, and Section VII – 12 but deferred (9-0) changes to Section VII – 13 until a policy could be drafted regarding the disposal of biohazardous agents.

D. **Disposal of Biohazardous Waste.** In conjunction with the discussion of IBC protocol 844, Committee members addressed the disposal of biohazardous waste. Several members were of the opinion that good laboratory practices dictate the inactivation of potentially infectious material by either bleach or autoclaving prior to disposal in the biohazard bins. Following discussion, it was determined that a policy should be drafted to address this issue for review at a later meeting.

V. **Updates:**

A. **FYI – Recent Action by Bush Administration That May Impact IBC.** Committee members were given a copy of a recent publication for their review announcing that the National Science Advisory Board for Biosecurity (NSABB) will soon begin issuing guidelines that will apply to "dual-use" research (i.e. research that has a legitimate scientific application but could also aid in the development of biological warfare agents).

The University of Chicago

Institutional Biosafety Committee

5841 S. Maryland Avenue
AMB S-152 ♦ MC 1108
Chicago, IL 60637

Minutes of June 8, 2004 Meeting
1:00 PM in [redacted]

In attendance:

Voting Members		Ex-Officio Members
Kenneth Thompson	Tong-Chuan He	Michael Holzhueter
Richard Hiipakka	Helena Mauceri	David Pitrak
Mark Abe	Louis Philipson	Markus Schaufele
Malcolm Casadaban	Gopal Thinakaran	Steve Seps
George Daskal	Craig Wardrip	
Jean Greenberg		

Staff

Pamela Postlethwait
Bill Pugh

Absent:

Voting Members	Ex-Officio Members	Staff
Clara Gartner	Steve Beaudoin	None
James Mastrianni	Russ Herron	
Mary Ellen Sheridan		

I. Minutes:

A. The minutes of the April 2, 2004 meeting were unanimously approved (8-0) with no corrections, additions or deletions.

II. Protocol Review:

The following protocols were reviewed at the meeting, with the disposition noted:

PR# Category/Investigator/*Disposition*

850 New/Lesniak, Maciej/*Pending Conditions* (11-0)

The research project involves the development of new techniques to bypass the blood-brain barrier in order to treat malignant brain tumors. The investigator had previously submitted a protocol to the Committee for the use of a retargeted replication competent adenoviral construct. Committee members had concerns regarding the use of a replication-competent adenovirus engineered to express a

recombinant DNA and the probability of dissemination of the agent within and outside of the laboratory under BL2 conditions and rejected the protocol. Given the Committee's concerns, the investigator has since submitted a protocol proposing to use a retargeted replication deficient adenoviral vector to assess cell and tissue type specificity of the virus, virus spread in tumor and normal tissue, impact of the virus on normal brain acutely and in the long term and efficacy of the retargeted virus to deliver gene therapy to brain tumors using a mouse model. During review of the protocol, Committee members thoroughly discussed the most appropriate method for testing of viral preparations for replication competent viruses. Additional comments were inclusion of pager numbers for emergency contact personnel and notification of Occupational Medicine for accidental exposure.

Pending Conditions:

1. In the event of an accidental exposure or needlestick, please indicate in Section VII, question 10, personnel will report to the University of Chicago Office of Occupational Medicine (UCOM L-156, 2-6757) for evaluation.
2. In Section VII, question 15, please provide a pager number and/or alternate number for the emergency contact.

738 AD02/Bendelac, Albert/*Pending Conditions* (11-0)

The research laboratory studies the role of various mouse genes involved in the development of CD1-specific T lymphocytes. Transgenic and knock-out/knock-in mice strains will be immunized with protein or lipid antigens to study their immune response. With this amendment, the investigator is proposing to inoculate mice with either heat-killed or live *Sphingomonas capsulata* to investigate the adjuvant effects of galactosylceramides. During discussion of the amendment, it was noted that the investigator had classified the use in animals of the heat-killed organism as ABSL1 and ABSL2 for the live organism. Committee members discussed the appropriate classification of the organism in order to determine the appropriate housing of the animals. Since the organism may pose a threat to immunocompromised animals in the facility, the veterinarians recommended the use of live agent in animals be classified as ABSL2. Committee members were in agreement with this recommendation. However, it was noted that tissues infected with live organism would be transported from the facility therefore the investigator would need to describe in detail the route of transport. Additional comment included removal of netilmycin since this antibiotic is not available.

Pending Conditions:

1. In the Supplemental Form B, Section VII, question 4, it is indicated that animal tissue is transported to [redacted] for analysis. Please describe the precise route of transport that will be used between the [redacted] and [redacted], specifying corridors and elevators used. Please be advised that patient elevators and corridors may not be used.
2. Since netilmycin is not available in this country, please remove from the protocol and supplemental forms all reference to the use of netilmycin as a treatment for exposure and indicate an alternative antibiotic.

811 AD01/Abe, Mark/*Approved* (9-0)

The research laboratory investigates the role of recently identified signal transduction proteins ERK7 and ERK8 in the regulation of other signaling proteins, cell cycle regulation, cell proliferation and apoptosis using a replication deficient VSV-pseudotyped Mouse Leukemia Virus retroviral system. With this amendment, the investigator is proposing to utilize a replication deficient VSV-pseudotyped Mouse Stem Cell Virus retroviral system and RNA interference technology in the form of short hairpin RNA (shRNA) to silence the expression of the endogenous signaling proteins of interest. Dr. Abe recused himself from discussion of the amendment. Upon review of the amendment, Committee members had no additional questions or comments and approved the amendment.

837 **AD01/Cai, Hua (Linda)/*Approved* (10-0)**
The research laboratory studies the regulation of endothelial nitric oxide synthase (eNOS) under disease conditions, i.e. hypertension. With this amendment, the investigator proposes to utilize adenoviral constructs to overexpress specific genes to examine their effect on eNOS expression. Upon review of the protocol, Committee members had no additional questions or comments and approved the amendment.

III. Old Business:

A. **Update on Rejected IBC Protocol #842.** At the April 2, 2004 meeting, the Committee reviewed an IBC protocol 842 involving the use of a retargeted replication competent adenoviral vector in vitro and in animals. After an in-depth discussion of the hazards associated with using a replication competent adenovirus engineered to express recombinant DNA, several Committee members had concerns that the proposed work could not be safely conducted under Biosafety Level 2 (BL2) conditions. Committee members determined that until additional information regarding the safe use of this agent in patients or lab animals could be submitted, the protocol as written could not be approved. The Committee has since been asked to review this decision. In preparation for the discussion, the Committee solicited the input of a number of individuals determined to possess sufficient knowledge and expertise to provide relevant insight. Committee members thoroughly reviewed and discussed the information received from the outside consultants. Based on the information provided from the consultants and the investigator, the Committee members found no information to indicate that its original decision to reject the protocol as written was inappropriate. Committee members were in agreement that the research could only proceed under BL3 conditions until such a time as information can be provided to indicate the research can be safely conducted under BL2 conditions. Several Committee members recommended forwarding a letter to the investigator indicating the issue had been discussed, the Committee's decision and the inclusion of additional concerns raised by the consultants not previously articulated to the investigator.

B. **Response to Stipulations for IBC #826.** IBC protocol 826 was approved on December 10, 2003 with the stipulation that prior to injection into animals, all batches of the replication deficient Herpes Simplex Virus (HSV) be tested for the presence of wild-type virus. The investigator submitted, for the Committee's review, test results confirming that the 03/24/2004 batch of HSV vectors was incapable of replication and free of wild-type virus. Upon review of the material, Committee members had no questions or comments but requested the investigator be sent a thank you letter.

IV. New Business:

A. **Injection of Proteins into Animals.** Currently, the Committee reviews protocols that involve the injection of plasmids, vectors or cells transfected with virus into animals. The question being brought before the Committee is whether proteins produced by recombinant means in the laboratory and purified for injection into animals should require the submission of the Supplemental Form B and review by the Committee. The question arose from an animal care and use protocol submission to the Institutional Animal Care and Use Committee (IACUC) whereby the investigator was producing proteins in a baculoviral system and following purification, injecting them into animals. The Committee discussed whether it was the production of the protein or the nature of protein that rendered the material hazardous and the appropriate way to acquire this information from the investigator. Several members questioned the appropriateness of the Supplemental Form B to ascertain the hazardous nature of the protein. After a lengthy discussion, the recommendation was made that if the investigator describes the use of recombinant means to produce a protein for subsequent injection into animals, then the research proposal needs to be fully described and a Supplemental Form B be submitted to describe the protein and any associated hazards. The Committee voted (6-4) to accept and implement the recommendation.

B. **Proposed Revisions to the IBC Protocol Submission Form.** In response to added regulatory attention by the Department of Transportation (DOT) and the Federal Aviation Administration (FAA), Mr. Marcus Schaufele proposed changes to Sections II and VII of the protocol submission

form to address the shipping of hazardous material and any associated training. Since Mr. Schaufele had to leave prior to the discussion of these proposed changes, the Committee agreed to defer discussion until the next scheduled meeting.

As a consequence of select agent review by various government agencies, a question pertaining to the deliberate transfer of a drug resistance trait to microorganisms was proposed for inclusion in Section III of the protocol submission form. After a brief discussion, Committee members voted (10-0) for inclusion of this question in the protocol submission form.

C. **Sunshine Project.** At the February 6, 2004 meeting, Committee members were informed that the Sunshine Project had made a request for copies of the minutes from the last two IBC meetings. NIH Guidelines state that IBC minutes must be made available to the public if requested. To accommodate this request, it was initially decided to invite a representative from the Sunshine Project to the University whereby the IBC meetings would be made available for their review. Mr. Pugh informed Committee members that the Sunshine Project informed his office in writing with the contention that our response was not in compliance with the NIH Guidelines and was now requesting the minutes of the last four IBC meetings. It was also pointed out to the committee that the NIH Office of Biotechnology Activities (OBA), as a result of queries from institutions regarding the Sunshine Project's request, has posted a series of questions and answers on their web site to assist institutions in developing policies and practices for the preparation of IBC meeting minutes that are in keeping with the intent of the NIH Guidelines. This guidance from NIH indicated that it was generally not appropriate to require a member of the public to travel to the site since this can entail significant time, effort and expense. As a response of this latest request from the Sunshine Project, redacted minutes from the last four IBC meetings were forwarded. Mr. Pugh informed the members that the University is now listed on the Sunshine Project's web site as being in compliance.

D. **Proposed Revision to Supplemental Form B.** Committee members were informed that the IACUC had endorsed removal of the investigator signature requirement on the Supplemental Form B. Since the Supplemental Form B is reviewed by both the IBC and IACUC, the Committee was asked to review the revised Form B upon which members indicated their agreement with the IACUC.

V. **Updates:**

A. **FYI – Article Regarding Commonly Used Viral Vectors.** Committee members were provided with an article discussing commonly used viral vectors for their review.

The University of Chicago

Institutional Biosafety Committee

5841 S. Maryland Avenue
AMB S-152 ♦ MC 1108
Chicago, IL 60637

Minutes of August 6, 2004 Meeting
1:00 PM in [redacted]

In attendance:

Voting Members		Ex-Officio Members
Kenneth Thompson	James Mastrianni	Russell Heron
Richard Hiipakka	Helena Mauceri	Michael Holzhueter
Mark Abe	Louis Philipson	David Pitrak
Malcolm Casadaban	Mary Ellen Sheridan	Steve Seps
Jean Greenberg	Gopal Thinakaran	
Tong-Chuan He	Craig Wardrip	

Guest	Staff
Jennifer Swanson	Pamela Postlethwait
	Bill Pugh

Absent:

Voting Members	Ex-Officio Members	Staff
George Daskal	Steve Beaudoin	None
Clara Gartner	Markus Schaufele	
Mary Ellen Sheridan		

I. Minutes:

A. The minutes of the June 8, 2004 meeting were unanimously approved (10-0) with no corrections, additions or deletions.

II. Protocol Review:

The following protocols were reviewed at the meeting, with the disposition noted:

PR# Category/Investigator/*Disposition*

852 New/Kroll, Todd/*Deferred* (12-0)

The research involves the investigation of abnormal gene arrangements from human thyroid cancers and the biochemical functions of the fusion proteins in cell growth control and transformation. Mammalian cell cultures will be transfected with expression vectors containing the fusion gene

constructs in order to analyze the cellular and biochemical effects of the expressed fusion protein. The protocol had been slated for subcommittee review however, since the expressed proteins may be oncogenic, had been called to full committee to determine if the work could proceed under BL1 conditions. Committee members also noted that the investigator's second protocol (#853) detailed the same experimental procedures but utilized lentiviral vectors to mediate the gene transfer. After thoroughly discussing the experimental procedures of both protocols, Committee members determined that the most appropriate biosafety level for conducting the proposed studies was BL2. Since both protocols describe the same experimental procedures and differ only in the method of gene transfer, the Committee agreed the protocols should be incorporated into one. Committee members voted to request the investigator to withdraw #852 and revise #853 to include the gene transfer methods described in #852.

Reason for Deferral:

1. The Committee requests the investigator withdraw this protocol and incorporate the information contained in Sections III and IV of the protocol into IBC protocol 853 (Characterization of t(2;3) in Human Thyroid Cancer – Lentivirus).

853 New/Kroll, Todd/*Pending Conditions* (12-0)

The research involves the investigation of abnormal gene arrangements from human thyroid cancers and the biochemical functions of the fusion proteins in cell growth control and transformation. Lentiviral vectors will be utilized to deliver the fusion gene constructs to mammalian cell cultures in order to analyze the cellular and biochemical effects of the expressed fusion protein. The Committee discussed this protocol in conjunction with #852 and had agreed the two protocols should be incorporated into one and conducted under BL2 conditions. Upon final review, it was also noted that the investigator needed to designate an individual to assume responsibility in the investigator's absence.

Pending Conditions:

1. Please incorporate the information contained in Sections III and IV of IBC Protocol 852 (Characterization of t(2;3) in Human Thyroid Cancer) into this protocol.
2. In Section VII, question 14, please indicate an individual to assume responsibility for day-to-day operations and personnel in the absence of the principal investigator. Please include contact information and relevant qualifications.

854 New/Zhang, Jian/*Deferred* (12-0)

The research laboratory will investigate the role of Cbl-b in CD40-mediated B cell activation by transfecting mouse B cell line in vitro with different Cbl-b cDNAs, either by retrovirus mediated gene transfer, electroporation, or Lipofectamine techniques. Committee members were informed that the biosafety cabinet certification date and staff signatures would be obtained when the investigator arrived on campus. During review of the protocol it was noted that in Section VII, regarding safety procedures, personal protective equipment and disposal methods the investigator had checked all options available. The Committee found this unnecessary and requested the investigator specify the requirements needed to work safely with this agent. The Committee also discussed the appropriateness of including descriptions of the live animal experiments when biohazardous agents were not being administered to live animals. In addition, the Committee discussed the two other IBC protocols (#855 and #856) submitted by the investigator that utilized the same agent but different recombinant DNAs and cell lines. Recognizing that all three protocols involved the same agent and would require the same revisions, Committee members agreed the investigator should incorporate the protocols into one that could then be reviewed at the next meeting.

Reasons for Deferral:

1. Since the investigator has submitted three IBC protocols (#854, #855 and #856) that utilize the same agents i.e. recombinant DNA, E. coli and VSV G-protein pseudotyped retrovirus, the IBC

requests the investigator incorporate the information and described procedures in protocols #855 and #856 into protocol #854.

2. The investigator has indicated that biohazardous agents are not being introduced into live animals therefore please remove all reference to experiments involving live animals in Section IV, Summary of Proposed Research.
3. When revising the protocol, please address the following items in Section VII:
   - Question 5. Rather than indicating all the options available, please indicate only the safety and security procedures necessary for admittance to the work area.
   - Question 8. Rather than indicating all the options available, please indicate only the personal protective equipment necessary to work with this agent.
   - Question 13. Rather than indicating all the options available, please indicate only the methods that will be utilized for disposal of the agent.

855 New/Zhang, Jian/*Deferred* (12-0)

The research objective is to understand the role of Cbl-b in T cell activation and autoimmunity. The research laboratory will investigate how CD28 co-stimulation controls ubiquitination of Cbl-b, whether Cbl-b regulates CD28-mediated formation of immunological synapse and whether Cbl-b regulates CD28-dependent autoreactive T cell activation in autoimmune arthritis using retrovirus-mediated gene transfer. The Committee discussed this protocol in conjunction with the two other protocols submitted by the investigator and determined the protocol should be withdrawn and the information and procedures described within be incorporated into protocol #854.

Reasons for Deferral:

1. Since the investigator has submitted three IBC protocols (#854, #855 and #856) that utilize the same agents i.e. recombinant DNA, E. coli and VSV G-protein pseudotyped retrovirus, the IBC requests the investigator withdraw protocol #855 and incorporate the information and described procedures into protocol #854.

856 New/Zhang, Jian/*Deferred* (12-0)

The research laboratory proposes to examine the effect of p38 MAPK on Fas ligand expression and T cell apoptosis using retrovirus-mediated gene transfer techniques to transfect primary mouse T cells in vitro. The Committee discussed this protocol in conjunction with the two other protocols submitted by the investigator and determined the protocol should be withdrawn and the information and procedures described within be incorporated into protocol #854.

Reason for Deferral:

1. Since the investigator has submitted three IBC protocols (#854, #855 and #856) that utilize the same agents i.e. recombinant DNA, E. coli and VSV G-protein pseudotyped retrovirus, the IBC requests the investigator withdraw protocol #856 and incorporate the information and described procedures into protocol #854.

857 New/Tang, Wei-Jen/*Pending Condition* (12-0)

The research objective is to study the effects of anthrax infection on cells that are vital for innate immunity utilizing the Bacillus anthracis Sterne strain, which lacks the pXO2 plasmid encoding proteins required for the generation of the bacterial capsule. In order to mimic the effects of anthrax infection on cell, macrophages or dendritic cells will be treated with a combination of heat-inactivated B. anthracis Sterne strain and anthrax toxins (edema factor and lethal factor). During review of the protocol, the Committee discussed the autoclave time appropriate for decontaminating both spores and vegetative bacteria.

Pending Condition:

1. The Committee recommends utilizing one autoclave time that would be sufficient for decontaminating both spores and vegetative bacteria. Please revise Section VII, question 9

(under 3a), question 12 and question 13 accordingly to indicate an autoclave time appropriate for decontaminating both spores and vegetative bacteria.

859 Renewal/Philipson, Louis/*Pending Conditions* (11-0)

The laboratory focuses on biophysical aspects of insulin secretion and glucose signaling. The focus is on specific ion channels and measurements of ion flux and other metabolic changes including visualization of exocytosis and endocytosis in the pancreatic beta cell using fluorescent reporter proteins. Replication deficient recombinant adenoviral vectors will be utilized to deliver genes into target cells. Before recusing himself from the discussion, Dr. Philipson presented the Committee with an overview of the research. After reviewing the protocol, the Committee had no questions or concerns regarding the described experimental and safety procedures but noted that the adenoviral work would be conducted in a dedicated but shared adenoviral facility. It was also noted by the committee that the identities of the agents to be utilized in the project needed to be indicated in Section II.

Pending Conditions:

1. In Section I, under Funding, please include the name of the grant agency and the Tracs ID number.
2. In Section II, question 2, please complete the following:
   - Indicate Human Cell Lines and provide the IRB information.
   - Indicate Animal Tissue and provide the IACUC information.
   - Under Microorganisms, include Adenovirus and indicate the Biosafety Level.

861 New/Roe, Michael/*Pending Conditions* (12-0)

The research laboratory utilizes fluorescence biosensor technology to study signal transduction mechanisms in cells. Wide-field and spinning disk confocal microscopy is used to perform real-time quantitative imaging of signaling events in cells. Replication deficient recombinant adenoviral vectors will be utilized to deliver genes into target cells. During review of the protocol, the Committee had no major concerns regarding the experimental procedures but noted that the adenoviral work would be conducted in a dedicated but shared adenoviral facility. The Committee also noted that since surveillance for adenovirus was not necessary, the investigator needed to remove the reference in the Biosafety Manual to performing PCR screening in the event of accidental exposure.

Pending Conditions:

1. In Section III, question 5b, please include mammalian cells.
2. Since surveillance for infections will not be done, please remove the reference to performing PCR screening from Section G of the Biosafety Manual.

610 AD03/Schneewind, Olaf/*Approved* (12-0)

The research objective is to characterize in molecular detail the mechanisms of cell wall sorting in Staphylococcus aureus and Listeria monocytogenes. The studies focus on the role of sortase genes in anchoring surface proteins to the cell wall and in mouse infection models. Additionally, the biochemical properties of the sortase enzymes and the sorting reaction will be characterized. With this amendment, the investigator is proposing studies to analyze the role of heme-iron uptake and utilization in staphylococcal endocarditis using a rat model. Studies will be initiated with the insertion of a jugular catheter in the animal and two days later bacteria will be injected in the tail vein. After three days, the animal will be sacrificed and tissue harvested for analysis. The major issues with the protocol concerned the location of the surgery and the isolation and transport of tissue. Upon review, Committee members were satisfied the investigator had addressed these concerns appropriately and approved the amendment.

622 **AD04/Tang, Wei-Jen/*Approved* (11-0)**

Using bacterial adenylyl cyclases including edema factor from Bacillus anthracis and CyaA protein from Bordetella pertussis, the research laboratory performs biochemical and structural analyses in order to develop chemical inhibitors to block the function of these proteins. With this amendment, the investigator proposes to test whether anthrax edema toxin (the combination of anthrax protective antigen and edema factor) can serve as an anti-angiogenic factor. Utilizing a mouse tumor model, the proteins will be injected intratumorally and the effect on tumor angiogenesis assessed. Although the amendment had been slated for subcommittee review it had been called to full committee to discuss the issue regarding the injection of recombinant proteins into animals. As a result of this amendment, the Committee initiated discussion on whether protocols and amendments involving the injection of proteins into animals should be reviewed at the subcommittee level or at full committee. After an in depth discussion of the issue, the Committee members agreed these types of protocols and amendments could be reviewed at the subcommittee level but the reviewer retains the option of sending to full committee for review and discussion. Upon conclusion of the discussion regarding the amendment, Dr. Mauceri recused herself from the vote at which time the Committee voted to approve the amendment.

649 **AD06/He, Tong-Chuan/*Pending Condition* (11-0)**

The research laboratory studies the molecular biology of bone formation and regeneration by investigating bone morphogenetic proteins (BMPs), their receptors(BMPR 1A and 1B) and other bone specific factors (Sox9 and Cbfa1) for their differential effects on the proliferation and differentiation properties of osteoblasts or chondrocytes. Replication deficient recombinant adenoviral vectors are utilized to deliver genes into target cells in vitro and in mice. With this amendment, the investigator is proposing to investigate the capacity of BMPs expressed by adenoviral vectors to induce or accelerate healing of both osseous (segmental defects in femur) and soft tissue (Achilles tendon) injuries in a rat model. As the principal investigator on this protocol, Dr. He recused himself from the discussion. Upon review of the protocol, the Committee had no questions but commented that the Supplemental Form B needed to be revised to clearly state [redacted] rather than [redacted].

Pending Condition:

1. In Supplemental Form B, Section VI, question 2, please indicate [redacted] instead of [redacted].

791 **AD01/Tang, Wei-Jen/*Approved* (11-0)**

The research studies involve the expression and purification of Bacillus anthracis protective antigen and lethal factor from E. coli to use as reagents to search for small molecular weight chemical inhibitors of this toxin complex in order to develop therapeutic agents against anthrax infection. With this amendment, the investigator proposes to test whether anthrax endema toxin (the combination of anthrax protective antigen and edema factor) can serve as an anti-angiogenesis factor. Utilizing a mouse tumor model, the proteins will be injected intratumorally and the effect on tumor angiogenesis assessed. The Committee thoroughly reviewed and discussed this amendment in conjunction with #622 AD04. Upon conclusion of the discussion regarding the amendment, Dr. Mauceri recused herself from the vote at which time the Committee voted to approve the amendment.

803 **AD01/Mauer, Ann/*Pending Condition* (11-0)**

The primary purpose of the study is to assess the effect of TNFerade (replication defective adenoviral vector containing the gene for tumor necrosis factor-alpha under the control of a radiation inducible promoter) on tumors in patients combined with fluorouracil, ciplatinol, and radiation therapy treatment. The data will also be used to assess the safety, feasibility, and tolerability of TNFerade, plus chemotherapy and radiation therapy. The investigator has submitted an amendment to update the protocol in response to the submission of sponsor amendment #2 dated 2/13/2004 and the revised

investigator's brochure dated 2/3/04 (Version 4). Changes to the protocol include revised language to correlate with more explicit exclusion criteria, allowing enrollment of an additional cohort at a dose of 4×10^{11} pfu if the maximally tolerated dose is not reached, increase the number of patients treated in the study and deletion of requirement for upper GI radiograph and chest x-ray. Upon review the Committee had no questions or comments regarding the amendment and voted to approve pending approval of the Institutional Review Board (IRB).

Pending Condition:

1. Institutional Review Board (IRB) approval is required.

III. Old Business:

A. Sunshine Project. Dr. Sheridan informed Committee members of an article in Science magazine regarding the Sunshine Project. This article outlines the group's activities and intentions, for those interested, since the Sunshine Project had previously requested, and received, the minutes of the last four meetings of the IBC.

B. Protocols Involving Select Agents. Committee members were reminded that there are several protocols involving the use of select agents (i.e., 707, 817) that had been approved with stipulations (i.e., SOPs, CDC approval, etc.). These stipulations need to be addressed prior to initiation of the studies. When these protocols were initially submitted, the work would be contained within the [redacted] (anthrax) or at [redacted] (yersinia). Earlier this year, the investigator submitted an amendment requesting permission to switch the yersinia work from [redacted] to [redacted]. This resulted in the IBC stipulating the need for that facility to be "commissioned". Since that amendment, the investigator submitted an amendment to the ames protocol, requesting that work also be expanded into the [redacted]. The committee was informed that during review of these new amendments to the ames and yersinia protocols, recommendations were made by the reviewers for the investigator to withdraw these amendments and submit freestanding IBC protocols for the ames and yersinia work in the [redacted] only. The committee was reminded that the Select Agent Planning Committee has been assisting, since the submission of the original protocols, with the planning of these facilities and with the development of the SOPs. Committee members were informed that the [redacted] has been reviewed by the commissioning agent and is near completion. Several members questioned whether it is appropriate to build the facilities prior to initiating dialogue with the IBC. Several other Committee members also recommended the Committee should play a facilitating role in faculty recruitment so as to be aware of the research needs of new faculty.

IV. New Business: None

V. Updates: None

The University of Chicago

Institutional Biosafety Committee

5841 S. Maryland Avenue
AMB S-152 ♦ MC 1108
Chicago, IL 60637

Minutes of September 30, 2004 Meeting
1:00 PM in [redacted]

In attendance:

Voting Members

Kenneth Thompson
Richard Hiipakka
Mark Abe
Malcolm Casadaban
George Daskal
Clara Gartner
Jean Greenberg
Tong-Chuan He
Helena Mauceri
Mary Ellen Sheridan
Gopal Thinakaran
Craig Wardrip

Ex-Officio Members

Steve Beaudoin
Russell Herron
David Pitrak
Markus Schaufele
Steve Seps

Guest

Debra Anderson
Kristen DeBord
Judd Johnson
Olaf Schneewind

Staff

Pamela Postlethwait
Bill Pugh
Jennifer Swanson

Absent:

Voting Members

James Mastrianni
Louis Philipson

Ex-Officio Members

Michael Holzhueter

Staff

None

I. Presentation by Dr. Olaf Schneewind

Dr. Schneewind provided an overview of his research and the BSL3 facilites.

II. Protocol Review:

Both of the protocols reviewed at this meeting involve the use of select agents and will be conducted in BSL3 facilities under similar SOPs. The Committee discussed the following issues, which pertain to both of these protocols.

The Committee discussed whole facility decontamination. In previous discussions, it was proposed that Vaporous Hydrogen Peroxide (VHP) decontamination would be performed annually and between the use of different select agents. However, as routine decontamination and environmental monitoring will be conducted, VHP decontamination will only be performed in response to off-normal conditions, spill of the select agent or detection of contamination through environmental monitoring. There are no regulations that require annual or between agent VHP decontamination.

The Committee discussed environmental monitoring procedures for the facilities. Quarterly monitoring will be conducted by the University Safety Office. When conducting environmental monitoring, the Safety Office follows departmental SOPs which outline sampling locations and number of samples to be collected. This information, however, was not included in the investigator's protocol submissions. Several members suggested that reference to these SOPs should be provided. After discussion of this issue, the Committee felt that summaries of the monitoring reports would be sufficient.

A member questioned whether or not environmental monitoring would be conducted after VHP decontamination. As biological indicators will be used during the decontamination process, environmental monitoring is not necessary.

The Committee discussed the need for decontamination of the ductwork. According to the Commissioning Agent, a plan should be in place for decontaminating the ductwork beyond the HEPA filter. In response to this issue, the University Safety Office indicated that contamination of the ductwork would be a rare event and that a plan would be developed at the time of need. Several members felt that a written plan should be incorporated into the protocol, as recommended by the Commissioning Agent. After discussing this issue further, the Committee agreed that an SOP for decontamination of the ductwork should be developed and included in the protocol prior to approval of the research.

The SOP for Fever Watch was discussed by the Committee. A member felt that the Fever Watch consent form should emphasize the need to seek medical attention in cases of known exposures. The Committee felt that this was not necessary, as this consent was developed strictly for Fever Watch and not for specific exposures. All staff members will be provided training on exposures and whom to contact in the event of an exposure. Furthermore, the two-person rule will be implemented at all times, and the exposed person would be assisted in seeking medical attention.

A member noted an area of the protocol submission form in which the investigator provided reference to an SOP, rather than providing an actual summary of the information. The member questioned whether or not this was appropriate. As the particular SOP is quite detailed, the Committee felt that it was acceptable to simply provide the reference.

The Committee discussed the use of human cell lines. HELA cells will be used, which are considered non-infectious.

The Committee noted items from the Commissioning Report work that need to be completed prior to approval of the research. This includes: testing of the emergency response system; installment and testing of bubble dampers; testing of the autoclave; completion of response to Item #34.

Administrative issues that need to be addressed include: clarification of routine decontamination procedures; removal of references to animal work.

In order to evaluate the SOPs and environmental monitoring, the Committee requested that the investigator submit summaries of two quarterly monitoring reports to the IBC.
The following protocols were reviewed at the meeting, with the disposition noted:

PR# Category/Investigator/*Disposition*

867 New/Schneewind/*Pending-Conditions & Stipulations* (11-0-0)

This research involves the use of *Yersina pestis* strains CO92 and KIM. The goal of this research is to identify new targets for vaccine and immunotherapies by screening for protective antigens and by elucidating the pathogenic features of immune protection.

Pending Conditions:
The PI must ensure that the following issues regarding the document entitled "[redacted] are addressed.

1. The U of C response to Item #1 indicates a 10/18/04 target completion date for work related to the second bubble tight damper. Confirmation of installation, testing and proper operation of the damper is needed.

2. The U of C response to Item #5 indicates a 10/18/04 target completion date for testing of the alarm notification time. Confirmation of the testing and proper operation of the emergency response plan is needed.

3. In Item #17, [redacted] assessment notes that a start-up report is needed for the autoclave. Confirmation of testing and proper operation of the autoclave is needed.

4. The U of C Response for Item #34 needs to be completed.

5. In Item #35, [redacted] recommends the development of procedures for decontamination of ductwork. The U of C response notes that contamination of ductwork would be a rare event, therefore, decontamination procedures for the ductwork will be generated upon a report of contamination. The Committee, however, requested that a plan be in place prior to approval of the research. The Investigator must provide a copy of the SOP that describes procedures for decontamination of ductwork. **(Vote 6-5-0)**

Stipulations:

The Investigator needs to submit summaries of the first two quarterly monitoring reports.

868 New/Schneewind/*Pending-Conditions & Stipulations* (13-0)

This research involves the use of Bacillus anthracis AMES. The goal of this research is to characterize (1) the role of sortase genes in surface protein anchoring and (2) the role of sortases and surface proteins in invasion of host cells.

The Committee discussed vaccination of staff members working with *Bacillus anthracis*. The University has concerns about mandatory vaccination. However, if the philosophy of the lab is to require vaccination, employees that wish to work with the agent would have to be vaccinated. If an employee refused vaccination, the University's legal office should be consulted, and alternative responsibilities would need to be assigned to the employee.

Pending Conditions:

The PI must ensure that the following issues regarding the document entitled "[redacted] are addressed.

1. The U of C response to Item #1 indicates a 10/18/04 target completion date for work related to the second bubble tight damper. Confirmation of installation, testing and proper operation of the damper is needed.

2. The U of C response to Item #5 indicates a 10/18/04 target completion date for testing of the alarm notification time. Confirmation of the testing and proper operation of the emergency response plan is needed.

3. In Item #17, [redacted] assessment notes that a start-up report is needed for the autoclave. Confirmation of testing and proper operation of the autoclave is needed.

4. The U of C Response for Item #34 needs to be completed.

5. In Item #35, [redacted] recommends the development of procedures for decontamination of ductwork. The U of C response notes that contamination of ductwork would be a rare event, therefore, decontamination procedures for the ductwork will be generated upon a report of contamination. The Committee, however, requested that a plan be in place prior to approval of the research. The Investigator must provide a copy of the SOP that describes procedures for decontamination of ductwork.

Stipulations:

The Investigator needs to submit summaries of the first two quarterly monitoring reports.

The University of Chicago

Institutional Biosafety Committee

5841 S. Maryland Avenue
AMB S-152 ♦ MC 1108
Chicago, IL 60637

Minutes of October 1, 2004 Meeting
1:00 PM in [redacted]

In attendance:

Voting Members		Ex-Officio Members
Kenneth Thompson	Tong-Chuan He	Michael Holzhueter
Richard Hiipakka	Helena Mauceri	David Pitrak
Mark Abe	Louis Philipson	Markus Schaufele
Malcolm Casadaban	Mary Ellen Sheridan	Steve Seps
George Daskal	Gopal Thinakaran	
Clara Gartner	Craig Wardrip	
Jean Greenberg		

Guest	Staff
None	Pamela Postlethwait
	Bill Pugh
	Jennifer Swanson

Absent:

Voting Members	Ex-Officio Members	Staff
James Mastrianni	Steve Beaudoin	None
	Russell Herron	

I. Minutes:

A. The minutes of the August 6, 2004 meeting were unanimously approved (12-0-0) with no corrections, additions or deletions.

B. The minutes of the August 27, 2004 meeting were approved (11-0-1) with no corrections, additions or deletions.

II. Protocol Review:

The following protocols were reviewed at the meeting, with the disposition noted:

PR# Category/Investigator/*Disposition*

854 Deferral/Zhang, Jian/*Pending Conditions* (13-0-0)

This protocol aims to assess the role of Cbl-b in T cell and B cell activation. The role of p38 in the regulation of Fas ligand and T cell apoptosis will also be investigated. Retroviral infection will be used to transfect mouse T and B cells.

This protocol was deferred at the 8/6/04 IBC meeting. One issue involved the investigator's submission of 3 protocols (854, 855 and 856) that would be utilizing the same agents. The Committee requested that the three protocols be combined into one protocol. The investigator addressed this issue and has incorporated the previously submitted protocols into the present protocol.

The Committee discussed the concern regarding use of live animals. The investigator has indicated that live animals will not be used in this protocol and all animal DNA will be obtained from other investigators. A member noted that there are still references to animals in this protocol. After a brief discussion, the Committee requested that the PI provide further clarification regarding this issue.

The reviewer indicated that the biosafety cabinet certification is still needed. The PI has indicated that the cabinet will be certified. This will need to be done prior to approval of the protocol.

Pending Conditions:

1. In Section IV, Experimental Plan, first paragraph, the Committee requested clarification on the statement "We will also study the effects of IL-4 on T cell apoptosis in autoimmune arthritis." The investigator needs to clarify whether an animal model of autoimmune arthritis is being generated and tissue harvested for use in *in vitro* experiments or whether biohazards are being administered to animals with autoimmune arthritis.

2. If the protocol does not involve experimentation in live animals, in Section V, Staff Group, the investigator needs to remove 'animal care' from Jian Zhou and Guilin Qiao responsibilities.

3. In Section VII, question 2a, the investigator needs to provide the certification date for the biosafety cabinet.

860 New/Pan, Tao/*Pending Condition* (13-0-0)

This protocol proposes to grow up an attenuated strain of *Yersinia pestis*. Cells will be lysed, RNA will be isolated and tRNA from these cells will be analyzed. There will be no removal of the cells from the facility and no animal work will be performed. Work will be conducted in [redacted] BSL2 facility.

A member questioned whether the PI plans to perform all laboratory work himself. As Dr. Schneewind is the only other individual listed in section V, it appears that the PI will perform all laboratory work. The

Committee noted that Melanie Marketon is listed as the individual responsible for oversight; however, she is not listed in section V as study staff. The Committee requested that she be added to section V.

A member questioned whether this strain of Yersinia will need to be registered. Administrative staff clarified that this strain is exempt.

A member noted that the protocol, under "Surveillance for Infection", lists symptoms (i.e. "non-specific syndrome" and "exitus lethalis") associated with other strains of *Yersinia* and questioned whether the language is appropriate for this particular strain. As clarified by the investigator, the strain is attenuated and not avirulent; therefore, the Committee felt that the language was appropriate and should not be removed from the protocol.

Pending Condition:

According to Section VII, #14, of the protocol submission form, Dr. Melanie Marketon is the individual responsible for oversight. Therefore, the Committee requested that she be added to the protocol. The investigator needs to submit a revised Section V of the submission form that includes Dr. Marketon's responsibilities and her signature.

862 New/Le Beau, Michelle/ *Pending Condition* (13-0-0)

The objective of this study is to elucidate the potential mechanisms by which the abnormal expression of endocytosis proteins might contribute to leukemogenesis. The investigator plans to use PCR to generate products that encode fusion proteins between endocytosis-related proteins and transcription factors. These fusion proteins are the result of chromosomal translocations and are associated with hematopoietic malignancies in humans. RNA isolated from human cell lines or human tissues will be amplified by PCR and either cloned into plasmid vectors, which will be propagated in E. coli for rDNA isolation, or cloned into MSCV-derived retroviral vectors, which will be transfected into packaging lines to produce ecotropic retrovirus. Murine and human lymphoid or myeloid cell lines will be transiently transfected with plasmids fused with various fluorescent proteins; Murine bone marrow and fetal liver progenitor cells will be transfected with replication defective ecotropic retrovirus. Transduced murine progenitor cells will be injected into lethally irradiated mice (IACUC protocol pending).

The reviewer requested clarification on the proper procedure for contacting UCOM in cases of exposure. The investigator has revised the protocol to include the 24 hour pager number. The Committee felt that this form of contact may not be necessary for this protocol, as the investigator will be using ecotropic retrovirus which is not infectious to humans.

The Committee discussed the use of human cell lines in this protocol and the need for staff members to complete bloodborne pathogen training. As the human cell lines could be considered potentially infectious, the investigator needs to confirm that all staff members will complete the training.

The Committee questioned whether or not bloodborne pathogen training should be mandatory for all protocols involving human cell lines. After a brief discussion, the Committee felt that a subcommittee should convene at a later date to further discuss the issue.

Pending Condition:

According to the Biosafety in Microbiological and Biomedical Laboratories (BMBL), human cell lines should be handled using Biosafety Level 2 (BL2) practices and containment. Additionally, all staff members working with human cells should be enrolled in the Institutional Bloodborne Pathogen Training program. Therefore, the investigator needs to confirm that all staff members participating in this protocol will receive Bloodborne Pathogen Training.

863 New/Kindler, Hedy/ *Pending Conditions* (12-0-0)

This protocol involves the use of viral vaccines, vaccinia and fowlpox, to stimulate the immune response in cancer patients. These recombinant viruses can infect antigen presenting cells and direct the expression of tumor associated antigens and co-stimulatory molecules that activate T cells. The investigator proposes that the use of these vaccines will help the immune system identify tumor cells and ultimately kill tumors.

The reviewer noted a concern regarding the infectious nature of vaccinia and the return of patients to the oncology clinic after receiving the vaccine. After receiving the first injection of vaccinia, patients could be infectious to immunocompromised patients for a period after the injection. As this study involves multiple injections of the viruses and requires patients to return to the clinic several times, the reviewer questioned whether the injections would be administered in areas separate from the outpatient clinic. The investigator indicated that patients who do not develop blisters or pustules within a 2-3 week time period would not be infectious. These issues are not relevant for fowlpox, as the virus is not infectious to humans.

A member noted that this protocol does not seem to be consistent with CDC guidelines for implementation of a vaccinia program. These guidelines include recommendations for vaccinating health care workers that will be administering the vaccine to patients, and designating separate areas of the hospital/clinic for administration of the vaccine and evaluation of vaccination sites. The protocol does not adequately address these issues. Implementation of a program of this nature would require involvement of Hospital Administration, University and Hospital Legal Departments and the Department of Infectious Disease. Approval by these departments would be necessary prior to IBC approval.

The Committee discussed the concern regarding training of staff members. The investigator indicated that a DVD and bio-safety materials, provided by the sponsor, would be used to train staff working with the vaccine. The Committee found receipt of these materials to be insufficient and requested that more information regarding staff training be provided by the investigator.

Pending Conditions:

1. Due to concerns with regards to potential infectivity, a vaccination program will need to be developed for the administration of vaccinia. The development of this program will need to be coordinated with, and eventually approved by, University Legal Counsel, University of Chicago Occupational Medicine and, if necessary, Human Resources. Other institutional (hospital and university) offices may need to become involved as this program is developed and defined. The following are some of the issues that will need to be taken into consideration during development of this program:
    - Potential need for vaccination of hospital care workers administering the vaccine
    - Location and logistics of vaccine administration
    - Process by which vaccination is determined to be successful
    - Plans for individuals (hospital care workers and patients) that are potentially contagious for 4-21 days after vaccination
    - Plans for patients who are vaccinated and then need admission to the hospital

   Since this is a multi-center study, information on how this issue is handled elsewhere may be helpful. The Committee recommended that the investigator contact Dr. David Pitrak, Chief Infectious Diseases Section, at 2-9078.

2. The Committee requested detailed information on the staff in-service on the vaccinia virus. Section B-4 of Appendix M indicates that the sponsor, Therion Biologics, will provide vaccinia-specific safety training to all sites participating in the study. The protocol submission form indicates that the investigator has received bio-safety materials and a DVD from the sponsor. A gastrointestinal nurse will use these educational tools to present an in-service to study staff. The Committee felt that additional information was needed in order to fully evaluate the training that will be provided to University of Chicago staff.

3. The investigator needs to submit Section V of the protocol submission form with Dr. Linda Skoog's signature.

Stipulations:

For a clinical trial site that is added after the RAC review process, no research participant shall be enrolled at the clinical trial site until the following documentation has been submitted to NIH OBA: (1) IBC approval (from the clinical trial site); (2) IRB approval; (3) IRB approved informed consent document; (4) curriculum vitae of the principal investigator(s) (no more than two pages in biographical sketch format); and (5) NIH grant number(s) if applicable.

864 New/Rock, Ronald/*Approved* (12-0-0)

The objective of this study is to express myosin, myosin fragments and mutated versions of myosin using E. coli or baculovirus. The purified products will be used in single-molecule force assays to study function.

The Committee had no issues with this protocol and recommended approval.

545 Renewal/Ragsdale, Clifton/*Approved* (13-0-0)

This protocol will investigate neuronal differentiation and patterning in embryonic chick brains. In ovo electroporation will be used to introduce recombinant DNA into chick embryos. Embryonic chick tissues will be harvested, fixed and processed for histology. The DNA to be used is non-infectious.

The Committee had no issues with this protocol and recommended approval.

757 AD 02/Preuss, Daphne/ *Approved* (13-0-0)

The goal of this protocol is to understand the genetic regulation of reproduction in flowering plants. Various genes will be introduced either by *Agrobacterial* transformation or particle bombardment. The protocol previously used only *Arabidopsis thaliana* as a model system. This amendment involves the addition of several plant species (DNA source and host) to the protocol: *Manihot esculenta*, *Oryza sativa*, *Phaseolus vulgaris*, and *Solanum tuberosum*. The amendment also involves addition of a new room and addition of staff members.

The Committee had no issues with this amendment and recommended approval.

869 New/Lesniak, Maciej/*Pending Conditions* (13-0-0)

The goal of this protocol is to use an adenoviral vector to treat malignant brain tumors in a mouse model. The adenoviral vector to be used is replication competent; however, the investigator has re-engineered this virus to limit infectivity. This retargeted virus will only bind to cells that express αvβ3/5 integrins.

The Committee discussed the tropism of the re-engineered virus. Based on data provided by the investigator, the virus had a 100-fold decrease in targeting to the liver, the primary target for adenovirus when administered IV. While the tropism has been altered, the protocol appropriately indicates a level of uncertainty with respect to viral infectivity.

The Committee discussed the proposed location of work. Several issues were raised regarding the use of replication competent adenovirus in an area that is not self-contained. The investigator plans to use multiple rooms, some of which are shared with other investigators, lack biosafety cabinets, and/or require transport of the agent across campus. After discussion of these concerns, the Committee requested that all *in vitro* work be conducted in a single, adequately controlled laboratory. Dr. He offered the use of his laboratory for this work and will discuss this option with the investigator. The Committee also requested that the investigator develop a plan for transporting the agents to the [redacted].

The Committee discussed whether or not the investigator should submit progress reports to the IBC. The Committee agreed that any changes to the protocol should be submitted as amendments. Therefore, progress reports are not necessary.

Pending Conditions:

1. The Committee has determined that all *in vitro* work involving the replication competent adenovirus must be confined to a single room or suite. Tong-Chuan He has agreed to make his laboratory available to the investigator for the preparation of the virus. The investigator needs to contact Dr. He (2-7169) to make arrangements regarding the use of his laboratory. Once a central location has been arranged, the investigator needs to revise the protocol accordingly (i.e., room number, certification date of cabinet, etc.).

2. While transport has been described, the details are not entirely consistent with what is described in the BMBL. Transport of the viral preparation to the [redacted] must be performed in a manner consistent with the transport description found in the BMBL for transport of biological agents (i.e., primary receptacle, water tight secondary packaging, and a durable outer packaging. Also, this packaging requires an "Infectious Substance" label. The investigator needs to revise the transport description accordingly.

534 Renewal/Mastrianni, James/*Pending Conditions* (12-0-1)

The objective of this protocol is to investigate the nature of infectious prions. Samples from individuals with prion disease will be obtained for prion protein analysis studies and transmission studies utilizing transgenic mice. Transgenic mice will be produced to study the genetic forms of prion disease and the nature of disease.

The Committee discussed the recommended biosafety level for work with prions. The investigator has been working in a BL2 facility with BL3 practices, which is appropriate for the scope of this protocol. However, he plans to move this work to a new BL3 laboratory that is currently under construction.

The Committee discussed construction of the BL3 laboratory with respect to decontamination methods. The investigator has indicated that all waste will be autoclaved and incinerated; however, the current construction plans to do not include installation of an autoclave. According to the BMBL, a BL3 facility must have access to an autoclave, but installation of an autoclave inside the BL3 laboratory is not required. Given the nature of the hazard, the Committee requested that an autoclave be installed in the BL3 facility.

The Committee noted other issues that need to be resolved prior to approval. The biosafety cabinet must be certified. In addition, the investigator needs to correct the following inconsistencies throughout the protocol: replace "autoclaved or incinerated" with "autoclaved and incinerated"; replace references to the BL3 and ABSL3 facility with "BL2 with BL3 practices" and "ABSL2 with ABSL3 practices" (as the BL3 facility is not yet complete); and harmonize the disinfection procedures throughout the protocol to be consistent with the 4th Edition of the BMBL.

Pending Conditions:

1. The investigator has indicated that waste from the BSL3 facility in [redacted] will be autoclaved in a facility across the hall. Given the hazards associated with this agent, the Committee requested that an autoclave be contained within the BSL3 laboratory in [redacted] so that waste may be autoclaved out of the facility.

2. Throughout the protocol submission form, supplemental forms and biosafety manual, reference is made to the use of a BSL3 or ABSL3 laboratory. Since the BSL3 laboratory in [redacted] is not yet completed nor has it undergone commissioning to ensure proper functioning, it is not appropriate to refer to the use of a BSL3 facility. Additionally, the prion room within the [redacted] is not an ABSL3 laboratory but rather an ABSL2 w/ABSL3 practices laboratory. Therefore, the investigator needs to revise the protocol submission form, supplemental forms and biosafety manual to reflect the use of either a BSL2 w/BSL3 practices laboratory or an ABSL2 w/ABSL3 practices animal prion room.

3. The investigator has previously established that animal carcasses and non-liquid waste contaminated with prions must be autoclaved and then sent for incineration. However, throughout the protocol submission form, supplemental forms and biosafety manual, it is indicated that this waste will either be autoclaved or incinerated. Therefore, the Committee requested that all prion-contaminated non-liquid waste and animal carcasses be autoclaved and then incinerated. The investigator needs to revise the protocol submission form, supplemental forms and biosafety manual appropriately.

4. When the biosafety cabinet in [redacted] has been certified, the investigator needs to indicate the certification date in Section VII, question 2a.

5. In Section VII, question 4 and in the biosafety manual (page 24), it is stated that waste will be steam autoclaved at 134 degrees centigrade for 1 hour and references the 3rd edition of the BMBL. Elsewhere in the protocol (e.g., #'s 12 and 13 of Section VII and in many locations within the biosafety manual) it is stated that waste is decontaminated at 134 degrees centigrade for 270 minutes as recommended by the 4th edition of the BMBL. The investigator needs to reconcile this issue.

865 AD04/Naclerio, Robert/*Pending Conditions* (12-0-0)

Dr. Thompson left the room for the vote, as he is a staff member on this protocol.

The goal of this protocol is to identify the role of viral infection in chronic sinusitis by measuring goblet-cell hyperplasia, nasal mucosa hyper-reactivity, and quantifying the cellular constituents of nasal mucosa after viral infection. The investigator plans to use Sendai virus to produce sinusitis in a mouse model.

The Committee discussed the Sendai virus, a paramyxovirus in the same family as human measles. Sendai is a rodent virus which poses no risk to humans; however, it is mildly contagious to mice, if housed in separate cages. While the investigator has indicated that work will be done in a BL2 facility with BL3 practices, the

Committee felt that the work could be done in a BL1 facility with BL2 practices, as the mice themselves are not considered biohazardous.

The Committee noted other issues that need to be addressed prior to approval: the protocol needs to be revised to replace Cidex with Clidox; the investigator needs to discuss housing arrangements and containment issues with the [redacted]; and, upon IACUC approval, the investigator needs to submit a copy of the approval letter to the IBC.

Pending Conditions:

1. Since the Sendai virus is a rodent pathogen and not a true human pathogen, the IBC has determined this protocol to be Risk Group 1 and the appropriate Biosafety Level (BL) to be BL1 w/BL2 practices. The investigator needs to revise the protocol submission form to reflect this determination. Additionally, it has been determined that although mice infected with the virus may be infectious to other mice, the mice themselves are not considered biohazardous, therefore the appropriate Animal Biosafety Level is ABSL1. The investigator needs to revise the Supplemental Form B to reflect this determination.

2. Given the infectious nature of the agent to rodents, the investigator will need to discuss with the [redacted] the housing arrangements and the proper containment for this agent in the animal facilities.

3. In Supplemental Form B, Section VII, the investigator needs to revise questions 4 and 5 to indicate the use of 'Clidox' rather than 'Cidex'.

4. The investigator needs to submit a letter of approval from the IACUC, as this protocol requires review and approval from the Institutional Animal Care and Use Committee (IACUC) prior to commencement.

III. Old Business: None

IV. New Business:

A. Frequency of Meetings for IBC **(12-0-0)**

The Committee discussed the need for monthly meetings. The Office of Biotechnology Activities (OBA) has clarified the guidelines regarding IBC review. All protocols must be reviewed and voted on at a convened meeting; therefore, subcommittees are no longer appropriate for the review of BL1 protocols. As all protocols will now have to go to full committee, the Committee voted to hold monthly meetings.

B. IBC Protocols for Microbiology Laboratories

The Committee discussed the need for IBC review of teaching protocols. As federal guidelines apply only to research protocols, implementation of a review process for teaching protocols is at the discretion of each institution. The Committee felt that more information was needed and deferred this issue to the next meeting.

V. Updates: None

The University of Chicago

Institutional Biosafety Committee

5841 S. Maryland Avenue
AMB S-152 ♦ MC 1108
Chicago, IL 60637

Minutes of November 5, 2004 Meeting
1:00 PM in [redacted]

In attendance:

Voting Members		Ex-Officio Members
Kenneth Thompson	Tong-Chuan He	Russell Herron
Richard Hiipakka	Helena Mauceri	David Pitrak
Mark Abe	Louis Philipson	Markus Schaufele
Malcolm Casadaban	Mary Ellen Sheridan	Steve Seps
George Daskal	Craig Wardrip	
Clara Gartner		
Jean Greenberg		

Guest	Staff
None	Bill Pugh
	Pamela Postlethwait
	Jennifer Swanson

Absent:

Voting Members	Ex-Officio Members	Staff
James Mastrianni	Steve Beaudoin	None
Gopal Thinakaran	Michael Holzhueter	

I. Minutes:

A. The minutes of the September 30, 2004 meeting were unanimously approved (11-0-0) with minor revisions to the discussion section of protocol 868.

B. The minutes of the October 1, 2004 meeting were unanimously approved (11-0-0) with no corrections, additions or deletions.

II. Protocol Review:

The following protocols were reviewed at the meeting, with the disposition noted:

PR# Category/Investigator/*Disposition*

870 New/Kalinichenko, Vladimir/*Approved* (11-0-0)

The purpose of this research is to determine the transcriptional targets of Foxf1 and the role of Foxm1b in endothelial proliferation, differentiation and migration. The research involves over-expression and inhibition of Foxf1 and Foxm1b in mouse endothelial cell lines and transgenic mice.

The Committee recommended approval.

871 New/Kee, Barbara/*Approved* (11-0-0)

This study will investigate the regulation of lymphocyte development by helix-loop-helix proteins. Mouse hematopoietic cells will be transfected with genes of interest using S003 and MigRI ecotropic retroviruses. Transduced cells will be introduced into irradiated mice.

The Committee recommended approval.

874 New/Bendelac, Albert/ *Pending Condition/Stipulation* (12-0-0)

This study will investigate the role of CD1 in host defense against *Ehrlichia muris* in mice. Mice will be inoculated with either heat-killed or live bacteria and sacrificed at various time points. Tissue will be harvested for immunological analysis.

The investigator has indicated that all work will be done in [redacted]. A member noted that the protocol indicates the use of a hood and questioned whether the investigator would be using a biosafety cabinet in his lab. If so, this section of the submission form would need to be completed; specifically, the biosafety cabinet certification date would be needed. The Committee believed that the investigator would not be working with live *Ehrlichia* in his lab, and that the hood must be referring to the biosafety cabinet in [redacted].

The Committee discussed the location of work. The Committee felt that the investigator would be able to work with heat-killed bacteria in his lab; however, all work with live bacteria must be done in [redacted].

The investigator has indicated that live and heat-killed bacteria will be received from the University of Texas and harvested tissue will be shipped back to Texas for analysis. The Committee stipulated that bacteria can be stored in the investigator's lab, but all unpacking of live bacteria, harvesting of tissue containing live cultures and packaging of these tissue samples must be conducted in [redacted]

Pending Condition:

1. The Institutional Animal Care and Use Committee (IACUC) must approve the corresponding amendment to ACUP [redacted].

2. Kristen DeBord needs to sign the staff signature page.

Stipulation:

1. Properly packaged vials containing live *Ehrlichia muris* may be stored in the laboratory however opening vials of live *E. muris* is restricted to a biosafety cabinet in [redacted]. In addition, all tissue harvested from mice infected with live *E. muris* must be properly packaged for transport in [redacted] but may be stored in the laboratory prior to shipping.

875 New/Bendelac, Albert/ ***Pending Condition/Stipulation*** **(12-0-0)**

This study will investigate the role of CD1 in immunoregulation during *Salmonella typhimurium* infection in mice. Mice will be inoculated with either heat-killed or live bacteria and sacrificed at various time points. Tissue will be harvested for immunological analysis.

The investigator has indicated that the bacteria will be provided by Dr. Schneewind. Growth and preparation (heat killing) of bacteria will be performed in Dr. Schneewind's laboratory in [redacted]. The Committee felt that it would be acceptable for the investigator to store the bacteria in his lab, as long as his staff received proper training on how to work with these organisms. The Committee stipulated that work with live organisms and tissues containing live culture would be restricted to [redacted]

A member noted that the investigator needs to revise the submission form to include updated methods of treatment for exposures.

The Committee discussed documentation of waste disposal. The Committee requested that the investigator confirm location and documentation of waste disposal. Live bacteria and tissue harvests containing live cultures must be disposed of in [redacted] or in [redacted], both of which document autoclaving and disposal.

Pending Condition:

1. The Institutional Animal Care and Use Committee (IACUC) must approve the corresponding amendment to ACUP [redacted].

2. Kristen DeBord and Olaf Schneewind need to sign the staff signature page.

3. In Section VII, question 10, under 'Other', the investigator needs to list the antibiotics that are listed in Supplemental Form B, Section VII, question 12.

4. The investigator needs to confirm that all waste containing live *Salmonella typhimurium* generated in [redacted] will be disposed of in accordance with the practices established for that facility. Additionally, please confirm that all waste containing live *S. typhimurium* generated in [redacted] will be disposed of in accordance with the practices established for that facility.

Stipulation:

1. Properly packaged vials containing live *Salmonella typhimurium* may be stored in the laboratory however opening vials of live *S. typhimurium* is restricted to a biosafety cabinet in [redacted] In addition, all tissue harvested from mice infected with live *S. typhimurium* must be

properly packaged for transport in [redacted] before transporting to [redacted] but may be stored in the laboratory.

551 Renewal/DiRienzo, Anna/ *Approved* (12-0-0)

The goal of this protocol is to study variation and linkage disequilibrium. Genomic DNA or mRNA will be extracted from tissue or lymphoblastoid cell lines, amplified and cloned. Clones will be used for sequencing, genotyping or expression in mammalian cell lines. All cell lines will be handled at BL2. The PI has confirmed that all staff will have appropriate training for work with human and non-human primate blood and cell lines.

The Committee recommended approval.

840 AD 01/Li, Yan-Chun/ *Approved* (12-0-0)

This amendment involves administration of replication-deficient recombinant adenovirus to mice for the treatment of alopecia. The vector is a type 5 adenovirus (with E1A and E1B deletions) containing a gene for a vitamin D receptor. The adenovirus will be administered subcutaneously to examine the effects of gene expression on the skin. The investigator describes this as a gene therapy model for alopecia.

The Committee recommended approval.

III. Old Business:

A. Clarification was provided for Protocol 865 AD04, which was discussed at the 10/1/04 meeting. The reviewer indicated that Sendai virus was previously described as a mouse virus which is not infectious to humans; however, further research indicated that the virus is replication competent in primates, causing a self-limiting infection. While the virus is not pathogenic, it can replicate in primates. Sendai virus is currently being used for Croup in Phase I clinical trials.

A member noted that older sources often list Sendai as a potential human pathogen. During outbreaks of disease in Japan in the 1950s, antibodies to the virus were found in patient samples. The medical community became concerned that the virus was crossing species and infecting humans. It was later determined that the antibodies were cross-reacting and not related to human infection.

The reviewer noted that the virus did cause infection in the nasopharynx region when administered to primates. Sendai is currently being administering to humans through the nasal passage as immunization against Croup. While the virus is related to virulent human viruses, there is no evidence of pathogenicity in humans.

The Committee felt that changes to the original recommendation were not necessary. The protocol should still be designated BL1 with BL2 practices.

B. IBC Review of Teaching Activities

The Committee discussed the idea of whether the IBC should review teaching activities that utilize the same agents and materials that the IBC currently reviews when it involves research. While NIH Guidelines require IBCs to review only research protocols, some institutions have also implemented a policy for review of teaching activities. Depending on the institution, the review may fall under the purview of the IBC or of the safety department. At the University of Chicago, the Safety Office

conducts an annual review of all research and teaching laboratories; however, it is unclear whether this process includes an evaluation of the activities in which students would participate.

The Committee discussed the type and number of courses that would need to be reviewed and noted that this may be difficult to determine without contacting each department. Furthermore, the courses could be offered by departments outside of the Biological Sciences Division.

The Committee felt that more information was necessary in order to fully assess the need for review of teaching activities and whether the IBC or University Safety would be the most appropriate entity to assume this responsibility. Additionally, the Committee felt that the decision to provide safety oversight of teaching activity with these biohazardous (i.e., as typically defined by the IBC) should be made by some appropriate University official, yet to be determined, not the IBC. This issue was deferred to the next meeting pending further information.

IV. New Business: None

V. Updates: None

The University of Chicago

Institutional Biosafety Committee

5841 S. Maryland Avenue
AMB S-152 ♦ MC 1108
Chicago, IL 60637

Minutes of December 3, 2004 Meeting
1:00 PM in [redacted]

In attendance:

Voting Members

Kenneth Thompson
Richard Hiipakka
Mark Abe
Malcolm Casadaban
George Daskal
Jean Greenberg
Tong-Chuan He
Helena Mauceri
Mary Ellen Sheridan
Craig Wardrip

Ex-Officio Members

Steve Beaudoin
Russell Herron
David Pitrak

Guest

John Bivona

Staff

Bill Pugh
Pamela Postlethwait
Jennifer Swanson

Absent:

Voting Members

Clara Gartner
James Mastrianni
Louis Philipson
Gopal Thinakaran

Ex-Officio Members

Michael Holzhueter
Markus Schaufele
Steve Seps

Staff

None

I. **Minutes:** The minutes of the November 5, 2004 meeting were unanimously approved (10-0-0) with no corrections, additions or deletions.

II. **Protocol Review:**
The following protocols were reviewed at the meeting, with the disposition noted:

PR# Category/Investigator/*Disposition*

534 Renewal (Response to Conditions)/Mastrianni, James/*Pending Conditions* (8-2-0)

The Committee discussed the investigator's response to the pending conditional letter from the last meeting. The Chair of IBC typically judges the adequacy of investigator responses to Pending-Conditions. All of the "conditions" were deemed adequately addressed by the Chair except for the one requiring the investigator to autoclave waste prior to removal from the laboratory. Due to the nature of the the response, the Chair determined that this required further consideration by the Committee.

The reviewer presented the condition and the investigator's response. At the last meeting, the Committee indicated that an autoclave should be installed in the investigator's laboratory; however, the investigator responded in disagreement, indicating that the BMBL recommends, but does not mandate, installation of the autoclave within the lab. The investigator also provided information from colleagues at the University of San Franscisco who do similar work, but do not have an autoclave within their lab.

In his response, the investigator also indicated space limitations as rationale for not having the autoclave installed in his lab. As per previous conversations between members of the Committee and University Facilities and Operations, installation of an autoclave in this space would be quite problematic. A member felt that it would be reasonable to request a cost estimate and further assessment of the space and types of autoclaves to determine if even a small unit could be installed. Other members noted that a small autoclave may not accommodate the amount of material generated by the investigator.

The Committee discussed the investigator's plan for using the autoclave across the hall. The plan includes procedures for transporting the materials and scheduling the autoclave cycle. Some members still questioned whether or not safety could be ensured, as the autoclave room is a multi-purpose area to which other investigators have access. Other members felt that using this room would be acceptable, but only under certain conditions determined by the Committee.

The Committee discussed and voted on the motion to require an autoclave in the investigator's lab. This motion was denied. (2-4-4)

The Committee discussed whether or not the investigator should provide cost estimates for installation of an autoclave in the lab. The Committee felt that they did not have the authority to require a cost estimate and the motion did not receive a second.

While the Committee felt that the safest option would be to install an autoclave in the lab, the investigator would be allowed to use the autoclave across the hall under the following conditions: The room must be locked during the autoclave cycle, and the lock must be a separate lock to which only the investigator and his staff have access; Properly trained staff must supervise the autoclaving process, being present for the start and end of the cycle; The investigator must submit a formal SOP for transport of material across the hall; All autoclaving must be documented and a 3-month report must be submitted to the Committee. (8-2-0)

Pending Conditions:

The protocol resubmission was reviewed at the October 1st meeting at which time the Committee requested an autoclave be contained within the laboratory in [redacted] in order to autoclave prion

contaminated waste out of the facility rather than transporting it to a multi-use facility across the hall. The following questions from the Committee are in response to additional information submitted by the investigator to address the issue regarding location of the autoclave.

Follow-Up Questions:

1. It is understood that the room containing the autoclave is in a corridor posted as restricted, however there is no entry barrier to this corridor. The Committee has concerns regarding access of the room by individuals not associated with the laboratory. Therefore, the Committee requests that the room be locked while prion contaminated materials are being autoclaved and an individual from the laboratory be present at the cycle's end to ensure the autoclave has functioned within specifications.

2. The Committee requests that in conjunction with University Safety & Environmental Affairs Office, a standard operating procedure (SOP) be developed for the transport and autoclaving of prion contaminated waste materials. Please contact John Bivona at 4-1130. Please note that records will need to be kept documenting the proper functioning of the autoclave. After 3 months, the Committee requests a report detailing any problems associated with the transport and autoclaving procedures.

572 Renewal/Prince, Victoria/*Approved with Comment* (10-0-0)

This protocol involves cloned zebrafish transcription factor genes, and their injection to create transgenic zebrafish. It was stated that cloned transcription factor genes could act as oncogenes, but that this has not been reported for zebrafish. As such, this would qualify as BSL1. However, the reviewer felt that it would be prudent, although not mandatory, to use BL2 practices such as sharps precautions and autoclave disposal.

The Committee discussed cases in which transgenic zebrafish were found in pet shops and the general population. The Committee felt that a warning comment should be added to the approval to ensure that the fish are not released into the environment.

Comment:

Given recent reports regarding the finding of transgenic zebrafish (particularly zebrafish expressing fluorescent proteins) in the general population, the Committee recommends reminding staff personnel that these fish should not be adopted as pets or released into the environment.

826 Amendment 01/Vezina, Paul/ *Approved* (10-0-0)

This amendment involves the addition of staff, change in room, change in transport and a change in the protocol. As the investigator's lab area is currently under renovation, he is requesting approval to transfer his work to another room in [redacted]. An appropriate route of transport is described in the amendment. The investigator also indicates that he will now be using full vials of the agent rather than small aliquots. A member questioned whether the disposal of vials was discussed in the original protocol. The protocol states that vials will be soaked in bleach overnight and either autoclaved or discarded as biohazardous material. The Committee found this method to be acceptable.

The Committee recommended approval.

III. Old Business: IBC Review of Teaching Activities

Representatives from the University Safety Office discussed the Laboratory Review Program. While teaching facilities are inspected annually, teaching activities are not reviewed, as this does not fall under the purview of the Safety Office. In order to assess the use of biohazards in teaching activities and the potential need for review of such activities, the Biosafety Officer and IBC Administrators will develop a survey that will be sent to faculty members. This issue was deferred to the next meeting, at which preliminary data from the surveys will be presented.

IV. New Business:

A. Revisions to Supplemental Form B

Administrative staff requested permission to revise Supplement B to indicate that a narrative is not necessary for BL1 protocols. The Committee felt that the change was appropriate.

B. Discussion of IBC Review Process

The Committee discussed the IBC review process and considered changes to the policy. Currently, protocols that have associated ACUPs are reviewed by two Committee Members, one being a veterinarian. As animal work will be reviewed in detail by the IACUC, and as all members receive copies of all protocols, the Committee felt that these protocols would not have to go to a veterinarian reviewer. With the exception of clinical protocols, the Committee agreed that IBC protocols would be assigned to only one reviewer. (10-0-0)

V. Updates: IBC Protocol 863—Principal Investigator: Hedy Kindler

Dr. Pitrak provided the Committee with an update on the status of IBC protocol 863, which was originally reviewed at the 10/1/04 meeting. This protocol involves the use of vaccinia virus as a vaccine for patients with metastatic prostate cancer. The virus is attenuated but has been modified to express tumor antigens. After receiving this vaccine, patients will also receive a fowlpox vaccine.

The main issue at the 10/1 meeting related to the potential infectivity of the virus and the need for a vaccination program at the institution. The investigator responded that a vaccination program was not necessary and recommended that members of the Committee speak with representatives from the sponsor.

After discussing the Committee's concerns with the Chief Medical Officer and Chief of Manufacturing for the sponsor, Therion Biologics, Dr. Pitrak indicated that there is still some risk associated with the use of this vaccine, but the chance for secondary spread seems to be reduced compared to the Dryvax vaccine that is used for smallpox vaccination. As indicated by the sponsor, vaccination is required for individuals who are doing animal work with this vaccine and who are involved in manufacturing. Health care workers who will be administering the vaccine to patients should be offered vaccination, but are not required to be vaccinated.

This trial is currently being conducted at other institutions. Contact information for some of the study sites has been provided so that further information can be gathered. Dr. Pitrak will contact these sites and ask the following questions:

1. Do you recommend or require personnel who will be giving the vaccine or evaluating the patients to receive the Dryvax Vaccinia vaccine?

2. What site do you use for subsequent clinic visits in order to evaluate the inoculation site and general condition of the vaccinated patient?

3. Do you let patients who have received this vaccine go to the clinics where other immunocompromised hosts may come in contact with the vaccinated patient?

4. What contingencies are in place for patients who have to be seen outside of the schedule of events for the study protocol?

5. What mechanisms do you use to insure that there are no susceptibles at home?

Additional information will be provided to the Committee upon receipt of responses from the other study sites and the updated version of the Investigator's Brochure that contains new safety data.

The University of Chicago

Institutional Biosafety Committee

5841 S. Maryland Avenue
AMB S-152 ♦ MC 1108
Chicago, IL 60637

Minutes of January 7, 2005 Meeting
1:00 PM in [redacted]

In attendance:

Voting Members		Ex-Officio Members
Richard Hiipakka	Tong-Chuan He	Russell Herron
Mark Abe	Helena Mauceri	David Pitrak
George Daskal	James Mastrianni	Steve Seps
Clara Gartner	Mary Ellen Sheridan	
Jean Greenberg	Gopal Thinakaran	

Guest	Staff
John Bivona	Bill Pugh
	Pamela Postlethwait
	Jennifer Swanson

Absent:

Voting Members	Ex-Officio Members	Staff
Kenneth Thompson	Steve Beaudoin	None
Malcolm Casadaban	Michael Holzhueter	
Louis Philipson	Markus Schaufele	
Craig Wardrip		

I. **Minutes:** The minutes of the December 3, 2004 meeting were unanimously approved (10-0-0) with no corrections, additions or deletions.

II. **Protocol Review:**
The following protocols were reviewed at the meeting, with the disposition noted:

PR# Category/Investigator/*Disposition*

851 New/Fu, Yangxin/*Approved with Recommendation* (10-0-0)

The research will involve the use of Influenza A virus to study the role of lymphotoxin in CD8 T cell-mediated protection, development of vaccines and development of methodologies to interfere with virus production.

The Committee discussed biosafety concerns related to use of the agent. The virus is an attenuated, mouse-adapted strain that was generated by a lab at MIT. Based on previous references, the virus appears to be safe and will not infect humans. A member noted that these strains have been used in labs for research purposes with no reported incidents of human infection.

The Committee recommended that the research staff be offered flu vaccine. The Committee noted, however, that the level of protection provided by the current vaccine cannot be determined, as the protocol does not include information on H and N types of this strain.

Recommendation:
The Committee recommends that all staff members working with this agent receive an influenza vaccination.

872 New/Fu, Yangxin/*Pending Conditions* (10-0-0)

This research will investigate the role of the tumor necrosis factor (TNF) family member LIGHT in T cell mediated protection against tumor progression. The investigator proposes to generate tumors in mice using a murine Ag104 tumor cell line, then use replication deficient adenovirus (Ad5 with E1/E3 deletions) to deliver a mutant form of LIGHT (lacking key proteolytic site) into the tumor(s). The mice will be sacrificed and tissues will be harvested for analysis. It also appears that the investigator will infect the Ag104 tumor cells *in vitro* prior to injecting them subcutaneously into the mice. An amendment to ACUP [redacted] to use replication deficient adenovirus in mice has been submitted.

The investigator plans to verify that the viral preparations do not contain replication-competent virus using a basic plaque assay. Plaques are only formed when the virus infects the cells, replicates and kills the cells. The absence of plaque formation should indicate replication defective viral preparations.

The virus will be made in the investigator's lab but will be shipped to National Cell Culture Lab for amplification and purification of the virus. The investigator has indicated that DOT/IATA training will be completed by all staff members working with the adenovirus.

A member questioned decontamination methods described in the research summary. The investigator indicates that adenovirus and PBS wash supernatants will be suctioned off into a detergent containing sealed flask. The Committee felt that it would be more appropriate to aspirate into a flask containing bleach.

An IRB exemption has been obtained for use of human cell lines. However, this protocol is pending IACUC approval.

Pending Conditions:

1. In Section IV, Research Summary, under Methods, item d needs to be revised to indicate that the adenovirus and the PBS wash supernatants will be aspirated into a flask containing a 1:10 dilution of bleach rather than a detergent-containing flask.

2. The Institutional Animal Care and Use Committee (IACUC) must review and approve the use of adenovirus in animals.

873 New/Glynn, Loretto/*Pending Conditions* (10-0-0)

This research will assess the effect of high molecular weight polyethylene glycol (PEG) on development of necrotizing enterocolitis (NEC) in rats. Rat pups will be taken by cesarean section and fed a select diet that includes DH5α E. coli, which is not considered to be a high-risk organism. The Committee determined that the protocol could be conducted under BSL1 conditions.

The Committee noted the following deficiencies in the submission form. The investigator needs to provide Dr. Alverdy's contact information and a list of antibiotics that can be used to treat this strain of E. coli.

Pending Conditions:

1. In Section VII, question 14, the investigator needs to provide contact information for Dr. Alverdy.

2. In the Supplemental Form B, Section VII, question 12, the investigator needs to list a few examples of antibiotics that E. coli is susceptible to. Also, this information needs to be included in the Form B narrative.

876 New/Reardon-Alulis, Catherine/*Pending Conditions* (10-0-0)

The research involves the use of lentivirus to transfect cells and whole animals with genes to produce proteins that affect lipid metabolism. Three types of experiments will be conducted. (1)Cultured or primary cells including hepatomas, macrophages, and neuronal cells, will be transfected and studied *in vitro*. (2)Fetal liver cells and bone marrow cells will be transfected, cultured for 20-24 hours, harvested and introduced into mice by retro-orbital sinus injections. The mice will be fed either chow or a high-fat cholesterol diet to determine how the expressed proteins will affect metabolism. Blood will be drawn every four weeks. Animals will be sacrificed 24 weeks later. Tissue will be harvested and transported back to the lab for analysis. (3)The viral vector will be injected directly into mice. Procedures for feeding, blood sampling and sacrifice are similar to experiments involving injection of transduced fetal liver and bone marrow cells.

The reviewer noted that there are inconsistencies in the protocol regarding the use of packaging cell lines. The investigator needs to clarify whether the viral vectors will be generated using stably transfected packaging cell lines or by transient transfection. Additionally, the investigator indicates that the vectors will be produced by recombination, which is incorrect. Therefore, the Committee requested that this section of the protocol be revised accordingly.

The investigator needs to clarify where work will be done. Cell work can be done at BL1 in the investigator's lab. Animal work, however, is considered BSL2 and must be conducted in [redacted]

Pending Conditions:

1. Since the viral vector is not being produced by recombination, the investigator needs to remove the words "by recombination" in the first paragraph in Section IV, Research Summary.

2. In Section IV, Research Summary, the investigator needs to clarify whether the viral vectors are produced by using stably transfected packaging cell lines or produced in cell lines by transient transfection.

3. In the Supplemental Form B for the lentiviral vector, Section VI, question 2 needs to be revised to indicate that these procedures will be carried out in [redacted] rather than [redacted].

877 New/Guevara-Patino, Jose/*Pending Conditions* (10-0-0)

This research involves the use of DNA vaccines for potential cancer therapy. The investigator plans to design, construct and validate the next generation of DNA vaccine for melanoma, prostate lymphoma and colorectal cancer. Confirmation of immongenicity will be evaluated in HLA*0201 transgenic mice. Mice will be immunized with DNA vaccines using a gene gun. Following immunization, animals are either used for tumor challenge experiments or euthanized for tissue harvest.

The Committee noted that no staff members are listed on the protocol. Administrative staff indicated that the PI recently submitted a staff list with signatures.

IACUC approval is pending.

Pending Conditions:
The Institutional Animal Care and Use Committee (IACUC) must review and approve the use of animals in this project.

878 New/Brorson, James/*Pending Conditions* (10-0-0)

The protocol involves the use of replication-defective adenoviral vectors to transfect mouse neurons with wild-type genes of interest (human SOD1, SOD2, catalase and CMVCre) in order to determine the effects of targeted proteins on neuronal activity.

The investigator will get the virus from an outside source, University of Iowa Gene Transfer Core, which will test for replication competence by PCR and plaque assay. The Committee found this to be acceptable.

The investigator was asked to provide additional contact information and he has provided this in the oversight section.

The Committee requested the following revisions to the protocol regarding risk management. The investigator needs to indicate that hazards are unknown, as the consequences of exposure to this agent have not been tested. The section listing PPE should include safety glasses and handwash sink, as these are BL2 requirements. Disposal methods should include general waste and sanitary sewer for decontaminated liquid waste and autoclaving of solid waste.

Pending Conditions:

Section VII of the protocol submission form needs to be revised to address the following issues.

1. The Committee requested that the response to question 4 be revised with a statement such as: "Although there are no known human hazards related to the expression of these transgenes, hazards associated with exposure to this agent are unknown, as the consequences of exposure have not been tested."

2. In question 8, safety glasses and hand wash sink need to be checked, as these are BL2 requirements.

3. In question 13, the investigator needs to check "General Waste and sanitary sewer" for decontaminated liquid waste and "Autoclaving" for solid waste, indicating the appropriate temperature and time. In addition, the Laboratory Biosafety Manual needs to be revised to describe these decontamination and disposal procedures.

561 Renewal/Staley, Jonathan/*Pending Conditions* (10-0-0)

This research will investigate the effects of mutations on spliceosome activity in yeast. The research team will perform *in vitro* reconstitution assays and *in vivo* experiments using recombinant yeast. Proteins involved in spliceosome activity will be produced in E. coli, baculovirus and yeast.

A member noted that baculovirus is replication competent and should be indicated as such in the protocol. In addition, the virus can infect non-insect cells; therefore, the investigator should list other cells, including mammalian, that can be infected by baculovirus.

Pending Conditions:

A revised protocol submission form is needed to address the following issues in section III.

1. Question 4c indicates that baculovirus is replication defective; however, the Committee believed that the virus is replication competent. Therefore, the investigator should check "Yes" for 4c or provide additional information about baculovirus regarding this issue.

2. While baculovirus is unable to replicate in non-insect cells, it can potentially infect other types of cells, including mammalian. Therefore, 5b needs to be revised to indicate other cell types that can be infected by baculovirus.

568 Renewal/He, Tong-Chuan/*Pending Conditions* (9-0-0)

This research will investigate the effect of signaling proteins, in particular Wnt/beta-catenin, on the development and proliferation of human osteosarcoma cells. Cells will be infected with a replication-deficient adenoviral system. Cells will be used for *in vitro* studies. Two types of *in vivo* experiments will also be conducted. (1) Tumor cells will be infected with the adenoviral vectors. The transduced cells will then be injected into mice. (2) Tumor cells will be injected into mice and allowed to grow. The adenoviral vectors will then be injected directly into the tumors.

IRB exemption for use of human cell lines is pending. IACUC approval has already been obtained.

A member noted that Supplemental Form B, question 10, needs to be revised to remove "n/a" and indicate only "needle sticks during subcutaneous injections."

A member questioned whether the investigator should be allowed to transport the animal carcasses from [redacted] to his lab for tissue harvests and further studies. Administrative staff clarified that carcasses are not under the purview of the IACUC. Therefore, the decision must be made by the IBC. After discussing the biosafety concerns, the Committee determined that it would be acceptable for the investigator to transport the carcasses to his lab for further analysis.

The Committee requested that Supplemental Form B be submitted for injection of the adenovirus into the animals.

Pending Conditions:

1. In Supplemental Form B for human tumor cells, the investigator needs to revise section VII, question 10, by stating only "needle sticks during subcutaneous injections."

2. The investigator needs to submit a separate Supplemental Form B for the adenovirus.

3. The investigator needs to submit a copy of the IRB Exemption Letter upon receipt.

666 AD 05/Webb, Gene/*Approval* (10-0-0)

This research involves the use of adenoviral vectors to transfect *in vitro* cultured cell lines and *in vitro* cultured mouse islet cell tissue to assess the function of beta cell kinase 1 (BCK1). In this amendment, the investigator requests approval to utilize a Clontech adenoviral vector system to transfect *in vivo* mouse liver.

The adenoviral vector will be injected into the mice via the tail vein. At several time periods after injection, blood samples for glucose testing will be obtained via tail snips. This work will be conducted in [redacted]. Animals will then be sacrificed for tissue harvest. Tissue will be transported from [redacted] to the investigator's laboratory. As the tissues may be considered hazardous for 3 days after injection, the investigator has agreed to use proper signage to indicate work with biohazardous materials.

The Committee discussed the location of the work and found the rooms to be acceptable, as the biosafety cabinets have been recently certified.

The Committee recommended approval.

766 AD 01/Villereal, Mitchell/*Pending Conditions* (10-0-0)

The research investigates the role of TRPC proteins in signaling pathways in mammalian cells. HEK293 cells are tranfected with antisense contructs to express genes of interest and assess protein function. GST-fusion proteins are used to study protein-protein interaction. In this amendment, the investigator requests approval for the addition of new plasmids (pSilencer 3.1-H1) and the siRNA technique to further explore calcium signaling mechanisms. siRNAs will be expressed in HEK293 cells and in neuronal cells.

IRB exemption is needed for the use of human cell lines. The investigator needs to submit a copy of the exemption letter and a revised protocol submission form including the IRB exemption number and date.

Pending Conditions:

As this protocol involves the use of HEK293 cells, a Claim of Exemption must be submitted to the IRB. Upon receipt of the exemption letter, a copy needs to be submitted to the IBC. In addition, section II of the protocol submission form needs to be revised to include the IRB protocol number and approval date under "Human Cell Lines."

798 AD 01/Qian, Zhijian/*Approval* (10-0-0)

This research investigates the role of FHL2 in the pathogenesis of acute myeloid leukemia by over-expressing the gene in mice. Ecotropic retrovirus is used to express the gene in primary bone marrow cells, which will then be injected into mice. In this amendment, the investigator requests approval for the addition of fetal liver cells.

The Committee recommended approval.

808 AD 02/Baron, Beverly/*Pending Conditions* (10-0-0)

This research investigates the expression of the BCL6 protein and potential target genes of the BCL6 protein. In this amendment, the investigator requests approval for the addition of ecotropic Moloney Murine Leukemia Virus for injection into mice. Mice transgenic for both BCL6 and LMP1 will be studied for lymphoma development and the capacity for lymph node germinal center formation.

The Committee discussed biosafety issues related to use of the virus. While the virus is ecotropic and cannot infect humans, it is replication competent and can be transmitted to other mice in [redacted]. A member clarified that transmission, if any, is generally vertical and [redacted] operating procedures are designed to minimize the risk of animal to animal transmission. The Committee had no additional concerns regarding this issue.

The Committee requested a minor revision to the submission form. The investigator needs to list the virus and the biosafety level in section II.

Pending Conditions:

In Section II, question 2, the investigator needs to check Microorganisms, list Moloney Murine Leukemia Virus (ecotropic) and indicate the biosafety level.

833 AD 03/Abraham, Clara/*Approval* (10-0-0)

This research investigates the role of CD18 in T-cell mediated responses to infection. In particular, the research team studies the ability of CD18-deficient T-cells to mediate effective responses to Listeria infection. Mice are injected with a very small dose of Listeria, which causes an immune response. Spleen and lymph nodes are harvested for analysis. In this amendment, the investigator requests approval for the addition of Flt3L-secreting B16 melanoma cells to expand dendritic cell populations of mice. Dendritic cells will be expanded *in vivo* through subcutaneous injection of B16 melanoma cells which have been stably transfected to over-express Flt3L, a natural growth factor for dendritic cells.

The Committee recommended approval.

782 AD 02/Greenberg, Jean/*Approval* (9-0-0)

The research team investigates the genetic regulation of pathogen resistance and programmed cell death in plants using Arabidopsis thaliana as a model and DNA from the plant pathogen Pseudomonas syringae. In this amendment, the investigator requests approval for the use of DNA from Ralstonia solanacaerum which is highly related to P. syringae. Experiments will involve only DNA from Ralstonia and not whole organism. DNA will be cloned in E. coli. The amendment also involves staff additions.

The Committee discussed biosafety issues related to the sources of DNA and the generation of transgenic plants. The work proposed in this amendment does not affect the risk level. The work can be conducted under BL1 conditions.

The Committee recommended approval.

785 AD 02/Greenberg, Jean/*Approval* (9-0-0)

The research team investigates the genetic regulation of pathogen resistance and programmed cell death in plants using Arabidopsis thaliana as a model and DNA from the plant pathogen Pseudomonas syringae. In this amendment, the investigator requests approval for the use of DNA from Ralstonia solanacaerum which is highly related to P. syringae. Experiments will involve only DNA from Ralstonia and not whole organism. DNA will be cloned in Agrobacteria. The amendment also involves staff additions.

The Committee discussed biosafety issues related to the sources of DNA and the generation of transgenic plants. The work proposed in this amendment does not affect the risk level. The work can be conducted under BL1 conditions.

The Committee recommended approval.

786 AD 02/Greenberg, Jean/*Approval* (9-0-0)

The research team investigates the genetic regulation of pathogen resistance and programmed cell death in plants using Arabidopsis thaliana as a model and DNA from the plant pathogen Pseudomonas syringae. In this amendment, the investigator requests approval for the addition of DNA from Ralstonia solanacaerum which is highly related to P. syringae. Experiments will involve only DNA from Ralstonia and not whole organism. DNA will be used to make transgenic plants. The amendment also involves staff additions.

The Committee discussed biosafety issues related to the sources of DNA and the generation of transgenic plants. The work proposed in this amendment does not affect the risk level. The work can be conducted under BL1 conditions.

The Committee recommended approval.

III. **Old Business:** IBC Review of Teaching Activities

The Biosafety Office has developed a survey to assess the use of biohazards in teaching activities and the potential need for review of such activities. The survey will be posted on the BSD website and an email will be sent to faculty members instructing them to complete the survey. This issue was deferred until preliminary data from the surveys can be presented.

IV. **New Business:** None

V. **Updates:** The Committee was informed that the Office of Biotechnology Activities (OBA) has indicated that site visits will be conducted to assess the function of Institutional Biosafety Committees. The notification did not include details on locations or dates of the visits. The Committee will be updated as new information is received from OBA.

Institutional Biosafety Committee

5841 S. Maryland Avenue
AMB S-152 ♦ MC 1108
Chicago, IL 60637

Minutes of February 4, 2005 Meeting
1:00 PM in [redacted]

In attendance:

Voting Members		Ex-Officio Members
Kenneth Thompson	Tong-Chuan He	Steve Beaudoin
Richard Hiipakka	Helena Mauceri	Russell Herron
Mark Abe	Louis Philipson	Michael Holzhueter
Malcolm Casadaban	Mary Ellen Sheridan	David Pitrak
George Daskal	Gopal Thinakaran	Markus Schaufele
Clara Gartner	Craig Wardrip	Steve Seps

Guests	Staff
Debra Anderson	Bill Pugh
Kristen DeBord	Pamela Postlethwait
Judd Johnson	Jennifer Swanson
Olaf Schneewind	

Absent:

Voting Members	Ex-Officio Members	Staff
Jean Greenberg	None	None
James Mastrianni		

I. **Minutes:** The minutes of the January 7, 2005 meeting were unanimously approved (8-0-0) with no corrections, additions or deletions.

II. Protocol Review:

The following protocols were reviewed at the meeting, with the disposition noted:

PR# Category/Investigator/*Disposition*

The following discussion items pertain to protocols 880 and 881.

The Committee discussed the following items in the [redacted] that have not yet been completed:

The main issue of concern pertained to the test decontamination of the BL3 suite. Results of the test indicated that there were leaks of vaporous hydrogen peroxide (VHP) out of the suite into adjacent areas. The cause of the leaks was determined to be air valves which were not adjusted properly. The valves have been readjusted to reduce flow into the suite. Additionally, a barrier has been placed between the suite and the animal holding area. Design engineers have developed a new sequence of operations so that the suite will exhaust under a slightly negative pressurization mode and this will be tested next week. Other issues discussed were the possible need for more caulking and repair of the autoclave panel which was damaged due to a steam leak. These will all be addressed during the next text decontamination.

The Committee discussed the results of decontamination of the ductwork. During the test, one of the two indicators in the ductwork tested positive. The possible cause of this positive result was that the bioindicator, which is placed downstream of the HEPA filter, may have been covered by duct tape and the VHP could not reach the indicator. This will be re-tested.

The [redacted] report indicated that the system was functioning properly, when in fact there were failures. The Committee expressed concern regarding this language. The Committee was assured by Safety and Environmental Affairs that additional testing is planned and a report of this testing will be sent to the IBC.

The Committee discussed training for individuals who work in or respond to situations involving these facilities. Proper labeling is in place on the roof to indicate biohazardous material and HEPA filters are in glove boxes. HEPA filters will be changed using bag in bag out procedures. A member questioned whether the filters needed to be autoclaved after removal. Since there may be times when the filters are changed without total decontamination of the ductwork, filters will have to be autoclaved. This issue needs to be specified in the SOP.

Testing of the autoclave was discussed. The autoclave is tested monthly using test cultures. There was some concern whether or not the autoclave would ever be tested with actual carcasses. The investigator indicated that carcasses are autoclaved for 3 hours, which is double the amount of time that is actually needed to kill the microorganisms in the carcass. The investigator will confirm that the autoclave is functioning properly.

Updates were provided regarding additional items from the [redacted]. The building automation system has been tested and is now functioning appropriately. All building engineers will be entered into the system by March 1. Select Agent Training of engineering staff is scheduled for next week. Fire Safety training will begin next week. Emergency Power still needs to be tested and confirmed.

The Committee questioned whether or not the Commissioning Agent needed to be notified after all items have been completed and a final commissioning report be obtained. The Committee decided that a report

did not need to be sent back to the Commissioning Agent, unless the Committee finds that additional expertise is necessary. The Committee felt that there is enough expertise on the Committee to adequately evaluate this information.

The investigator will submit a final response to confirm completion of all outstanding items from the [redacted] Additionally, test decontamination and environmental monitoring reports will be submitted to the IBC.

Additional issues were discussed about the protocols:

The main issue of concern related to the need for total decontamination of the facility between agents. The current protocol indicates that total decontamination, including ductwork, will be done annually. Total decontamination between agents will not be performed. The investigator indicated that total VHP decontamination is not necessary when switching from *Yersinia pestis* to any other agent, as *Yersinia* does not survive outside of an animal for very long. However, the Committee felt that the investigator did not provide sufficient scientific justification for not conducting total VHP decontamination when switching from *Bacillus anthracis* to any other agent. The Committee discussed the risk involved with not conducting total decontamination after using anthrax in the lab. Since *Bacillus anthracis* is a spore former, the bacteria may last indefinitely. Some members of the Committee questioned whether surface decon was sufficient. Safety and Environmental Affairs noted that environmental monitoring will be conducted between agents and will determine if total decontamination is necessary. Reports of environmental monitoring will be provided to the IBC. A member noted that the sampling methodology is not clearly described in the protocol, so it is difficult to determine the efficacy of the environmental monitoring. Safety and Environmental Affairs assured the Committee that detailed information regarding the sampling methodology would be incorporated into the standard operating procedure. A member also noted that if total decontamination was not performed when switching from anthrax to any other agent, spores could potentially exist in the ductwork. In the interior lab, all air is exhausted through the biosafety cabinet which contains a HEPA filter. However, there are some air paths out of the facilities, such as in the animal holding area, which do not pass through HEPA filters before entering the ductwork. Ultimately, the Committee decided to require total VHP decontamination when switching from anthrax to any other agent. If the investigator does not agree, he will need to provide further justification. (7-4-1)

The Committee discussed the Fever Watch Protocol. The protocol indicates that all non-vaccinated personnel working with strain AMES will be put on fever watch. A member questioned whether vaccinated staff should also be on fever watch. The investigator indicated that this is not a practice followed by other agencies and institutions. A member also noted that the language in the protocol needs to clarify that fever watch should be for the entire time that staff are working with the agent, not just after work is completed. A member noted that if a research staff member developed a fever and had to visit a clinic outside of U of C, that individual would have to report back to U of C. The University has a policy for cases of this nature and this will be reiterated in the SOPs for this research.

A member noted that a research staff member who had respiratory symptoms, possibly due to *Yersinia* infection, may be putting others at risk if he/she went to UCOM or another clinic. Another member clarified that if the staff member tested positive, everyone who visited the clinic on that day would be contacted for further testing. Additionally, precautions will be taken, for example, patients with respiratory symptoms are given masks upon arrival at the clinic. No further questions were raised about this issue.

A member noted that the *Yersinia* will be passaged in mice to maintain virulence. Blood from the mice will then be transported back to [redacted]. The member questioned whether it would be possible to

keep the stock samples in the small inner lab of [redacted] to limit transport across campus. The investigator clarified that stocks of *Yersinia pestis* and *Bacillus anthracis* cannot be stored in the same area for security reasons. Additionally, the blood samples need to be processed in the [redacted] laboratory. Transport of the samples will only be done when injections are performed. The Committee had no further questions regarding this issue.

Since these protocols have associated IACUC protocols, the Committee requested a detailed list describing all changes to IBC and IACUC protocols to ensure consistency between the documents.

880 New/Schneewind, Olaf/*Pending Conditions and Stipulation* (12-0-0)

This research will involve the study of the pathway that anchors surface proteins to the cell wall envelope of gram-positive bacteria. Different doses of wild type and mutant *Bacillus anthracis* will be injected into mice and guinea pigs to determine if the mutations affect the pathogenicity of the bacteria. Most of the mutations will be in genes that are involved in expression and display of surface proteins. This research also involves the injection of anthrax spores and various inhibitors (single chain antibodies, selected small peptides and small molecules) into guinea pigs to determine if these agents can affect the pathogenesis of the bacteria in the animals.

Pending Conditions:

1. The investigator needs to provide a written report to the Institutional Biosafety Committee (IBC) that addresses the following issues detailed in Appendix E, Response to [redacted]:

   a. In Item #3, "Laboratory Environmental Control and Monitoring", it is indicated that the programming of the remaining dial out pages will be completed by 03/01/2005. The investigator needs to provide confirmation that the programming of the Building Automation System (BAS) has been completed and successfully tested.

   b. In Item #10, "HEPA Filters, Housing", it is indicated that additional training needs to be provided to engineering staff. The investigator needs to provide confirmation that training has been completed. Please note in the report, there are two items listed as #10, Strobic Exhaust Fans and HEPA Filters, Housing.

   c. In Item #11, Bubble-Tight (Bioseal) Dampers, a 03/01/05 completion date regarding the operation of the bubble tight damper is indicated. The investigator needs to provide confirmation of the testing and proper operation of the damper.

   d. In Item #14, Emergency Power, it is indicated that emergency lighting needs to be tested. The investigator needs to confirm that testing has been completed.

   e. In Item #15, Autoclave, the investigator needs to confirm that the autoclave process has been proven with efficacy testing.

   f. In Item #16, Decontamination/Interaction with HVAC System, it is indicated that during a decontamination test with vaporous hydrogen peroxide (VHP) on 12/10/2004, leakage of the VHP was identified. The accompanying [redacted] report identifies leakage occurring around pressure sensors, parts of the autoclave, 2 doors and an electronic

shower sign. In investigator needs to confirm that leakage at these points has been resolved and the facility has been successfully decontaminated.

g. In Item #17, Fire Suppression and Fire Alarm Systems, a completion date of 03/01/2005 for the Chicago Fire Department including the Hazardous Materials Team to receive an orientation to the laboratory is indicated. The investigator needs to provide confirmation that this orientation has been completed.

h. In Item #18, Training of U of C Staff, a completion date of 03/01/2005 for the training of all employees required to work in or respond to situations involving these facilities is indicated. The investigator needs to provide confirmation of completion.

2. A positive result was reported for one of the biological indicators placed in the duct work for the decontamination test performed on December 10, 2004. It is surmised that this may be the result of improper positioning of the indicator rather than failure to appropriately decontaminate the area. It is the Committee's understanding that the decontamination test will be repeated in which the positioning of the indicators will be checked. Once a successful decontamination has been completed, the investigator needs to provide the Committee with the final report.

3. The investigator needs to clarify in the first paragraph of SOP UCOM-SAL-001, Anthrax Fever Watch Protocol, that temperature monitoring must take place every 12 hours while working with the agent and for 10 days after such work. Additionally in the second paragraph, if an individual must report to an emergency room outside of the area, the investigator needs to reference the appropriate University Policy or provide instructions on notifying the University of this occurrence.

4. Section 5.12 (Quarterly Environmental Monitoring Program for Bacillus anthracis and Yersinia pestis) of the University of Chicago Safety Manual indicates that the University Responsibility Official (RO) will report results to the Select Agent Committee and a written report to the University Deans Office and UCH Hospital. The Committee requests that a report also be submitted to the IBC.

5. Since both the IBC and the Institutional Animal Care and Use Committee (IACUC) will review and comment on associated documentation regarding work with this agent, the Committee requests a list detailing all the changes requested by both Committees that have been incorporated into the protocol submission be submitted for inclusion in the protocol file.

6. The IACUC must review and approve the corresponding animal care and use protocols.

Stipulation:

Unless further scientific justification to the contrary can be provided, the Committee requires a complete vaporous hydrogen peroxide decontamination of the facility when switching from experiments utilizing *Bacillus anthracis* to experiments utilizing *Yersinia pestis* before work with *Y. pestis* can commence.

881 New/Schneewind, Olaf/*Pending Conditions and Stipulation* (12-0-0)

The aim of this study is to identify new targets for vaccine and immunotherapies against *Y. pestis* by screening for protective antigens and by elucidating the pathogenic features of immune protection in experimental animals. Surface antigens will be identified. Mice will be immunized and then challenged with *Yersinia*. Animals will also be infected with mutant forms of *Yersinia*.

Pending Conditions:

1. Please provide a written report to the Institutional Biosafety Committee (IBC) that addresses the following issues detailed in Appendix E, Response to [redacted]:

   a. In Item #3, "Laboratory Environmental Control and Monitoring", it is indicated that the programming of the remaining dial out pages will be completed by 03/01/2005. The investigator needs to provide confirmation that the programming of the Building Automation System (BAS) has been completed and successfully tested.

   b. In Item #10, "HEPA Filters, Housing", it is indicated that additional training needs to be provided to engineering staff. The investigator needs to provide confirmation that training has been completed. Please note in the report, there are two items listed as #10, Strobic Exhaust Fans and HEPA Filters, Housing.

   c. In Item #11, Bubble-Tight (Bioseal) Dampers, a 03/01/05 completion date regarding the operation of the bubble tight damper is indicated. The investigator needs to provide confirmation of the testing and proper operation of the damper.

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   e. In Item #15, Autoclave, the investigator needs to confirm that the autoclave process has been proven with efficacy testing.

   f. In Item #16, Decontamination/Interaction with HVAC System, it is indicated that during a decontamination test with vaporous hydrogen peroxide (VHP) on 12/10/2004, leakage of the VHP was identified. The accompanying [redacted] report identifies leakage occurring around pressure sensors, parts of the autoclave, 2 doors and an electronic shower sign. The investigator needs to confirm that leakage at these points has been resolved and the facility has been successfully decontaminated.

   g. In Item #17, Fire Suppression and Fire Alarm Systems, a completion date of 03/01/2005 for the Chicago Fire Department including the Hazardous Materials Team to receive an orientation to the laboratory is indicated. The investigator needs to provide confirmation that this orientation has been completed.

   h. In Item #18, Training of U of C Staff, a completion date of 03/01/2005 for the training of all employees required to work in or respond to situations involving these facilities is indicated. The investigator needs to provide confirmation of completion.

2. A positive result was reported for one of the biological indicators placed in the duct work for the decontamination test performed on December 10, 2004. It is surmised that this may be

the result of improper positioning of the indicator rather than failure to appropriately decontaminate the area. It is the Committee's understanding that the decontamination test will be repeated in which the positioning of the indicators will be checked. Once a successful decontamination has been completed, the investigator needs to provide the Committee with the final report.

3. Please clarify in the first paragraph of SOP UCOM-SAL-001, Anthrax Fever Watch Protocol, that temperature monitoring must take place every 12 hours while working with the agent and for 10 days after such work. Additionally in the second paragraph, if an individual must report to an emergency room outside of the area, the investigator needs to reference the appropriate University Policy or provide instructions on notifying the University of this occurrence.

4. Section 5.12 (Quarterly Environmental Monitoring Program for Bacillus anthracis and Yersinia pestis) of the University of Chicago Safety Manual indicates that the University Responsibility Official (RO) will report results to the Select Agent Committee and a written report to the University Deans Office and UCH Hospital. The Committee requests that a report also be submitted to the IBC.

5. Since both the IBC and the Institutional Animal Care and Use Committee (IACUC) will review and comment on associated documentation regarding work with this agent, the Committee requests a list detailing all the changes requested by both Committees that have been incorporated into the protocol submission be submitted for inclusion in the protocol file.

6. The IACUC must review and approve the corresponding animal care and use protocol.

Stipulation:

Unless further scientific justification to the contrary can be provided, the Committee requires a complete vaporous hydrogen peroxide decontamination of the facility when switching from experiments utilizing *Bacillus anthracis* to experiments utilizing *Yersinia pestis* before work with *Y. pestis* can commence.

662 AD 03/Kang, Un Jung/*Pending Conditions* (11-0-0)

The purpose of this research is to use recombinant viruses to modify gene expression in the rat brain on experimental models of neurodegeneration to produce biological effects. With this amendment, the investigator requests approval to use shRNA sequences for DJ-1 and parkin using adeno-associated virus vectors.

The investigator has indicated that the vectors are replication deficient. The Committee felt that the investigator should add language to describe testing of AAV for replication-competence, and indicate that each batch will be tested.

Members indicated that there are minor inconsistencies in the protocol regarding terminology and Supplemental B needs to be updated.

Pending Conditions:

1. In Section III, question 4a, the investigator needs to provide a description of the replication deficient adenovirus and the replication deficient adeno-associated virus.

2. In Section III, question 4d, the investigator needs to revise to indicate mammalian cells are susceptible however replication only occurs in host cells expressing the genes necessary for replication.

3. In Supplemental Form B, the investigator needs to address the following:

   a. Since vectors will be administered, in Section III, question 2, the investigator needs to indicate 'Yes' and specify the vector and how it is being administered.

   b. It is standard practice in [redacted] to autoclave cages and carcasses out of the facility therefore in Section VII, question 4, the investigator needs to revise to indicate this practice.

   c. In Section VII, question 5, the investigator needs to indicate that cages will be decontaminated by autoclaving.

   d. In Section VII, question 7, the investigator needs to clarify that standard protective clothing for [redacted] is required. Additionally, the protocol indicates the need for safety eyewear when handling virus.

   e. In Section VII, question 16, it is indicated that virus is periodically tested for the ability to infect non-helper cells such as 293 cells however the protocol indicates that 293 is used as the helper cells. The investigator needs to clarify how the virus is tested for replication competency. Also, the investigator needs to clarify if each batch of prepared virus is tested.

   f. As the animal is considered hazardous for 72 hours following the administration of the agent, the information provided in Section VIII, question 1, appears to be incorrect. The investigator needs to clarify who will train the ARC staff.

794 AD 05/Missiakas, Dominique/*Pending Conditions* (11-0-0)

The research objective is to characterize the genetic determinants of the *S. aureus* pathway for protein secretion across the cell wall envelope. With this amendment, the investigator is adding procedures regarding measurement of immune response. Additionally, the investigator has updated the protocol to include information regarding antibiotic resistance and staff participation.

The Committee had no issues regarding the protocol. However, the amendment must be reviewed by the Institutional Animal Care and Use Committee (IACUC) prior to approval by the IBC.

Pending Conditions:

The Institutional Animal Care and Use Committee (IACUC) must review and approve the corresponding amendment to ACUP [redacted].

839 AD 02/Grdina, David/*Approved* (12-0-0)

This research involves the use of plasmid vectors containing the mutated IκBα gene to transfect SA-NH mouse sarcoma cells. The new cell lines are used *in vitro* to determine the activity of the transcription factor NFκB and clonogenic survival following exposure to x-rays. *In vivo* work involves the injection of the cells into mice to determine their ability to spontaneously metastasize and form tumors in the lungs. With this amendment, the investigator wishes to use liposome-encapsulated manganese superoxide dismutase (MnSOD) antisense and scrambled sequence 21 base pair oligonucleotides for injection into tumors to assess the role of MnSOD in preventing metastases formation and Lewis Lung Carcinoma cells.

The Committee recommended approval.

III. Old Business: None

IV. New Business

A. Review of Animal Biosafety Level for Protocol 670—PI: Philip Ashton-Rickardt (11-0-0)

The animal protocol that is associated with this IBC protocol is up for triennial review. There was a question regarding the biosafety level needed for the animal work. The investigator wants to use a viral vector that is identified as Moloney Murine Virus which is strictly a mouse pathogen. However, language that was approved 3 years ago indicates that there is some risk of the virus infecting human cells. A member clarified that this depends on packaging. The protocol did not specify the actual virus, only retrovirus. As written, the protocol would require BL2 conditions and the animals would have to be housed in [redacted]. According to the investigator, the virus itself will not be injected into the mice. Only the cells that have been exposed to the virus will be introduced into the animals. Therefore, lab work would be performed under BL2 but the animal work could be ABSL1. Animals could then be kept in the [redacted]. The Committee determined that BSL2 is appropriate for the lab work and ABSL1 is appropriate for the animal work. (11-0-0)

B. Amendment Review Process

The Committee discussed a change in policy regarding the amendment review process. The Committee determined that minor changes that do not affect risk group or biosafety level can be sent to the Chair for review and approval.

V. Updates: None

The University of Chicago

Institutional Biosafety Committee

5841 S. Maryland Avenue
AMB S-152 ♦ MC 1108
Chicago, IL 60637

Minutes of March 4, 2005 Meeting
1:00 PM in [redacted]

In attendance:

Voting Members

Kenneth Thompson
Richard Hiipakka
Mark Abe
Malcolm Casadaban
George Daskal
Clara Gartner
Tong-Chuan He
Helena Mauceri
Mary Ellen Sheridan
Gopal Thinakaran
Craig Wardrip

Ex-Officio Members

Russell Herron
Michael Holzhueter

Guest

John Bivona

Staff

Bill Pugh
Pamela Postlethwait
Jennifer Swanson

Absent:

Voting Members

Jean Greenberg
James Mastrianni
Louis Philipson

Ex-Officio Members

Steve Beaudoin
David Pitrak
Markus Schaufele
Steve Seps

Staff

None

I. Minutes: The minutes of the February 4, 2005 meeting were unanimously approved (10-0-0) with no corrections, additions or deletions.

II. Protocol Review:
The following protocols were reviewed at the meeting, with the disposition noted:

PR# Category/Investigator/*Disposition*

879 New/Nash, Piers/*Pending Conditions* (11-0-0)

This research involves the use of adenoviral vectors and TAT-protein. The research team studies protein-protein interactions involved in signal transduction.

A member noted that there are inconsistencies in the protocol regarding animal work. Administrative staff clarified that the investigator had originally planned to use mouse tissue but has since decided to use only cell lines from ATCC. Therefore, references to animal work need to be removed from the protocol submission form.

The Committee discussed the investigator's methods for decontamination and requirements for personal protective equipment. Information provided in the protocol does not conform to the Minimum Guidelines for TAT Protein Use. Therefore, the investigator needs to revise the protocol to be consistent with these guidelines.

A member noted that Section VII, question 4, should include a description of the hazards associated with the recombinant adenovirus.

The Committee recommended approval after the noted issues have been appropriately addressed.

Pending Conditions

1. It is the Committee's understanding that mice and tissue harvested from mice will not be utilized in the initial phases of this project but rather will entail the use of commercially available lines. Therefore in Section II, the reference to the use of animal tissue needs to be removed and in Section IV, the reference to *in vivo* work needs to be removed. Prior to initiation of work involving animals or animal tissue, there must be an approved animal care and use protocol and the biosafety protocol must be amended.

2. In Section VII, question 4, the possible consequences of exposure to wild-type adenovirus is clearly specified however the possible consequence of exposure to the replication deficient recombinant adenovirus indicates only that risk depends on dose and nature of the transgene. The investigator needs to elaborate on the risk of exposure to the replication deficient recombinant adenovirus and the transgenes.

3. The investigator needs to revise Section VII to comply with the attached Minimum Guidelines for TAT Protein Use. Specifically, the following need to be addressed:
    - In Section VII, question 6, the investigator needs to indicate that the Minimum Guidelines for TAT Protein Use will be followed in the handling of the TAT and TAT-fusion proteins.
    - The personal protection specified in Section II.B of the TAT Guidelines needs to be indicated in Section VII, question 8.
    - The decontamination and disposal procedures specified in Sections III and IV of the TAT Guidelines, respectively, need to be indicated in Section VII, questions 9, 12 and 13 where appropriate.

882 New/Lang, Deborah/*Pending Condition* (11-0-0)

This research involves the use of recombinant DNA, mouse cell lines and transgenic mice to study PAX3 protein interactions.

Administrative staff noted that the protocol has yet to be reviewed by the Institutional Care and Use Committee (IACUC). The Committee had no other issues with this protocol and recommended approval after the investigator has received approval from IACUC.

Pending Condition:

Approval by the Institutional Biosafety Committee (IBC) is contingent upon approval by the Institutional Care and Use Committee (IACUC).

565 Renewal/Hoff, Wouter/*Approved* (11-0-0)

This research involves the use of plasmid vectors to express photoactive yellow proteins (PYPs) from *Halorhodospira halophila* in *E. coli*. PYPs will be purified for spectroscopic studies. The investigator also plans to examine swimming behavior in *H. halophila*.

The Committee had no issues with this protocol and recommended approval.

570 Renewal/Thinakaran, Gopal/*Pending Conditions* (10-0-0)

This research involves the use of cultured human and animal cell lines and transgenic mice to study underlying mechanisms of Alzheimer's disease and related neurological disorders.

The Committee discussed the use of African monkey kidney COS cells in this research. Typically, when a protocol involves the use of non-human primate tissue or cells, the Institutional Animal Care and Use Committee (IACUC) requires investigators to submit a Tissue Use Short Form. The main purpose of this form is to ensure proper oversight when tissues or cells are being directly harvested from the animals. When this resubmission was initially submitted, it was unclear whether investigators who purchased non-human primate cell lines from commercial sources would also be required to submit the form. The IACUC has since revised the policy to require Short Form submission for use of tissue, preserved vertebrates, or non-human primate primary cells that are directly isolated from animals or tissues. Therefore, since this research involves non-human primate cell lines purchased from ATCC, the Short Form is not necessary. The Committee had no further comments regarding this issue.

A member noted that "etc" is used in the protocol submission form and recommended that it be replaced with complete information or be removed.

The Committee recommended approval after the noted issues have been appropriately addressed.

Pending Conditions:

The investigator needs to submit a revised Protocol Submission Form to address the following issues:

1. In section III, questions 3 and 9a, the investigator needs to replace "etc" with complete information or remove the term entirely.

2. In section IV, paragraph 1, line 3, the investigator needs to replace "etc" with complete information or remove the term entirely.

571 Renewal/Thinakaran, Gopal /*Pending Conditions* (10-0-0)

This research involves the use of cultured human and animal cell lines to investigate biogenesis/folding, secretory trafficking and metabolism of amyloid precursor protein. Plasmid or retroviral vectors will be used to express wildtype and mutant proteins.

The Committee noted that this protocol involves the use of non-human primate cell lines that have been purchased from a commercial source. The investigator is not required to submit a Tissue Use Short Form to the Institutional Animal Care and Use Committee (IACUC).

A member noted that "etc" is used in protocol submission form and recommended that it be replaced with complete information or be removed.

The Committee recommended approval after the noted issues have been appropriately addressed.

Pending Conditions:

The investigator needs to submit a revised Protocol Submission Form to address the following issues:

1. In section III, questions 3, 4 and 9a, the investigator needs to replace "etc" with complete information or remove the term entirely.

2. In section IV, end of paragraph 1, the investigator needs to replace "etc" with complete information or remove the term entirely.

574 Renewal/Schwartz, Eric/*Approved* (11-0-0)

This research involves the use of transgenic zebrafish and human cell lines to study vesicle cycling in photoreceptor cells of the vertebrate eye. The Avian Leukosis and Sarcoma Virus will be used to transfect cells.

The Committee questioned whether this virus was on the USDA list of prohibited agents and requested that administrative staff look into this issue further prior to granting approval.

III. Old Business: None

IV. New Business: Transport of Biohazardous Animals—R. Weichselbaum (Protocols 633 and 686)

As part of the triennial review of ACUP [redacted] (Gene Therapy for Metastatic Adenocarcinoma), the Institutional Biosafety Committee reviewed new routes of animal transport that are now required by the Section of Infectious Disease. Following discussion, the Committee approved the new route of transport of biohazardous animals to [redacted] and [redacted]. (11-0-0)

Recognizing that these routes were applicable to all of the investigator's IBC and IACUC protocols, the Committee agreed to grant a blanket approval for the new route of transport. A letter will be sent to the investigator to indicate the approved route of transport for all of these protocols.

V. Updates:

A. Environmental Monitoring Report: [redacted] ABSL3 Facilities

As stipulated in Dr. Schneewind's protocols, the Committee will receive quarterly environmental monitoring reports of the BL3 facilities. The Committee reviewed and discussed the first monitoring report that was received from the Safety Office. The Biosafety Officer indicated that the methods used to monitor the facilities are based on CDC recommendations. Samples were analyzed by U of C and an outside laboratory and were found to be negative for the agent. A member questioned whether the monitoring methodology included the use of positive controls, as this was not clear from the report. The Biosafety Officer will query the testing laboratories and provide additional information to the Committee upon receipt.

B. Preliminary Data from Teaching Surveys

The Biosafety Officer updated the Committee on preliminary survey results regarding the use of biohazards in teaching activities. The survey was sent to all faculty members and 24 responses have been received, some of which indicate the use of biohazards in teaching. A second attempt will be made to obtain results from faculty members who did not respond to the initial survey.

As preliminary survey results did indicate some use of biohazards in teaching, the Committee discussed possible options for oversight of such activities. While federal regulations do not require the IBC to review and approve teaching activities, members of the Committee felt that the University should take a proactive approach to ensure the safety of University employees and students. For example, rather than requiring faculty to submit protocols to the IBC, the University could develop policies and/or guidelines for the use of biohazards in teaching. Additionally, biohazard training could be required of all faculty members and teaching assistants.

As the use of biohazards in teaching cannot be fully determined due to incomplete survey results, the Committee deferred the issue until more information can be presented.

The University of Chicago

Institutional Biosafety Committee

5841 S. Maryland Avenue
AMB S-152 ♦ MC 1108
Chicago, IL 60637

Minutes of April 1, 2005 Meeting
1:00 PM in [redacted]

In attendance:

Voting Members		Ex-Officio Members
Kenneth Thompson	Tong-Chuan He	Russell Herron
Richard Hiipakka	Helena Mauceri	David Pitrak
Mark Abe	Louis Philipson	
Malcolm Casadaban	Mary Ellen Sheridan	
George Daskal	Gopal Thinakaran	
Clara Gartner		

Guest	Staff
John Bivona	Bill Pugh
	Pamela Postlethwait
	Jennifer Swanson

Absent:

Voting Members	Ex-Officio Members	Staff
Jean Greenberg	Steve Beaudoin	None
James Mastrianni	Michael Holzhueter	
Craig Wardrip	Markus Schaufele	

I. **Minutes:** The minutes of the March 4, 2005 meeting were unanimously approved (9-0-0) with no corrections, additions or deletions.

II. **Protocol Review:**
The following protocols were reviewed at the meeting, with the disposition noted:

PR# Category/Investigator/*Disposition*

883 New/Rebay, Ilaria/*Approved* (11-0-0)

This research involves the study of gene expression during development using *Drosophila* as a model system. In particular, the research team investigates how the activity of transcription factors is modulated during *Drosophila* eye development.

The Committee discussed whether the protocol also needed to be submitted to the Institutional Animal Care and Use Committee (IACUC). As this protocol does not involve work with vertebrate animals, IACUC approval is not needed.

The Committee had no issues with the protocol and recommended approval.

884 New/Puri, Neelu/*Pending Condition* (11-0-0)

This research involves the study of telomere 3' overhang DNAs and their effect on melanoma. Plasmid vectors containing inserts for mutated tumor suppressor genes (p53 and p73) will be used to transfect melanoma cells, which will subsequently be exposed to T-oligo and evaluated for apoptosis.

A member noted that the "Microorganisms" box needs to be checked in the protocol. In addition, the Committee requested that the investigator check "yes" for the use of oncogenes, as mutated forms of p53 and p73 could lead to oncogenesis.

The Committee recommended approval after the noted issues have been appropriately addressed.

Pending Condition:

1. In Section II, question 2, the investigator needs to check the 'Microorganisms' box.

2. In Section III, question 3b, the investigator needs to indicate 'Yes' and indicate that p53 and p73 are tumor supressor genes and not oncogenes. However, it should be noted by the investigator that mutant forms of these genes may result in loss of tumor suppression and lead to oncogenesis.

580 Renewal/Abe, Mark/ *Pending Condition* (10-0-0)

This research involves the characterization of signaling pathways involving ERK7 and ERK8 and identification of signaling intermediates that interact with these proteins to determine how they regulate lung cell differentiation. Characterization of signaling pathways involved in airway epithelial cell cytokine expression will also be examined. The investigator plans to use shuttle and/or expression vectors for *in vitro* studies with bacteria, yeast and/or mammalian cells.

The Committee discussed areas that needed to be addressed by the investigator. In Section III of the protocol, question 9a, the phrase "and other signaling molecules" should be specified. In question 5, mice should be listed, as transgenic mice will be generated. Additionally, IACUC approval is needed.

The Committee recommended approval after the noted issues have been appropriately addressed.

Pending Condition:

1. In Section III, question 5, the investigator also needs to include mice.

2. In Section III, question 9a, the investigator needs to specify the 'other signaling molecules' or remove the statement.

3. The associated animal care and use protocol (ACUP [redacted]) describing the use of these agents in animals must be reviewed and approved by the Institutional Animal Care and Use Committee (IACUC).

583 Renewal/Wang Chyung-Ru/*Pending Conditions* (11-0-0)

This research involves the use of class Ib-deficient mice and transgenic mice to examine the contribution of MHC class Ib-restricted response during primary and secondary infection by *Listeria monocytogenes*. Liver and spleen will be harvested 3-21 days post injection. Homogenates will be grown on agar plates to evaluate bacterial growth and determine the effect of genotype on *Listeria* infection.

As the investigator plans to conduct work in the [redacted] and [redacted], the Committee requested clarification regarding packaging and transport of the agent.

The Committee discussed language in the protocol regarding pregnant staff members. In a list of issues that will be reviewed with staff, the investigator indicates that pregnant staff members should avoid work on this project. While the language may be important for risk assessment and management, some members questioned its appropriateness from a legal standpoint. Legal assured that the statement was appropriate, as it makes no reference to termination due to pregnancy. The Committee had no further concerns.

The Committee recommended approval after the noted issues have been appropriately addressed.

Pending Conditions:

As work with this agent will be performed in both [redacted] and [redacted], in Section IV, Summary of Research, the investigator needs to include a description of how the agent will be packaged (i.e. triple packaged) for transport to [redacted] and how tissues will be packaged for transport back to [redacted]. Also, the investigator needs to include the route of transport. The investigator needs to be advised that triple packaging requires the agent to be contained within a primary container that is contained within a secondary container containing absorbent packing material which is then contained in a durable outer package and each is labeled with a biohazard sticker.

584 Renewal/Hamann, Kimm /*Pending Conditions* (10-0-0)

This research will investigate the effects of PLA2, H-Ras signaling proteins and PI3 kinase on IL-5 induced eosinophil adhesion and other functional activities to determine whether these proteins can block antigen-induced airway eosinophilia and hyperresponsiveness in mice.

The reviewer noted that the investigator will need to obtain an exemption from the Institutional Review Board (IRB) for the use of human cell lines.

The Committee discussed several issues that need to be resolved in the protocol. Handling of waste and packaging/transport of the agent need to be described, [redacted] needs to be listed on page 1, and "Animal Tissue" needs to be checked in Section II.

The Committee recommended approval after the noted issues have been appropriately addressed.

Pending Conditions:

1. In Section I, the investigator needs to include [redacted] in the 'Location of Proposed Work/Experiments' section.

2. In Section II, question 2, the investigator needs to check the 'Animal Tissue' box.

3. In Section IV, Summary of Research, the investigator needs to describe how the agent will be packaged (i.e. triple packaged) for transport to [redacted] and how harvested tissue will be packaged for transport to the laboratory. Also, the investigator needs to include the route of transport. The investigator needs to be advised that triple packaging requires the agent to be contained within a primary container that is contained within a secondary container containing absorbent packing material which is then contained in a durable outer package and each is labeled with a biohazard sticker.

4. The investigator needs to provide a letter of exemption from the Institutional Review Board (IRB) for the use of human cells lines.

587 Renewal/Strauss, Bernard/*Approved* (11-0-0)

This research involves the systematic mutagenesis of *E. coli* by random insertion of a transposon and identification of the insertion sites by sequencing. The investigator plans to use bacteriophage P1 for the insertion.

The Committee had no issues with the protocol and recommended approval.

811 AD 03/Abe, Mark/ *Pending Condition* (10-0-0)

This research involves the characterization of signal transduction proteins ERK7 and ERK8 through the transfection of cultured cells using retroviral vectors. With this amendment, the investigator requests approval for the use of lentiviral vectors to transfect non-dividing or slowly dividing cells, addition of a tetracycline-inducible retroviral system, and addition of a new staff member.

Administrative staff noted that IACUC approval is pending.

The Committee recommended approval after the noted issues have been appropriately addressed.

Pending Condition:

The associated animal care and use protocol (ACUP [redacted]) describing the use of these agents in animals must be reviewed and approved by the Institutional Animal Care and Use Committee (IACUC).

III. Old Business: None

IV. New Business: None

V. Updates:

A. NIH Update

The Director of Regulatory Compliance for Laboratory Programs provided a summary of a recent conversation he had with Allan Shipp from the NIH Office of Biotechnology Activities regarding the IBC review process. All IBC protocols, except those exempt from the NIH guidelines, must be reviewed at a full committee meeting. Currently, the IBC is not allowed to approve protocols through an expedited review process. As the Institutional Animal Care and Use Committee (IACUC) and the Institutional Review Board (IRB) have successfully implemented policies for expedited review, it seems reasonable that the IBC could do the same. Allan Shipp indicated that he would consider this issue.

B. Use of Biohazards in Teaching

The Biosafety Officer provided an update regarding the use of biohazards in teaching. The Safety Office will be developing a biosafety training program for Teaching Assistants. The training will be offered through a full day course in biosafety; chemical hygiene; fire safety; Hazard Communication (HAZCOM); Personal Protective Equipment (PPE); and spill clean-up, and will be taught through lecture and hands-on activities. The Safety Office will develop a plan for identifying and contacting the individuals who would be required to complete the training. The Biosafety Officer will update the Committee as more information becomes available.

C. Environmental Monitoring Report for ABSL3 Facilities

At the IBC meeting of 3/4/05, the Biosafety Officer presented results of environmental monitoring in the ABSL3 facilities. While the agent was not detected in the samples, it was unclear from the report if positive controls were used in the analysis. After contacting the testing laboratories, the Biosafety Officer confirmed that positive controls were used.

The University of Chicago

Institutional Biosafety Committee

5841 S. Maryland Avenue
AMB S-152 ♦ MC 1108
Chicago, IL 60637

Minutes of May 6, 2005 Meeting
1:00 PM in [redacted]

In attendance:

Voting Members

Kenneth Thompson
Richard Hiipakka
Mark Abe
George Daskal
Jean Greenberg
Tong-Chuan He
James Mastrianni
Helena Mauceri
Louis Philipson
Gopal Thinakaran

Ex-Officio Members

Russell Herron
David Pitrak
Markus Schaufele

Guest

John Bivona
Lois Zitzow

Staff

Bill Pugh
Pamela Postlethwait
Jennifer Swanson

Absent:

Voting Members

Malcolm Casadaban
Clara Gartner
Mary Ellen Sheridan
Craig Wardrip

Ex-Officio Members

Steve Beaudoin
Michael Holzhueter

Staff

None

I. Minutes: The minutes of the April 1, 2005 meeting were unanimously approved (8-0-0) with no corrections, additions or deletions.

II. Protocol Review:
The following protocols were reviewed at the meeting, with the disposition noted:

PR# Category/Investigator/*Disposition*

885 New/Ho, Robert/*Pending Conditions (8-0-0)*

This research involves the production of transgenic fish to study transcription factors, gene function and gene regulatory elements. The research team will perform microinjections of embryos for embryonic studies and creation of transgenic lines.

The Committee requested that the investigator provide more information about the transcription factors and fluorescent proteins to be studied in the research.

The Committee recommended approval after the noted issues have been appropriately addressed.

Pending Conditions:

In Section III, question 3, the investigator needs to provide a concise list of the transcription factor genes and the fluorescent protein genes to be utilized in this project.

886 New/Lengyel, Ernst/*Pending Conditions (8-0-0)*

This research will involve the use of human ovarian cancer cells in mice to study potential new treatments related to signaling receptors and adhesion molecules (integrins) specific to the tumor growth. These studies will use several tumor lines, three of which are named in the protocol: SKOV-3, CAOV-3 and ID-8 (another line named OVMZ-6 has been eliminated from use due to Mycoplasma contamination in cultures). The research group will produce small-interfering RNA (siRNA) molecules, using BSL-1 techniques and commercially available kits containing E. coli. The effect of the siRNAs will be to interfere with various tumor cell receptors, such as tyrosine-kinase c-Met. These siRNA molecules will be delivered to human tumor cells in culture or to human tumor cells implanted into nude mice, using a replication-defective adenoviral vector, in order to evaluate their ability to stop or slow tumor growth. Injection of tumor-bearing mice will be accomplished under ABSL-2 conditions in [redacted]. Batches of viral preps will be tested for presence of deleted E1 and E3 genes (which might indicate reversion to replication competence) before use. Decontamination processes are appropriately described for BSL-1 bacterial work, and BSL-2 viral work, respectively. Potential risks to humans are addressed well in the protocol – no gene expression in the animals or viral shedding from the animals is expected. Needlesticks are not a risk for caretakers, and the risk to investigators is minimal: collaborators of the PI at another institution have injected these siRNAs into human volunteers with no effect from down regulation of c-Met apparent.

A member noted that the investigator has checked BL1 and BL2 and questioned whether only the highest level should be checked. As the investigator is working with E. coli which is RG1, and adenovirus which is RG2, some members felt that it was appropriate to check both. Other members felt that the investigator should check only one box to account for the highest biosafety level needed for this research. As the form is unclear, the Committee did not request a change by the investigator; however, administrative staff will revise the form for better clarity.

The Committee noted several issues that needed to be clarified. The investigator needs to indicate the location where work will be conducted, describe transport of the agent to [redacted], indicate time to sacrificed after injection, and describe packaging and transport of carcasses. In addition, under PPE, "mask" needs to be checked for work with adenovirus and animals

The Committee recommended approval after the noted issues have been appropriately addressed.

Pending Conditions:

1. In Section IV, Research Summary, the investigator needs to include a description of how the agent will be packaged (i.e. triple packaged) for transport to [redacted] and how carcasses will be packaged for transport to [redacted]. Also, the investigator needs to include the route of transport. The investigator should be advised that triple packaging requires the agent to be contained within a primary container packaged within a secondary container with absorbent packing material which is placed in a durable outer container and each being labeled with a biohazard sticker.

2. In Section IV, Research Summary, the investigator needs to clarify the time to sacrifice following injection of the adenoviral vector.

3. In Section VII, question 8, the investigator needs to check 'Mask'.

4. In Supplemental Form B, question 2, the investigator needs to specify [redacted].

5. In Supplemental Form B, question 3 indicates that animal carcasses will be transported to [redacted]. The investigator needs to indicate what building. Also, the investigator needs to specify that the carcasses will be transported in closed containers.

887 New/Claud, Erika/*Approval (8-0-0)*

This research involves the use of a rat model of necrotizing enterocolitis (NEC) to evaluate potential prevention of this condition in humans with secreted factors from probiotics. Probiotics are naturally occurring bacteria organisms, which may be given in live form orally, in order to colonize or recolonize the gastrointestinal tract. In order to avoid actual bacterial infection, but still provide beneficial effects from bacterially-secreted factors, bacteria (Lactobacillus GG and Lactobacillus plantarum) will be cultured in the PI's lab under BSL-1 conditions. Conditioned media will be sterile-filtered free of live bacteria (tested by culture to prove this), and gavage fed to rat pups stressed by prematurity, hypoxic stress and cold stress to evaluate the efficacy in preventing development of NEC. Standard rat handling and housing in a neonatal incubator in the [redacted] will adequately provide the needed ABSL-1 conditions.

A member questioned whether Supplemental Form B was needed for this protocol. Administrative staff clarified that the form is not needed in this case, as the investigator is not administering identifiable biohazards to the animals.

A member questioned whether the investigator needed to indicate where the Lactobacillus will be grown. The Committee felt that this could be taken care of administratively.

Administrative staff noted that the protocol also needs to be reviewed and approved by the Institutional Animal Care and Use Committee (IACUC); however, in this case, as the animals will be injected with conditioned media and not an identifiable agent, IBC approval is not contingent upon IACUC approval.

The Committee had no issues with this protocol and recommended approval.

569 Renewal/Clark, Marcus*/Pending Conditions (9-0-0)*

This research involves the use of replication-deficient, VSV-pseudotyped retroviral vectors to express mutants of the murine B cell antigen receptor and downstream signaling molecules in murine B cells and primary cells.

The Committee discussed the genes to be expressed. The reviewer had concerns that some of the genes could be oncogenic, but noted that the investigator has removed the use or Ras, a potential oncogene. The Committee discussed the use of dominant and negative cyclins and requested that the investigator fully describe the hazards associated with these transgenes.

The Committee discussed the retrovirus to be used in this research. In the protocol, the investigator indicated that the virus was replication-deficient and provided justification for not testing viral preparations for replication-competent virus. The Committee, however, felt that testing was still necessary and requested that the investigator describe an appropriate method for testing viral preparations. In addition, the Committee felt that more information was needed regarding the hazards associated with this virus, given that it is VSV-pseudotyped and can infect human cells. Therefore, the Committee requested that the investigator discuss the consequences of integration and expression of transgenes in human cells.

A member noted that the investigator plans to decontaminate with 10% bleach for a period of 30 seconds and questioned whether this amount of contact time was adequate. The Committee requested that the investigator revise the protocol to indicate a contact time of at least 10 minutes.

The Committee recommended approval after the noted issues have been appropriately addressed.

Pending Conditions:

1. In Section III of the Protocol Submission Form, question 4c indicates that the MIGRI retrovirus is replication-defective and that recombination events resulting in replication-competent virus would be unlikely. The Committee, however, still requests that viral preparations be tested for replication-competent virus. Therefore, the investigator needs to replace the information in question 4c with appropriate methods for testing viral preparations.

2. In Section VII, question 4, please provide more information regarding the hazards associated with the use of an amphotropic retrovirus. In particular, the investigator needs to describe the consequences of integration and expression of the transgenes in human cells.

3. In Section VII, questions 9 and 12 indicate that bleach will be used for 30 seconds. The Committee recommends that bleach be used for at least 10 minutes. Therefore, the investigator needs to revise the form accordingly.

573 Renewal/Fu, Yang-Xin/ *Pending Conditions (8-0-0)*

This research involves the use of Listeria monocytogenes in a mouse model to study the response of primary and secondary T-cells to intracellular bacteria. Listeria will be cultured and suspended in culture medium for injection into mice. Mice will be sacrificed at either one week or one month post injection for tissue harvest of spleen and lymph nodes.

The Committee requested that the investigator revise #9, 13 and the narrative of Supplemental Form B to provide more information on infection of humans, route of transmission, symptoms and methods of treatment of a Listerial infection.

A member noted that laboratory accidents need to be reported to employee health. The Committee requested that the investigator indicate this in the protocol.

The Committee recommended approval after the noted issues have been appropriately addressed.

Pending Conditions:

1. In Supplemental Form B, question 9, the investigator needs to indicate that the biohazardous agent can be infect humans and indicate the route of transmission.

2. In Supplemental Form B, question 13, the investigator needs to identify any potential effects of an infection and the risks of treatment.

3. In the Supplemental Form B narrative, in response to the question "What is an exposure?", the investigator needs to describe what constitutes an exposure to the agent.

4. In the Supplemental Form B narrative, in response to the question "What do I do if I am exposed?", the investigator needs to indicate that individuals should report to Occupational Medicine (UCOM L-156, 2-6757).

581 Renewal/Peter, Marcus/ ***Approved (8-0-0)***

This protocol involves the use of replication-deficient, VSV-pseudotyped retroviral vectors to infect human tumor cell lines for the study of apoptosis signaling molecules and their function in these cells. All studies are in vitro.

The Committee had no issues with this protocol and recommended approval.

568 AD 01/He, Tong-Chuan/ ***Pending Conditions with Comment (8-0-0)***

This study will examine the potential role of activation of the Wnt/beta-catenin and BMP pathway in development of human osteosarcoma. Recombinant adenovirus will be used to infect osteosarcoma cells. With this amendment the investigator is requesting the addition of Moloney Murine Leukemia Virus derived retroviral vectors to establish stable cell lines for in vitro and in vivo studies.

The Committee discussed the animal biosafety level of this protocol. As the investigator uses the viruses for transduction of cultured cells and not for direct injection into animals, the Committee felt that the animal work could be conducted at Animal Biosafety Level 1 (ABSL1) if the transduced cells were not infectious at the time of injection.

The Committee discussed the potential infectivity of cells transduced by retroviruses. The retrovirus will be used to establish stable osteosarcoma cell lines in the laboratory, and since retroviruses have a relatively short half-life in culture (8-12 hours), the Committee determined that the retrovirally transduced cells would not be shedding virus at the time of injection and could be handled under ABSL1 conditions. The Committee stressed, however, that the retroviral lab work must still be conducted at Biosafety Level 2 (BL2).

The Committee discussed whether or not the cells transduced by adenoviruses could also be handled under ABSL1 conditions. Adenovirus is considered potentially infectious for 72 hours, yet the investigator plans to infect cells with adenovirus 20-24 hours prior to injection. The Committee determined that these cells could still carry live virus and would have to be handled under ABSL2 conditions unless the investigator could confirm that the cells were no longer infectious. This could be accomplished by with a suitable Polymerase Chain Reaction (PCR) test to rapidly detect the presence of replication-competent virus. Or, the investigator could do a mock test whereby after 20 hours, supernatant is placed on a suitable cell line and assayed. The Committee requested that this point be communicated to the investigator.

Administrative staff noted that the amendment is pending review and approval by the Institutional Animal Care and Use Committee (IACUC).

The Committee recommended approval after the noted issue has been resolved.

Pending Conditions:

The Institutional Animal Care and Use Committee (IACUC) must review and approve the corresponding Animal Care and Use Protocol (ACUP). The investigator needs to submit a letter of approval from the IACUC upon receipt.

Comment:

The Committee has determined that experiments involving the introduction of retrovirally transduced cells into animals may be conducted at Animal Biosafety Level 1 (ABSL1). However, experiments involving introduction of cells transduced with adenoviral vectors into animals must be conducted at Animal Biosafety Level 2 (ABSL2). If it can be demonstrated that the cell lines infected with adenovirus are free of viral particles prior to injection into animals, then the Committee may also consider downgrading these experiments to ABSL1.

571 AD 01/Thinakaran, Gopal/ ***Approved (8-0-0)***

This research involves the use of plasmid and replication-deficient retroviral vectors to transduce cultured cells for the study of biogenesis/folding, secretory trafficking and metabolism of amyloid precursor protein. With this amendment, the investigator requests approval for the addition of replication-deficient adenoviral vectors, addition of a room and changes in staff.

The Committee had no issues with this protocol and recommended approval.

648 AD 01/Clark, Marcus/ ***Pending Conditions (8-0-0)***

The primary goal of this research is to understand how components of the B cell antigen receptor complex couple to and activate receptor associated tyrosine kinases. Mutants of the B cell antigen receptor and downstream signaling molecules will be expressed in murine B cell lines via a replication-defective, VSV-psuedotyped retrovirus. With this amendment, the investigator requests approval for the addition of new procedures: retroviral infection of ex vivo cultured primary murine bone marrow cells and injection of the transduced cells into irradiated mice. The amendment also involves a staff addition.

The Committee noted that this protocol has issues similar to those discussed for protocol 569. The investigator needs to describe testing for replication-competent virus and hazards associated with the use of amphotropic retrovirus. Additionally, decontamination methods need to be revised to indicate 10% bleach for at least 10 minutes.

The Committee discussed aspects of the animal work. The investigator will be using the viral vector to infect murine bone marrow cells which will subsequently be injected into animals. While the retroviral work must be conducted under Biosafety Level 2 (BL2), the Committee determined that the animal work could be conducted under Animal Biosafety Level 1 (ABSL1), as the transduced cells will not contain live virus at the time of injection.

The Committee noted several issues that need to be resolved in Supplemental Form B. The investigator needs to add home phone numbers to the form, describe transport of carcasses and clarify whether ecotropic or amphotropic virus will be used.

A member noted that the investigator needs to check the animal biosafety level in section 2 of the protocol.

The Committee recommended approval after the noted issues have been appropriately addressed.

Pending Conditions:

1. While the laboratory work for this protocol must be done at BSL2, the Committee determined that the animal work can be done at ABSL1. Therefore, the investigator needs to check ABSL1 in the Protocol Submission Form, Section II, under "Whole Animals" and in Supplemental Form B, Section IV. In addition, as animal location and containment will change for work under ABSL1, the investigator needs to make additional revisions to Form B, as needed.

2. In Section III of the Protocol Submission Form, question 4c indicates that the MIGRI retrovirus is replication-defective and that recombination events resulting in replication-competent virus would be unlikely. The Committee, however, still requests that viral preparations be tested for replication-competent virus. Therefore, the investigator needs to replace the information in question 4c with appropriate methods for testing viral preparations.

3. Section IV indicates that VSV-pseudotyped retrovirus will be used to infect cultured cells; however, Supplemental Form B (Section VII, question 10; Section VIII, 2A[1, 3 and 6]) indicates that the virus is ecotropic and cannot infect humans. The investigator needs to reconcile this issue.

4. In Section VII, question 4, the investigator needs to provide more information regarding the hazards associated with use of an amphotropic retrovirus. In particular, the investigator needs to describe the consequences of integration and expression of the transgenes in human cells.

5. In Section VII, questions 9 and 12 indicate that bleach will be used for 30 seconds. The Committee recommends that bleach be used for at least 10 minutes. Therefore, the investigator needs to revise the form accordingly.

6. In Supplemental Form B, the investigator needs to list home telephone numbers. These numbers will remain confidential and will only be used for emergency purposes.

7. The Institutional Animal Care and Use Committee (IACUC) must review and approve the corresponding Animal Care and Use Protocol (ACUP). The investigator needs to submit a letter of approval from the IACUC upon receipt.

683 AD 01/Macdonald, R. Loch/ *Pending Condition (9-0-0)*

This research involves the use of gene transfection by electroporation and liposome delivery to manipulate angiogenesis in the brain of mouse embryos. With this amendment, the investigator requests approval to transfect the basilar artery of dogs with plasmid DNA or siRNA by electroporation to determine the feasibility of in vivo transfection of smooth muscle.

Administrative staff noted that the amendment has to be reviewed and approved by the Institutional Animal Care and Use Committee (IACUC). Prior to that review, the IBC must determine the animal biosafety level. The Committee decided that the animal work could be conducted under Animal Biosafety Level 1 (ABSL1).

The Committee had no issues with this protocol and recommended approval.

Pending Condition:

The Institutional Animal Care and Use Committee (IACUC) must review and approve the corresponding Animal Care and Use Protocol (ACUP). The investigator needs to submit a letter of approval from the IACUC upon receipt.

687 AD 04/Weichselbaum, Ralph/*Deferred (8-0-0)*

This research involves the use of Herpes Simplex Virus I (HSV I) vectors in conjunction with irradiation to study the effects of combining antitumor and antiangiogenic therapies with radiotherapy on human and murine tumor model systems. With this amendment, the investigator requests approval for the addition of a new HSV I vector, addition of new procedures (tumor excision and homogenization), change in emergency contact information and addition of new staff members.

The Committee discussed the vector used in this research. The vector is a replication-competent, neuro-attenuated Herpes Simplex Virus. The investigator has already been working with HSV vectors, but is now requesting approval for the addition of a new HSV vector containing the luciferase gene.

While the Committee did not have concerns with expression of luciferase, they were concerned with the HSV vectors. These particular vectors are neuro-attenuated and cannot infect neuronal cells or produce a latent HSV infection. They can, however, infect non-neuronal cells and, as replication-competent viruses, have the potential to produce a local infection.

A member questioned how the investigator plans to transport the agents to [redacted]. Administrative staff clarified that the agent is not being transported to [redacted]; the animals are being transported, via a previously approved route, to the investigator's lab for injection of the agent.

The Committee discussed the procedures being added with this amendment. The investigator plans to inject the agent into tumors growing in the hind limbs of mice and then treat the tumors with irradiation. Tumors will then be excised and homogenized. As the excised tumors may harbor live virus, the Committee requested more information about the tissue harvest and homogenization procedures, location of those procedures and packaging/transport of the tissue samples. Also, as luciferase activity in the tumor homogenates will be analyzed with a luminometer, the Committee requested that the investigator specify the location of the luminometer.

As part of this amendment, the investigator has changed the emergency contact information to Dr. David Pitrak. The Committee indicated that all exposures should now go to employee health rather than Dr. Pitrak and requested that the form be revised accordingly.

The Committee felt that there was not enough information to adequately assess this amendment and recommended that it be deferred until the noted issues can be appropriately addressed.

Reasons for Deferral:

1. While attenuated, the vector being used is replication competent therefore the Committee would like additional information regarding the tumor excision and homogenation procedures. In Section IV, Research Summary, the investigator needs to address the following questions:
    - Where will the tumor excision and homogenation take place?
    - How will the tumor be homogenized?
    - Where is the location of the luminometer?
    - How will homogenized tissue be transported to this location?

2. In Section VII, question 5, the investigator needs to clarify that in the event of an exposure, staff should report to Occupational Medicine (UCOM L-156, 2-6757) rather than paging Dr. Pitrak.

736 AD 02/Naclerio, Robert/ ***Pending Conditions (9-0-0)***

This research involves the use of Streptococcus pneumoniae to induce sinusitis in mice in order to investigate the mechanism by which allergic rhinitis worsens acute sinusitis, evaluate the kinetics and inflammatory response to treatment of acute sinusitis and test if leukotrienes are responsible for increased bacterial infection. With this amendment, the investigator is adding a staff member and new experimental procedures in association with ACUP [redacted] to determine if RC 527, a TLR 4 agonist, reduces an allergic reaction and the increased bacterial infection that occurs during an allergic reaction.

A member questioned whether this strain of Streptococcus could cause pneumonia. Another member clarified that the strain used in this research is non-encapsulated, therefore, avirulent.

The Committee recommended approval after the amendment has been reviewed and approved by the Institutional Animal Care and Use Committee (IACUC).

Pending Conditions:

The Institutional Animal Care and Use Committee (IACUC) must review and approve the corresponding Animal Care and Use Protocol (ACUP). The investigator needs to submit a letter of approval from the IACUC upon receipt.

881 AD 01/Schneewind, Olaf/ ***Pending Conditions (9-0-0)***

The goal of this research is to identify new targets for vaccine and immunotherapies against Yersinia pestis by screening for protective antigens and by elucidating the pathogenic features of immune protection in experimental animals. With this amendment, the investigator is requesting approval for the addition of

protective index experiments in mice, addition of experiments involving rats as hosts, and addition of staff members.

Administrative staff noted that the amendment is pending review and approval by the Institutional Animal Care and Use Committee (IACUC).

The Committee recommended approval after the noted issue has been resolved.

Pending Conditions:

The Institutional Animal Care and Use Committee (IACUC) must review and approve the corresponding Animal Care and Use Protocol (ACUP). The investigator needs to submit a letter of approval from the IACUC upon receipt.

III. Old Business: None

IV. New Business: Transport of Biohazardous Animals—H. Halpern (ACUP [redacted]/IBC 632)

As part of the triennial review of ACUP 71151, the investigator is requesting approval to transport the animals from [redacted] to [redacted] for injection of the biohazardous agent and then to four different labs for imaging studies. The Institutional Animal Care and Use Committee (IACUC) has already approved the transport. Since these animals will be biohazardous, the Institutional Biosafety Committee must review and approve the routes of animal transport. In order to approve Dr. Halpern's transport changes, the Committee felt that an amendment should be submitted for the associated IBC protocol (Weichselbaum—632).

V. Updates: The Committee members were provided with copies of the Final Rule for Select Agents and an article entitled "Biosafety Committees Come Under Scrutiny." The Committee had no comments regarding these documents.

The University of Chicago

Institutional Biosafety Committee

5841 S. Maryland Avenue
AMB S-152 ♦ MC 1108
Chicago, IL 60637

Minutes of June 3, 2005 Meeting
1:00 PM in [redacted]

In attendance:

Voting Members

Kenneth Thompson
Richard Hiipakka
Mark Abe
Malcolm Casadaban
George Daskal
Clara Gartner
Jean Greenberg
Tong-Chuan He
Helena Mauceri
Mary Ellen Sheridan
Gopal Thinakaran
Caig Wardrip

Ex-Officio Members

Russell Herron
David Pitrak
Markus Schaufele

Guest

Lois Zitzow

Staff

Bill Pugh
Pamela Postlethwait
Jennifer Swanson

Absent:

Voting Members

James Mastrianni
Louis Philipson

Ex-Officio Members

Steve Beaudoin

Staff

None

I. Minutes: The minutes of the May 6, 2005 meeting were unanimously approved (12-0-0) with minor clarifications.

II. Protocol Review:
The following protocols were reviewed at the meeting, with the disposition noted:

PR# Category/Investigator/*Disposition*

889 New/McKee, Mark/*Pending Conditions (11-0-0)*

The study objective is to examine T cell response to carcinoembryonic antigen (CEA) epitopes using vaccination strategies. Peptide antigens or DNA constructs will be delivered by either subcutaneous injection or gene gun and differences in the immune response will be examined.

The investigator proposes to immunize mice against human CEA and/or specific CEA epitopes in order to generate an anti-tumor immune response. He has generated a mammalian expression vector construct utilizing a CMV promoter encoding human CEA. Either the wild-type, mutant forms of CEA (containing multiple epitopes with improved binding to MHC-I molecules) or a control will be introduced into mice using gene gun technology. Alternatively, mice will be immunized using specific CEA-based peptide antigens. CEA levels will be determined pre- and post-immunization and some mice will undergo tumor challenge.

Administrative staff noted that the Animal Care and Use Protocol is pending approval by the IACUC. The Committee recommended approval after IACUC approval has been granted.

Pending Condition
The Institutional Animal Care and Use Committee (IACUC) must review and approve the associated animal care and use protocol.

890 New/Chong, Anita/*Pending Conditions (12-0-0)*

The research involves the use of recombinant DNA for the production of transgenic mice. Mice will express a B-cell receptor with alloreactivity for transplantation antigens. The transgenic mice will be generated by [redacted]

A member noted that, in Supplemental Form B, the investigator checked ABSL2 but did not complete the necessary questions for this biosafety level. A member clarified that this work should actually be done under ABSL1; therefore, the investigator does not have to complete the entire form.

A member noted that the investigator has described the production of transgenic mice in this protocol, when in fact, those procedures are being conducted under a separate Animal Care and Use Protocol (ACUP) by [redacted] The member felt that the transgenic production should not be described in this IBC protocol. Furthermore, since the investigator is not the person who will be introducing the DNA into mice, Supplemental Form B should not be included either. Administrative staff clarified that [redacted] ACUP is a generic protocol that does not indicate specific gene inserts. Therefore, if the IBC protocol does not include a description of transgenic production or form B, there will be no documentation of the specific transgenic work. The Committee felt that it would be acceptable for the investigator to remove references to animal work, but include a statement that the genes would be provided to [redacted] for the production of transgenic animals. The Committee requested that the submission form be revised accordingly and that Supplemental Form B be removed from the submission. In addition, the Committee requested that [redacted] submit a generic IBC protocol for the production of transgenic mice.

The Committee recommended approval after the noted issues have been appropriately addressed.

Pending Conditions
While this protocol describes the generation of the gene fragments for use in the production of transgenic animals, it is [redacted] that will actually be manipulating and producing the transgenic mice. Therefore, the investigator needs to remove references to the use of live mice from the following sections:

1. In Section II, question 2, the investigator needs to deselect "Whole Animals" and remove the information regarding the animal care and use protocols.

2. In Section III, question 5, the investigator needs to remove mice as host.

3. In Section IV, the investigator needs to revise the research summary to describe the production of the linearized DNA and indicate that generated DNA will be provided to [redacted] for production of transgenic mice which will then be utilized under the approved ACUP [redacted].

4. The Committee has determined that submission of the Supplemental Form B is not necessary; therefore, the form will be administratively removed from the protocol submission.

892 New/Bendelac, Albert/*Deferred (11-0-0)*

The research objective is to immunize mice with heat-killed Rickettsia conorii to evaluate the CD1d-specific T lymphocyte immune response. Heat-killed Rickettsia conorii will be prepared at the University of Texas. Viability testing of each heat-killed preparation of Rickettsia conorii will also be done at the University of Texas. Wild-type and CD1 null adult B6 mice will be injected intravenously with one of three different amounts of heat-killed Rickettsia conorii. The immunized mice will be euthanized at five different time points. Serum and various tissues will be collected, homogenized and analyzed. LPS will be used as a control. The injections and tissue harvest will be performed in the investigator's lab.

The Committee discussed the biosafety level of this protocol. Rickettsia conorii, a RG3 agent, is usually handled under BL3 conditions; however, the investigator has indicated BL1, as the agent will be heat-inactivated. The reviewer contacted the collaborators at the University of Texas for further information regarding the biosafety level and heat-inactivation methods. They indicated that all work with Rickettsia conorii (live or heat-killed) is conducted under BL3/ABSL3 conditions; however, it was unclear from their response if BL3 was absolutely necessary for heat-killed organisms. They also indicated that work involving formalin-inactivated Rickettsia is conducted at BL2.

The Committee questioned whether the investigator could use formalin-inactivated Rickettsia rather than heat-killed. If that is not possible, the Committee requested that the investigator obtain information from the University of Texas as to why they use BL3/ABSL3 for heat-killed organisms. Additionally, the Committee requested confirmation that the organisms would be effectively heat-inactivated and could be handled under BL1/ABSL1 conditions.

The Committee recommended that the protocol be deferred until more information can be obtained from the investigator and his collaborators at the University of Texas.

Reason for Deferral
The Committee has concerns regarding the use of the heat killed Rickettsia conorii under Biosafety Level 1 and Animal Biosafety Level 1 (BL1/ABSL1) practices, especially since investigators at the University of Texas manipulate the heat killed organism using BL3/ABSL3 practices. The only exception is when the

organism has been chemically inactivated (i.e. formalin, acetone, etc), at which point BL2 practices are utilized. Please clarify whether it is possible to utilize chemically inactivated R. conorii in the proposed experimental studies. If not, the Committee would like information indicating why BL3/ABSL3 practices for the heat killed organism are utilized by the investigators at the University of Texas. As the University of Texas investigators are experts on R. conorii, perhaps they would be willing to provide their opinion on the use of the heat killed organism under BL1/ABSL1 conditions. The Committee would find this helpful in determining the appropriate Biosafety Level.

560 Renewal/Lin, Anning/*Pending Conditions (11-0-0)*

This research will investigate Bax-mediated cell death in B cell lymphoma. Adenoviruses will be propagated in 293 cells and then used to infect cultured cells, which will then be fixed for morphological or protein assays.

The Committee noted several issues that the investigator needs to resolve. The PI needs to sign section VI. In section VII, the investigator needs to provide the biosafety cabinet certification date, check "mask" and "safety glasses," and provide the bleach concentration.

The Committee recommended approval after the noted issues have been appropriately addressed.

Pending Conditions

1. The investigator needs to sign and date section VI of the protocol.

2. In section VII, the investigator needs to address the following issues.

    a. Question 2a indicates that the biosafety cabinet was last certified 5/2004. All biosafety cabinets must be certified annually; therefore, the investigator needs to indicate the certification date for 2005.

    b. The Committee requested that all staff members working with adenovirus wear eye protection and a mask; therefore, in question 8, the investigator needs to check "safety glasses" (or "safety goggles/shield") and "mask."

    c. In question 12, the investigator needs to indicate the concentration of bleach (10%, as indicated in question 9, #5) to be used for decontamination.

575 Renewal/Gupta, Mahesh/*Pending Conditions (12-0-0)*

The research utilizes primary cultures of rat cardiac myocytes as an *in vitro* model of cardiac hypertrophy. Expression of endogenous genes will be modified using recombinant adenoviral vectors. The genes that will be expressed are transcription factors and deacetylases. There are no known hazards associated with the gene inserts. After 48 hours of infection, myocytes will be harvested and cell-lysates analyzed using various molecular biology techniques for protein and RNA analyses.

A member noted that contact information is needed for the oversight person. Additionally, in section VII, question 4, the investigator needs to describe possible consequences of exposure to the recombinant agent and transgenes.

The Committee recommended approval after the noted issues have been appropriately addressed.

Pending Conditions

1. In Section VII, question 4, the hazards associated with accidental exposure to replication deficient adenovirus are thoroughly described; however, information regarding the possible consequences of exposure to the replication deficient adenovirus carrying a transgene is not provided. The investigator needs to describe the possible consequences of exposure to replication deficient adenovirus expressing the contractile genes, transcription factors, deacetylases and reporter genes being utilized in this project.

2. In Section VII, question 11, the investigator needs to provide a contact number for Dr. Pillai.

578 Renewal/Ashton-Rickardt, Philip/*Pending Conditions (12-0-0)*

The laboratory will examine the effect of an inhibitor of apoptosis, which will be expressed in T cells of transgenic mice, on the development of memory cytotoxic T lymphocytes after infection with lymphocytic choriomeningitis virus (LCMV). The virus will be obtained through a collaborator at either Emory University or University of Massachusetts Medical Center. The virus will be administered to the transgenic mice by intravenous injection. Spleen and thymus will be harvested. Work will be conducted in [redacted] and in the investigator's lab.

In section VII of the protocol and in Supplemental Form B, the investigator described waste incineration as a required method of disposal. The reviewer questioned whether incineration was still being performed at this institution. A member clarified that [redacted] does not incinerate waste, although that was the procedure years ago when this protocol was originally approved. Currently, waste requiring incineration is placed in designated containers and incinerated by the University's contracted waste disposal company. The Committee felt that incineration is not necessary for this agent and requested that the investigator remove all references to waste incineration from the forms.

A member noted that, in Supplemental Form B, the investigator has incorrectly described the agent as "not a natural pathogen of humans and cannot be passed from mice to humans." As the agent can be transmitted from mice to humans through inhalation of aerosolized rodent urine, feces, saliva or other body fluids, the Committee requested that this statement be revised. Additionally, the Committee requested that a statement be added to clearly identify the increased risk to immunocompromized individuals.

A member noted the investigator's reference to a "momentary infection." The Committee believed that the investigator was referring to a local infection, but requested that this be clarified.

The Committee recommended approval after the noted issues have been appropriately addressed.

Pending Conditions

1. In Supplemental Form B, Section VII, question 9, it is indicated that accidental injection with Lymphocytic Choriomeningitis Virus (LCMV) can result in a "momentary infection" of humans. The investigator needs to clarify what is meant by "momentary infection."

2. The Supplemental Form B Narrative states that LCMV is "not a natural pathogen of humans and can not be spread from mice to humans." As LCMV may be transmitted to humans from mice by inhaling infectious aerosolized particles of rodent urine, feces or saliva, or by contamination of mucous membranes with infected body fluids, the investigator needs to revise the Form B narrative accordingly.

3. As immunocompromised individuals are at particular risk of infection with LCMV, the investigator needs to clearly indicate in the Supplemental Form B Narrative that immunocompromised individuals should not enter rooms containing this biohazardous agent.

4. The Committee has determined incineration of waste is not necessary. Therefore, in Section VII, question 13, the investigator needs to deselect "Waste incineration required" and indicate that disposal of animal carcasses will be done by the [redacted] staff according to the procedures of [redacted] Additionally, the investigator needs to revise Supplemental Form B, Section VII, question 4 and the supplemental material entitled "Manipulations and Procedures" accordingly.

626 AD 05/Weichselbaum, Ralph/*Pending Conditions (10-0-0)*

The research laboratory uses HSV-1 7020 to transfer therapeutic genes to vacuolar tissue in an effort to make bypass grafts last longer and prevent arterial restenosis. With this amendment, the investigator is adding experimental procedures involving surgical implant of recombinant HSV-1 coated stents into rabbits to evaluate inhibition of neointimal hyperplasia. Elution of recombinant HSV-1 into surrounding tissue will be assessed by Vero titer protocol.

The Committee discussed the consequences of exposure to HSV-1 7020. The virus is neuro-attenuated, which will not cause a latent infection; however, it is replication-competent and can cause a local infection at the site of exposure.

A member noted that, in Supplemental Form B, the investigator has indicated that a bottle of Acyclovir will be kept in the [redacted]. As the [redacted] no longer maintains a supply of this drug, the investigator needs to remove that statement.

The Committee recommended approval after the noted issues have been appropriately addressed.

Pending Conditions
In Supplemental Form B, Section VII, question 11, the reference to maintaining a vial of oral Acyclovir in [redacted] and paging Infectious Diseases needs to be revised to indicate exposed individuals will report to Occupational Medicine (L-156; 2-6757). Additionally, the Form B narrative, the supplement entitled "Rabbit Herpes Simplex Virus Vector Biocontainment Practices" and Section VII, question 10 of the protocol submission form need to be revised accordingly.

687 AD 04 (*Revised Deferral*)/Weichselbaum, Ralph/*Approved (10-0-0)*

The research examines the effects of combining antitumor and antiangiogenic therapies with radiotherapy. HSV-1 vectors are used in conjunction with ionizing radiation to achieve tumor control and cure. With this amendment, the investigator requests approval for addition of a new vector (HSV-1-GCluc); addition of new procedures (tumor excision and homogenation); and staff additions.

This amendment was deferred at the May 6th meeting due to several issues regarding the tumor excision and homogenation procedures. The investigator has since submitted a revised protocol that appropriately addressed the Committee's concerns. The Committee recommended approval of this amendment.

III. Old Business: None

IV. New Business: Administrative review and approval of staff additions and room changes.

The Committee discussed whether or not it was appropriate for administrators to review and approve changes to protocols that involve staff and room additions. As there are no special requirements for staff additions, the Committee agreed that administrators could sign off on them (11-0). However, for room additions, the Committee questioned whether a more extensive review would be required to ensure that the added rooms were properly equipped for the type of work conducted by the investigator. Currently, the IBC does not inspect rooms, nor does it require the investigator to provide information about the rooms aside from the type and certification date of the biosafety cabinet. The research laboratories are inspected annually by the Environmental Health and Safety Office; however, it is unclear if new rooms are also inspected, as the safety office may not be aware of room additions. Currently, the IBC does not specifically notify safety when rooms are added to IBC protocols; however, a representative from the University Safety Office is a member of the IBC and does receive copies of all protocol submissions (i.e. during distribution of the protocol meeting packet). A member suggested that room additions be handled between the IBC administrative staff and Environmental Heath and Safety. The Committee requested that administrative staff discuss the issue with the safety office and report back to the Committee at the next meeting. The IBC Chair will continue to sign off on room additions until more information can be presented.

V. Updates:

A. Environmental Monitoring Report: [redacted] ABSL3 Facilities

The Committee discussed the first environmental monitoring report for the [redacted] ABSL3 facility as well as supplemental information from [redacted], the outside testing laboratory, regarding testing methodology and positive controls. The Committee noted that there were inconsistencies between the testing methodologies described in the environmental monitoring report and those described by [redacted]. The report indicates that all samples were tested by PCR; however, [redacted] indicates testing by traditional culture and, if necessary, PCR. When culturing samples, [redacted] uses a medium that selects for all *Yersinia* species. If *Yersinia* colonies are present, they are sent for further analysis by PCR to rule out Y. pestis. The Committee questioned why the outside lab is now using culturing methods rather than the previously described method of PCR.

The Committee discussed the information on positive controls. According to [redacted], *Yersinia enterocolitica* is the positive control used during culturing. The Committee questioned why the lab uses *Y. enterocolitica* when the species of interest is *Y. pestis*.

A member noted that the environmental monitoring report does not include a description of positive controls or results of those controls. The Committee requested that the report be revised to reflect this information.

The Committee requested that the Environmental Heath and Safety Office provide clarification for the issues noted above.

B. Change in Institutional Review Board (IRB) Policy—Use of Human Cell Lines

The Committee was informed that use of human cell lines no longer requires submission to the IRB. The Office of Human Research Protections (OHRP) has determined that human cell lines are not considered human subjects; therefore, use of these cells does not require review and approval by the IRB. The University of Chicago's IRB has changed its policy accordingly.

The University of Chicago

Institutional Biosafety Committee

5841 S. Maryland Avenue
AMB S-152 ♦ MC 1108
Chicago, IL 60637

Minutes of July 8, 2005 Meeting
1:00 PM in [redacted]

In attendance:

Voting Members

Gopal Thinakaran
Richard Hiipakka
Malcolm Casadaban
George Daskal
Clara Gartner
Jean Greenberg
Tong-Chuan He
Helena Mauceri
Louis Philipson
Mary Ellen Sheridan
Craig Wardrip

Ex-Officio Members

Russell Herron
David Pitrak

Guest

None

Staff

Bill Pugh
Jennifer Swanson

Absent:

Voting Members

Mark Abe
James Mastrianni
Lois Zitzow

Ex-Officio Members

Steve Beaudoin
Markus Schaufele

Staff

Pamela Postlethwait

I. Minutes: The minutes of the June 3, 2005 meeting were unanimously approved (9-0-0).

II. Protocol Review:
The following protocols were reviewed at the meeting, with the disposition noted:

PR# Category/Investigator/*Disposition*

891 New/Viswanathan, Natarajan/*Deferred (9-0-0)*

This work involves the use of replication deficient adenovirus recombinants with several mammalian genes, at least one of which is oncogenic (Src). The adenoviral vectors will be used to investigate the role of LPA in airway inflammation and lung cancer.

A number of committee members mentioned that the investigator provided insufficient information in that protocol and that this did not permit an adequate review of the research. In addition to several minor items in the submission form that need to be completed or revised, the investigator needs to provide more information in the research summary, in particular, an explanation of the rDNA and how it will be used in animals; if and how tissue harvests will be performed; and how the viruses will be obtained and used.

The protocol was deferred until the noted issues have been appropriately addressed by the investigator.

Reason for the Deferral

1. In Section I, the investigator needs to provide the University of Chicago contact information for the investigator, location of the work/experiments, name of the grant agency funding the project and Tracs ID or FAS account number.

2. According to the protocol, animal tissue will be utilized in the project. Therefore, in Section II, question 2, the investigator needs to indicate "Animal Tissue Only" and provide the species, Animal Care and Use Protocol (ACUP) number and approval date.

3. In Section II, question 3, the investigator needs to indicate "No".

4. In Section III, question 3a, the investigator indicate only "Yes".

5. In Section III, question 3b, the investigator indicate only "Yes".

6. As the protocol indicates Src kinase has oncogenic properties, in Section III, question 3c, the investigator needs to indicate "Yes" and describe how the recombinant DNA sequence is potentially harmful.

7. In Section IV, Summary of Proposed Research, the investigator needs to provide further clarification regarding the experimental procedures to be performed. The investigator needs to explain from where the adenovirus will be obtained and how it will be used in the experimental procedures. The investigator needs to clarify the role of animals and/or animal tissue in this project. If biohazards are being administered to animals, the investigator needs to clarify how they will be administered, where procedures will be performed, how tissues will be harvested and what safety precautions will be utilized during these procedures. Also, to avoid confusion, the investigator needs to spell out all abbreviations (i.e. LPA, BAL, etc).

8. In Section V, Staff Group, the investigator needs to obtain the signatures of all staff members listed.

9. In Section VI, the principal investigator must sign the protocol.

10. In Section VII, the investigator needs to provide the laboratory room number(s) and phone number(s).

11. In Section VII, question 2a, the investigator needs to provide the certification date for the biosafety cabinet.

12. In Section VII, question 4, the investigator needs to provide further clarification regarding the hazards associated with using a replication deficient adenoviral vector AND the hazards associated with expression of any transgenes carried by the adenoviral construct. In particular, the investigator needs to describe how individuals can be exposed to the adenoviral vectors, the consequence of exposure to the adenoviral vector and the consequence of expression of a transgene (Src kinase, LPA receptors, protein kinase C isoforms, etc.) carried by the vector.

13. In Section VII, question 6, it is indicated that the work area will be cleaned using alcohol spray. However, this is not consistent with the decontamination procedures listed in question 12. The investigator needs to reconcile this discrepancy.

14. In Section VII, question 10, it is indicated that effective post exposure treatment is available. The investigator needs to provide details of the treatment available.

15. In Section VII, question 11, the investigator needs to address whether surveillance is appropriate and justify whether or not sera banking/testing is needed.

16. In Section VII, question 13, waste incineration is indicated as being required. The University of Chicago does not have an on-site incinerator and if incineration is necessary, the investigator will need to make arrangements to have the waste incinerated.

17. In Section VII, question 14, the investigator needs to list an individual who will assume responsibility in the absence of the investigator. The investigator needs to describe the qualifications of the individual and provide contact information (phone number, pager, etc).

18. In Section VII, question 15, the investigator needs to provide his contact information.

893 New/Abe, Mark/*Approved (9-0-0)*

This research involves the study of signal transduction proteins ERK7 and ERK8. The investigator plans to isolate cells and tissues from mice with loxP sites flanking the ERK7 gene. TAT protein will be used to introduce Cre-recombinase into these cells and tissues, which may allow for conditional knockout of the ERK7 gene in a temporal and cell/tissues specific manner. Beta-galactosidase and green fluorescent protein will be used as markers of efficient gene transfer. Modulation of cell signaling pathways, cellular growth, cellular death, gene expression and tissue morphometry will be examined.

The Committee had no concerns with this protocol and recommended approval.

894 New/Randall, Glenn/*Pending Conditions (10-0-0)*

This research investigates interaction of hepatitis C virus (HCV) with its host cell. Replication-deficient retroviral vectors will be used to generate stable cell lines that either over-express host cell genes or express shRNAs which will silence host cell genes. The cells will then be infected with HCV to evaluate the effects of altered host gene expression on HCV replication. The investigator also plans to conduct genetic analyses

of HCV replication, study the effects of chemical inhibitors on HCV replication, and conduct biochemical analyses of HCV-host interaction.

The Committee discussed the Biosafety Manual for this agent and requested that the investigator instruct staff members to go to UCOM in the event of an exposure and provide the contact information for UCOM. A member noted that the manual contains incorrect information about prophylaxis and response to treatment for HCV; therefore, the investigator needs to revise the plan for handling exposures and infections. The Committee recommended that Dr. Pitrak discuss these issues with the investigator to ensure that the biosafety manual provides accurate and complete information to staff members. In addition, staff should not read and sign the protocol until the biosafety manual has been appropriately revised.

A member noted that the investigator plans to screen staff members for HCV when they join the lab. The Committee discussed the legal aspects of employee screening and requested that Legal Counsel advise the administrative staff on comments to be sent to the investigator.

The Committee discussed the mutant HCVs that will be used in this research. While the investigator describes the hazards associated with wild-type HCV, he does not include any information about the mutants. The Committee requested that the investigator describe these hazards, if known, or indicate that no studies have been done to determine whether there are additional hazards associated with the mutants.

The Committee noted other issues that need to be addressed by the investigator: University of Chicago contact information is needed for the investigator and primary contact; the biosafety cabinet needs to be certified; PI, Staff and Department Chair signatures are needed.

A member noted that the investigator plans to keep stocks of the virus in his lab and questioned whether the biosafety level should be changed to BL3. A member requested that the administrative staff look into this issue further and bring the protocol back to the Committee if a change in biosafety level is necessary.

The Committee recommended approval after the noted issues have been appropriately addressed.

Pending Conditions

1. In the Biosafety Manual, under "Pre-Exposure Evaluation," the investigator indicates that employees will be asked to provide blood samples which may be stored for at least 30 years. University of Chicago Occupational Medicine (UCOM) has indicated that there is no mechanism at the University to provide serum banking. Instead, they recommend baseline and annual HCV antibody testing of all personnel working on this protocol. The investigator needs to revise the biosafety manual and the protocol (Section VII, question 11, "Surveillance for Infections") as appropriate and contact Dr. Geoffrey Korn in UCOM (834-9190) to make arrangements for employee screening.

2. In the Biosafety Manual, under "Post-Exposure Evaluation and Follow-Ups," the investigator refers to post-exposure prophylactic treatment. At present, there is no prophylactic treatment for exposures. UCOM recommends the following post-exposure follow-up schedule: HCV testing at baseline, 6 weeks, 12 weeks, and 6 months. The investigator needs to revise the biosafety manual accordingly. In addition, the investigator needs to revise the manual and protocol (Section VII, questions 4 and 10) to indicate that there is no prophylactic treatment for HCV exposures. Also, the investigator needs to provide contact information for UCOM and instruct employees to go to UCOM in cases of exposure.

3. The Committee requested that the Biosafety Manual include a plan for handling HCV infections. Please provide this information. For further information or questions about these issues, the investigator should contact Dr. David Pitrak, Chief of Infectious Diseases (702-9078).

4. The investigator needs to address the following issues in the Protocol Submission Form.
   A. In Section I, the investigator needs to provide his U of C e-mail, phone and fax. In addition, the investigator needs to provide contact information for the Primary Lab Contact.

   B. In Section V, the investigator needs to provide staff member names, responsibilities and signatures. *The investigator must ensure that the protocol and biosafety manual are appropriately revised and found to be acceptable by Dr. Pitrak before any staff members are asked to read and sign the protocol.*

   C. In Section VI, the investigator needs to sign and date the protocol. In addition, the Department Chair needs to sign and date the protocol, as this is required for internally funded protocols.

   D. Please address the following issues in Section VII.

      i. At the top of page, the investigator needs to provide his new U of C phone number.

      ii. In question 2a, the investigator needs to provide the biosafety cabinet certification date.

      iii. In question 4, the investigator needs to describe the hazards associated with the mutant HCVs used in this research. Otherwise, if no information is available, the investigator should indicate that there are no known hazards associated with the mutant HCVs, other than those associated with wildtype HCV, as studies to test for such hazards have not been conducted.

      iv. In question 14, the investigator needs to provide contact information for the individual who will assume responsibility for oversight (this individual should be someone other than the PI).

      v. In question 15, the investigator needs to provide his U of C phone number and pager number.

896 New/Garcia, Joe/*Pending Conditions (9-0-0)*

The research laboratory investigates the role of various genes in acute lung injury processes. Using cell cultures or mouse models, the genes of interest will either be over-expressed or silenced and the resultant phenotypes investigated.

A member noted that several questions in Supplemental Form B were not answered by the investigator. Other members clarified that the investigator is not required to complete the entire form for this protocol because rDNA will be used solely for the production of transgenic mice. Since transgenic animals are not considered biohazardous, the Committee requested that the investigator change the length of time that animals are biohazardous from "lifetime" to "none."

The Committee noted that the research summary provides well-written explanation of general laboratory techniques; however, some members felt that it should also include more details about the investigator's

research. After much discussion, the Committee determined that the research summary provides sufficient information about the investigator's project and is acceptable as written.

Administrative staff noted that two of the investigator's staff members still need to read and sign the protocol. As these individuals have not yet arrived at the institution, they may need to be added to the protocol with an amendment.

The Committee recommended approval after the noted issues have been appropriately addressed.

Pending Conditions

1. In Supplemental Form B, section II. Material Details, the investigator needs to change the length of time animals will be hazardous to "none," as the transgenic animals will not be hazardous to humans.

2. The Institutional Animal Care and Use Committee (IACUC) must review and approve the corresponding Animal Care and Use Protocol (ACUP).

3. Eddie Chiang and Sara Camp cannot be approved for work on this project until they read and sign the protocol. Therefore, the investigator needs to submit Section V (staff signature page) of the protocol with their signatures. Otherwise, if they are not yet at the University, they can be added upon their arrival by submitting an amendment to the approved protocol.

581 AD 01/Peter, Marcus/*Pending Conditions (10-0-0)*

The objective of this research is to use VSV-pseudotyped retroviral vectors to transduce human tumor cell lines for the study of apoptosis signaling molecules and their function in these cells. The investigator is amending the previous protocol to use GeneNet siRNA libraries to perform a genome wide RNAi knock down screen of genes in human and mouse cell lines that confer resistance to FasL induced apoptosis. The siRNA will be delivered using a feline immunodeficiency virus based lentiviral system. An animal component not in the previously approved protocol involves growing mouse tumor cell lines in mice. These mouse tumor cell lines will have specific genes identified as potential tumor promoters knocked down by RNAi using a human immunodeficiency virus based lentiviral system.

The Committee discussed the biosafety level and determined that the *in vitro* work must be conducted at BL2 but the animal work can be conducted at ABSL1 since the transduced cells will not be infectious at the time of injection into animals.

The Committee noted the issues that need to be resolved prior to approval of the protocol. The investigator requested a title change but still needs to add the new title to the submission form. In addition, the protocol needs to be reviewed and approved by the Institutional Animal Care and Use Protocol (IACUC).

The Committee recommended approval after the noted issues have been appropriately addressed.

Pending Conditions

1. As a change in the protocol title to "Expression and Suppression of Genes Using Retroviruses" has been requested, the investigator needs to submit a revised Section I, Project, which reflects the new protocol title.

2. The Institutional Animal Care and Use Committee (IACUC) must review and approve the use in mice of tumor cell lines that have been stably transfected using replication deficient, self-inactivating lentiviral vectors.

744 AD 02/McNally, Elizabeth/*Approved (10-0-0)*

This research laboratory investigates the role of muscle proteins in heart, skeletal and smooth muscle cells. With this amendment, the investigator is including the production of transgenic/knockout mice to study these proteins.

The Committee had no concerns with this amendment and recommended approval.

III. Old Business:

A. Administrative review and approval of room changes.

At the 6/3/05 meeting, the Committee discussed whether room changes or additions to approved protocols could be reviewed and approved by the administrative staff, instead of the IBC Chair as is currently done. Since the IBC does not inspect rooms or request specific information about the rooms (except for location and biosafety cabinet certification), the Committee felt that administrative review would be appropriate if Safety and Environmental Affairs Office would also be involved in the process. The Committee deferred the issue until the administrative staff could have a discussion with Safety. At this meeting, the administrative staff summarized the discussion with Safety. Initially, Safety indicated that they did not need to be notified of room changes because new labs would be inspected at the time of annual review. After discussing the issue further, Safety indicated that they should be notified and that they will confirm laboratory approval (BL2 research only) prior to approval of the rooms. This may involve new lab inspections. The Committee questioned whether the inspections would include an assessment of biohazard use in the lab. As a representative from Safety was not in attendance, the Committee requested that the lab review process be presented by Safety at the next meeting.

The Committee approved administrative review and approval of room additions (BL1 and BL2 rooms only). (10-0-0)

B. Environmental Monitoring Reports:

At the 6/3/05 meeting, the Committee noted several issues with the environmental monitoring reports for [redacted] and the use of positive controls during sample analysis. A response to those issues was received from Safety and Environmental Affairs and was discussed by the Committee. According to the response, samples from [redacted] were analyzed by traditional culture rather than PCR. The Committee questioned whether a second set of samples would be collected for analysis by PCR. In addition, the Committee requested that all documents from Safety and Environmental Affairs be submitted with cover letters to explain the documents and all pages of the submission should have proper headers/footers (author, date, page #). The Committee requested that the environmental monitoring reports also include the original reports from the testing laboratories and Safety's interpretation of the results. A meeting will be scheduled to discuss these issues with Safety.

IV. New Business:

The Committee discussed the proposed change in meeting day/time and determined the best day/time to be Friday at 1:45-3:45. The Committee requested that administrative staff contact all members to determine whether or not this change would be acceptable.

V. Updates: None

The University of Chicago

Institutional Biosafety Committee

5841 S. Maryland Avenue
AMB S-152 ♦ MC 1108
Chicago, IL 60637

Minutes of August 5, 2005 Meeting
1:45 PM in [redacted]

In attendance:

Voting Members		Ex-Officio Members
Richard Hiipakka	Helena Mauceri	Steve Beaudoin
Clara Gartner	Mary Ellen Sheridan	Russell Herron
Tong-Chuan He	Craig Wardrip	David Pitrak
Jean Greenberg	Lois Zitzow	Markus Schaufele
James Mastrianni		

Guest	Staff
John Bivona	Bill Pugh
	Pamela Postlethwait
	Jennifer Swanson

Absent:

Voting Members	Ex-Officio Members	Staff
Gopal Thinakaran	None	None
Mark Abe		
Malcolm Casadaban		
George Daskal		
Louis Philipson		

I. **Minutes:** The minutes of the July 8, 2005 meeting were unanimously approved (9-0-0).

II. **Protocol Review:**
The following protocols were reviewed at the meeting, with the disposition noted:

PR# Category/Investigator/*Disposition*

590 Renewal/Sharma, Kamal/*Pending Conditions (9-0-0)*

This research laboratory will use recombinant and transgenic methods to understand how neurons are generated in the spinal cord. Transgenic mice will be produced by [redacted] for the study of gene mis-expression in mouse embryos. *In ovo* electroporation and mammalian expression vectors will be used to introduce and transiently over-express genes in the spinal cords of chick embryos. Genes will also be introduced and expressed in cultured cells.

The Committee discussed the use of animals in this protocol. In Section II, the investigator checked "Animal Tissue Only;" however, in the research summary, he described production of transgenic mice and use of adult mice in locomotion experiments. The Committee requested that the investigator submit Supplemental Form B to clarify the use of whole animals in this research and to identify the genes that will be expressed in the transgenic animals.

The Committee recommended approval after the noted issues have been appropriately addressed.

Pending Conditions:

1. In Section V, Staff Signatures, the principal investigator's name and signature are needed.

2. The investigator needs to complete and submit Sections I - IV of the Supplemental Form B to describe all the genes to be expressed in the transgenic mice utilized in this project. Specifically in Section III, question 3, the investigator needs to list each gene being expressed and describe whether the gene product poses any risk to individuals having contact with the animal or its excreta.

897 Renewal/Kraig, Richard/*Pending Conditions and Stipulation (9-0-0)*

This research involves the preparation of enhanced green fluorescent protein (EGFP)-expressing plasmid for loading into polyethylene glycol (PEG)-based nanoparticles. The nanoparticles will be introduced into rats to determine expression and distribution of EGFP within harvested brain, liver and lung tissue.

The Committee discussed the biosafety issues related to the use of the PEG-based nanoparticles. As the protocol lacked specific information about the nanoparticles (composition, bioavailability and half-life), the Committee was unable to fully assess the safety issues. The Committee requested that this information be provided in the protocol.

The Committee discussed the animal work. The investigator has indicated that the particles will be administered intranasally; however, since the specific method of intranasal administration (injection, painting, spraying) was not included, the Committee was unsure if there would be potential for aerosolization. As there was insufficient information about administration and safety of the particles, the Committee requested that all procedures involving the PEG-based nanoparticles be conducted in a biosafety cabinet.

The Committee determined that the lab work must be conducted at BL1 with BL2 practices. The animal work must be conducted at ABSL2, unless the investigator is able to provide sufficient information to ensure that the nanoparticles are safe to work with under ABSL1.

The Committee recommended approval after the noted issues have been appropriately addressed.

Pending Conditions:

1. The investigator needs to provide additional information regarding the composition, bioavailability and half-life of the polyethylene glycol (PEG) based nanoparticles.

2. The Committee has concerns regarding shedding and the possible exposure of animal care workers to the agent. Therefore, the protocol has been classified as Animal Biosafety Level 2 (ABSL2) which will require housing the animals in [redacted]. If additional safety data can be presented, the Committee will reconsider the Animal Biosafety Level.

Stipulation:

The Committee has classified this protocol as Biosafety Level 1 with Biosafety Level 2 practices and determined that a biological safety cabinet must be used for all work involving the PEG-based nanoparticles (loading of cDNA into nanoparticles and inoculation of animals with nanoparticles).

III. Old Business:

A. The Director of Laboratory Programs updated the Committee on previous concerns with the format of environmental monitoring reports for the BSL3 facilities. A meeting was held with Safety and Environmental Affairs to discuss the issues. Safety indicated that the reports are being revised and will be submitted to the IBC.

B. At the July 8th IBC meeting, the Committee voted to accept administrative review and approval of room additions to BL1 and BL2 protocols. Room additions to existing BL2 protocols and rooms indicated for new BL2 protocols will be assessed by Safety and Environmental Affairs prior to approval. Safety will conduct inspections of the facilities to ensure that they are equipped for BL2 work. In response to the Committee's request at the last meeting, safety presented the laboratory inspection process and indicated that the inspection checklists have been updated to include new criteria which will allow for the assessment of biohazards and biosafety equipment.

IV. New Business:

The Committee approved the use of new administrative forms (PI Response Form and Protocol Comments Sheet).

V. Updates:

A. Safety and Environmental Affairs updated the Committee on two incidents involving the [redacted].

- The first case involved access to the BL3 facility by an authorized individual but by an unauthorized method. The authorized staff member had swipe card access but recently obtained a new ID that would not allow access to the facility. The individual was then allowed access by a supervisor. The Responsible Official was immediately notified, along with the University and the Chicago Police Departments and the problem was immediately corrected. Staff members working in the [redacted]

were notified that such incidents will result in termination or other appropriate disciplinary action. In addition, all staff members are required to complete additional security training.

- The second case involved a potential exposure to BL3 select agent. A research staff member experienced percutaneous contact with an instrument that was used on an infected animal. The Responsible Official and Biosafety Officer were immediately notified. The staff member was escorted to the Emergency Room and prophylactic treatment was administered. As a result of this incident, the protocol and Standard Operating Procedures will be reviewed and, if necessary, revised to avoid future incidents.

B. The Committee received an updated IBC Roster.

The University of Chicago

Institutional Biosafety Committee

5841 S. Maryland Avenue
AMB S-152 ♦ MC 1108
Chicago, IL 60637

Minutes of September 2, 2005 Meeting
1:45 PM in [redacted]

In attendance:

Voting Members

Gopal Thinakaran
Richard Hiipakka
Mark Abe
George Daskal
Clara Gartner
Tong-Chuan He
James Mastrianni
Helena Mauceri
Louis Philipson
Mary Ellen Sheridan
Craig Wardrip
Lois Zitzow

Ex-Officio Members

Steve Beaudoin
Russell Herron
David Pitrak

Guest

John Bivona

Staff

Bill Pugh
Pamela Postlethwait
Jennifer Swanson

Absent:

Voting Members

Malcolm Casadaban
Jean Greenberg

Ex-Officio Members

Markus Schaufele

Staff

None

I. **Minutes:** The minutes of the August 5, 2005 meeting were approved with minor clarification regarding the report of unauthorized access to the BL3 facility. The minutes were revised to correctly indicate that an authorized staff member had swipe card access but recently obtained a new ID that would not allow access to the facility. (11-0-0)

II. Protocol Review: The following protocols were reviewed at the meeting, with the disposition noted:

PR# Category/Investigator/*Disposition*

898 New/Glotzer, Michael/*Approved with Stipulation* (11-0-0)

This research involves the study of genes that regulate cytokinesis. Plasmid and baculoviral vectors will be used to introduce wildtype and mutant genes into cultured cells. Genes will be expressed in C. elegans, bacteria, yeast, insect and human cells.

A Committee member noted that the research summary includes an incomplete sentence that needs to be corrected. The Committee had no other issues with the protocol and recommended approval with the stipulation that the investigator correct the incomplete sentence.

Stipulation

In the Protocol Submission Form, please clarify the following issue for your research staff. In Section IV, paragraph 2, line 4, please complete the sentence: "The genes will be _____ to bacteria..."

595 Renewal/Crispino, John/*Pending Conditions* (12-0-0)

The research laboratory investigates the mechanisms of blood cell development using in vivo and in vitro techniques. This work will involve the study of protein-protein interactions using the yeast two-hybrid screen and expression of fusion proteins in bacteria. Retroviral transduction strategies will also be used to express the proteins in mouse hematopoietic primary cells and cell lines. TAT protein will be introduced into murine and human hematopoietic cell lines to investigate whether blocking protein-protein interactions will block leukemic cell growth in tissue culture. Ecotropic murine retroviral vectors will be generated and used to transduce primary murine bone marrow cells. The infected cells will then be injected into lethally and sub-lethally irradiated mice. Additional studies will involve sequencing of DNA isolated from human blood and bone marrow.

The Committee noted several issues that need to be resolved. Supplemental Form B needs to be revised to include updated information (primary lab contact, location where work will be conducted and date of move to [redacted]). Additionally, the sections that describe cage decontamination and carcass disposal need to be revised to indicate standard ARC procedures. The protocol and biosafety manual need to be revised to clarify spill procedures, location of pertinent safety equipment and the meaning of "utility gloves" and "freshly prepared bleach." Additionally, contact information for the oversight person is needed in the protocol.

The Committee recommended approval after the noted issues have been appropriately addressed.

Pending Conditions

1. Please address the following issues in Section VII of the Protocol Submission Form.
    a. In question 12, under "Other," please clarify what is meant by "freshly prepared 10% bleach solution" and "fresh solution of 10% bleach." In particular, please indicate how often the bleach solution will be replaced.
    b. In question 14 please provide contact information for Hui Liu.

2. In the attachment entitled "Spills," please make the following clarifications:

    a. Please identify the location of the hand sinks, eye wash stations and showers to be utilized in the event of a spill.

    b. For spills that involve TAT-fusion proteins, please specify the step by step procedures (i.e. cover with paper towels, working from the outer edges inward apply detergent with a protease enzyme, allow for a 10 – 20 minute contact time and waste is placed in biohazard waste drum for pick-up by EVS) to be followed.

    c. In "Spill of Human Blood or Blood Products/Retroviral Supernatants," under item 6, please clarify what is meant by "utility gloves."

3. In Supplemental Form B, please make the following changes.

    a. In Section I, please update lab contact information.

    b. In Section II, under "Length of time the animal is considered hazardous," please indicate none.

    c. In Section VI, question 2, please update to reflect the new procedure rooms in [redacted].

    d. As the animal biosafety level (ABSL) has been determined to be ABSL1, in Section VII, question 4, please revise to indicate that carcasses will be bagged and placed in the morgue refrigerator as per ARC procedures for barrier facilities.

    e. As the ABSL has been determined to be ABSL1, in Section VII, question 5, please revise to indicate that cages will be decontaminated per ARC procedures for barrier facilities.

610 AD 09/Schneewind, Olaf/*Pending Conditions with Comment* (12-0-0)

The study objective is to characterize the sortase genes and the secretion pathways in Staphylococcus aureus and Listeria monocytogenes. Additionally, the role of bacterial heme-iron uptake and utilization in staphylococcal disease will be studied in a rat model of infection. With this amendment, the investigator is adding a mouse model of pneumonia and changing the primary contact.

The Committee discussed safety issues related to the mouse model of pneumonia. The Committee felt that the necessary precautions will be taken, as the mice will be handled in a biosafety cabinet. However, the Committee recommended that the investigator use scissors rather than scalpels for tissue harvest.

The Committee noted several issues that need to be resolved. A staff member needs to sign the protocol. The PI needs to provide the biosafety cabinet certification date, change the concentration of ethyl alcohol to 70% and clarify "rise in body temperature," "medical officer" and "air filtration mask." There are also numerous typos throughout the submission that should be corrected and "other" should be checked on the amendment form.

The Committee recommended approval after the noted issues are appropriately addressed.

Pending Conditions

1. In Section II of the Amendment Form, please check "other."

2. In Section V of the Protocol Submission Form, please add Yukiko Stranger-Jones to the staff list, as she was added to the protocol with amendment 10 (approved 8/3/05). In addition, please have Juliane Bubeck Wardenburg sign the updated staff signature page, as she is being added with this amendment.

3. Please address the following issues in Section VII of the Protocol Submission Form.

    a. In question 2a, please update the biosafety cabinet certification date.

    b. In question 9, please change the concentration of ethyl alcohol to 70% in order to be consistent with the biosafety manual.

    c. In questions 10 and 11 as well as in the Form B narrative under "Is it treatable?", please clarify what is meant by "medical officer."

    d. In question 11, please clarify what is meant by "a rise in body temperature." In particular, please use and define the term "fever" and indicate the actual temperature range that may cause concern.

    e. In question 14, please provide contact information for Dr. Skaar.

    f. In question 15, please provide contact information for Dr. Schneewind.

    g. In Supplemental Form B, Section VI, question 1, it is indicated that liver, spleen, lung and heart blood are removed by scalpel or syringe-needle aspiration. The Committee recommends that staff members use scissors rather than scalpels to harvest tissue.

    h. In Supplemental Form B, Section VII, question 7, please clarify what is meant by "air filtration mask" (i.e. surgical mask?).

Comment

Please review all revised material (amendment, protocol submission and supplemental forms) for misspellings prior to submission.

626 AD 06/Weichselbaum, Ralph/*Pending Conditions* (11-0-0)

Dr. Mauceri recused herself, as she is listed as a staff member on this protocol.

The research laboratory uses HSV-1 in studies of vein patches, stent procedures, intimal hyperplasia and restenosis in rabbits. With this amendment, the investigator is modifying the experimental procedures: inclusion of a control group and slightly modified operative procedures; addition of a rabbit iliac and carotid model for stent placement.

The Committee discussed the nature of the amendment and determined that there were no changes related to the biohazardous agent. The amendment involves only the addition of procedures to the associated animal protocols. The Committee felt that the protocol contained great detail regarding animal work but little

information about the agent and rationale for its use. Therefore, the Committee requested that the research summary be revised to provide rationale for using the agent.

The Committee noted other minor issues that need to be resolved. Supplemental Form B needs to be revised to indicate that staff should contact UCOM in the event of an exposure. In addition, the form must be revised to incorporate changes requested by the Institutional Animal Care and Use Committee (IACUC).

The Committee recommended approval of the amendment after the noted issues have been appropriately addressed.

Pending Conditions

1. In Section IV, Research Summary, please provide an initial statement explaining the rationale for using the neuro-attentuated, replication competent Herpes Simplex Virus I (HSV-1 R7020) in the described studies.

2. In the "Biohazardous Agent Orientation" narrative for each of the Supplemental Form B, please revise the information provided in item 9 (What do I do if I am exposed) to direct individuals to contact the University of Chicago Occupational Medicine (UCOM) rather than the Infectious Diseases section.

3. Please submit revised Supplemental Form B for ACUPs [redacted] and [redacted] containing the revisions requested by the Institutional Animal Care and Use Committee (IACUC).

697 AD 03/LeBeau, Michelle/*Pending Conditions* (11-0-0)

The research goal is to evaluate candidate tumor suppressor genes to identify a myeloid-leukemia gene in 5q31. Ecotropic retroviral vectors encoding candidate transcripts are used to transduce mouse ES cells in vitro. With this amendment, the investigator is expanding the studies to include transduction of progenitor bone marrow cells with retroviral vectors expressing RNAi constructs for the transcripts encoded by the genes in 5q31. The transduced mouse bone marrow cells will be transplanted into lethally irradiated mice.

A member noted that Supplemental Form B indicates red bagging, red drums and use of the biohazard facility. Since this work will be conducted under ABSL1 conditions, the form needs to be revised to remove these references.

The Committee discussed the animal biosafety level of the protocol. Since the investigator plans to use ecotropic viruses that will only infect mice, there is no risk to humans. Also, since the virus can only be spread vertically, there is very little risk of infecting other mice in the facility. Therefore, ABSL1 conditions are appropriate for this work.

The Committee recommended approval after the noted issues are appropriately addressed.

Pending Conditions

In Supplemental Form B, Section VII, questions 4 and 5, please remove the references to red bagging, biohazard bins and biosafety facility, as this protocol is classified as ABSL1.

III. Old Business:

A. Protocol 897: Review of Dr. Kraig's response to pending conditions

At the 8/5/05 IBC meeting, the Committee discussed Dr. Kraig's protocol involving the use of polyethylene glycol (PEG)-based nanoparticles in animals. Due to limited information provided about composition and safety of the nanoparticles, the Committee determined that lab work must be conducted at BL1 with BL2 practices and animal work must be conducted at ABSL2. However, if the investigator could provide pertinent safety data and information regarding the composition, bioavailability and half-life of the nanoparticles, the Committee would reconsider the biosafety level.

In response to the Committee's comments, the investigator submitted two papers for review. The papers provided information about nanoparticles with similar, but not identical, properties. In addition, the safety information provided was for use in humans, not animals. Since there was still uncertainty regarding the use of these nanoparticles in animals, the Committee felt that the animal biosafety level could not be downgraded to ABSL1. The Committee upheld the original stipulations: lab work must be conducted at BL1 with BL2 practices; animal work must be conducted at ABSL2.

The Committee recommended approval with the noted stipulations (10-1-0).

Stipulations:

1. Please be advised that the Committee has classified this protocol as Biosafety Level 1 with Biosafety Level 2 practices and determined a biological safety cabinet must be used for all work involving the PEG-based nanoparticles (loading of cDNA into nanoparticles and inoculation of animals with nanoparticles).

2. The Committee reviewed the literature that was provided and determined that there is still uncertainty regarding the potential risk of shedding and possible exposure of animal care workers to the agent. Therefore, the protocol has been classified as Animal Biosafety Level 2 (ABSL2) which will require housing the animals in [redacted]. If additional references can be submitted, in particular, those that address shedding and safety for animal care workers, the Committee will reconsider the Animal Biosafety Level.

B. Safety and Environmental Affairs: Revised Environmental Monitoring Reports

Safety and Environmental Affairs provided revised environmental monitoring reports for the BSL3 facilities. The reports were revised according to the Committee's requests and now include clarification of the testing methodology and results of the positive controls. In addition, the reports follow the format requested by the Committee (letterhead, headers/footers, etc.). The committee had no comments.

IV. New Business: None

V. Updates: None

The University of Chicago

Institutional Biosafety Committee

5841 S. Maryland Avenue
AMB S-152 ♦ MC 1108
Chicago, IL 60637

Minutes of October 7, 2005 Meeting
1:45 PM in [redacted]

In attendance:

Voting Members

Gopal Thinakaran
Richard Hiipakka
Mark Abe
Malcolm Casadaban
George Daskal
Tong-Chuan He
Mary Ellen Sheridan
Craig Wardrip
Lois Zitzow

Ex-Officio Members

Russell Herron

Guest

John Bivona

Staff

Bill Pugh
Pamela Postlethwait
Jennifer Swanson

Absent:

Voting Members

Clara Gartner
Jean Greenberg
James Mastrianni
Helena Mauceri
Louis Philipson

Ex-Officio Members

Steve Beaudoin
David Pitrak
Markus Schaufele

Staff

None

I. **Minutes:** The minutes of the September 2, 2005 meeting were unanimously approved (9-0-0).

II. Protocol Review: The following protocols were reviewed at the meeting, with the disposition noted:

PR# Category/Investigator/*Disposition*

891 Revised Deferral/Natarajan, Viswanathan/*Pending Condition and Stipulation* (9-0-0)

This research will investigate the role of lysophosphatidic acid (LPA), spingosine-1-phosphoate (S1P) and NAPDH oxidase in airway inflammation and lung cancer. Replication-deficient adenoviral vectors will be used to study overexpression of LPA and S1P in human epithelial cells and harvested animal tissue.

The Committee discussed the investigator's plan for obtaining the adenovirus. The University of Iowa will prepare the virus; however, it was unclear whether they will test the preparations for replication-competent virus before shipping it to the investigator. The investigator needs to describe how the preparations will be tested for replication competence. In addition, the investigator must be notified that every batch of virus must be tested.

The Committee recommended approval after the noted issues have been appropriately addressed.

Condition:

In Section III, question 4c, the investigator needs to indicate and describe the method(s) that will be utilized to test viral preparations for the presence of replication competent virus.

Stipulation:

Each adenoviral preparation obtained from the University of Iowa Core Facility must be tested for the presence of replication competent virus. If the adenoviral vector will be amplified within the investigator's laboratory, he must test each preparation for the presence of replication competent virus.

895 New/Sisodia, Sangram/*Pending Conditions* (9-0-0)

This research will investigate the effects of familial Alzheimer's Disease (FAD)-linked presenilin-1 variants on notch signaling pathways in adult neural progenitors. Replication-deficient lentiviral vectors will be generated using the three-plasmid expression system. The vectors will then be used to transduce neural stem cells for the study of wild type and mutant proteins of interest.

The Committee discussed several issues that need to be resolved. The investigator needs to: remove "etc" from the submission; list the lentiviral proteins that will be expressed; replace "randomly" with the actual frequency of testing; describe the studies/analyses that will be conducted with the transduced cells; describe the hazards associated with integration of the recombinant virus; check "Authorized Access Only" and describe specific BL3 practices that will be used; remove the term "consolidated"; and clarify decontamination procedures.

The Committee recommended approval after the noted issues are appropriately addressed.

Conditions:

1. The Committee requests that the abbreviation "etc" be deleted from the protocol, as it does not provide information that is pertinent to risk assessment. Therefore, the investigator needs to remove "etc" from Section III, questions 3, 4 and 9; and Section IV, paragraph 2, line 6.

2. Section III, question 4c, and Section IV, second to last line, indicate that the viral preparations will be "randomly" tested for replication competent virus. The Committee requested that the term "randomly" be replaced with the actual frequency of testing. *The investigator was informed that every batch must be tested for replication competent virus.*

3. In Section III, question 9, the investigator needs to indicate the lentiviral proteins that will be expressed.

4. In Section IV, the investigator needs to describe the studies/analyses that will be conducted after the neural progenitor cells have been infected with lentivirus.

5. In Section VII, the investigator need to address the following issues.
   a. In question 4, the investigator needs to describe the hazards associated with integration of the virus.

   b. In question 5, the investigator needs to check "Authorized Access Only," as this is a BL3 requirement.

   c. In question 6, the investigator needs to remove the term "consolidated."

6. In the SOP for Lentivirus Usage, the investigator needs to address the following issues.
   a. In #3, the investigator needs to revise to describe BL3 practices.

   b. The investigator needs to provide a list of specific BL3 practices that will be used in this research.

   c. The investigator needs to specify which materials should be decontaminated with bleach and which should be autoclaved. *The investigator was informed that materials containing bleach should not be autoclaved due to the potential for autoclave damage and generation of toxic by-products.*

900 New/Goldstein, Steve/ *Approved* (9-0-0)

This research involves the study of potassium channel structure and function. Plasmid vectors will be used to introduce potassium channel genes into S. cerevisiae, mammalian cells and frog oocytes. Proteins of interest will be studied *in vitro* using standard electrophysiological or biochemical techniques.

The Committee had no concerns with this protocol and recommended approval.

902 New/Keenan, Robert / *Approved with Stipulation* (9-0-0)

This laboratory investigates the relationship between a protein's sequence, three dimensional structure and resulting function. In particular, this project focuses on two model systems—fluorescent proteins from C. californica and bacterial N-acetyltransferase from B. licheniformis. Wild-type and variant genes encoding

these proteins will be cloned into standard E. coli expression plasmids, which will then transformed and expressed in standard E. coli strains. Proteins will be characterized in terms of structure and function.

The Committee discussed the investigator's use of live bacteria in the lab. The investigator indicated that he obtained a sample of B. licheniformis in order to isolate a particular gene. It was unclear whether this work was conducted prior to submission of the protocol. The Committee requested that the investigator be informed that this type of work requires IBC approval prior to initiation. Therefore, if he decides to work with the live organism in the future, he must amend the protocol and receive IBC approval before the work begins.

The Committee recommended approval with the noted stipulation.

Stipulation:

The investigator was notified that all work involving live bacteria must be approved by the IBC. If, at any time, this research changes to involve work with live bacteria, an amendment must be submitted and approved prior to initiation of the work.

905 New/Schreiber, Hans/ *Pending Conditions* (9-0-0)

The research goal is to develop novel gene therapy approaches to promote rejection of established tumors. Studies will utilize replication-deficient adenovirus expressing murine T cell receptor to transduce murine lymphocytes for inoculation into tumor bearing mice.

The Committee recommended approval after the associated animal protocol is reviewed and approved by the Institutional Animal Care and Use Committee (IACUC).

Condition:

The associated amendment to ACUP [redacted] for the use of replication deficient adenovirus in mice must be reviewed and approved by the Institutional Animal Care and Use Committee (IACUC).

906 New/Hara, Manami/ *Approved* (9-0-0)

Using genetic approaches, the investigator will characterize genes involved in the formation and function of endocrine and exocrine tissue of the pancreas. Genes will be cloned and inserted into E. coli or S. cerevisiae for *in vitro* studied.

The Committee had no concerns with this protocol and recommended approval.

907 New/Zhuang, Xiaoxi/ *Approved* (9-0-0)

This research will investigate the role of SK3 (a calcium activated potassium channel) in firing patterns of dopamine cells in response to learning and memory. Transgenic mice will be generated to overexpress either the wild-type SK3 or a naturally occurring mutant form, SK-1B, which lacks the N-terminus and the first transmembrane portion. SK-1B has been shown to act as a dominant-negative mutant. The rDNA will be prepared using standard techniques and the transgenic mice will be generated [redacted].

The Committee had no concerns with this protocol and recommended approval.

585 Renewal/Mastrianni, James/ *Pending Conditions* (9-0-0)

The proposed research is designed to generate wild-type non-pathogenic prion protein (PrP) and mutant prion protein with various mutations associated with human disease (PrP-Sc). Expression vectors will be used to generate prion protein in yeast and cell cultures. Purified preparations of pathogenic PrP-Sc protein will be injected into the cerebrum of hamsters. Transgenic mice will also be generated by injection of fertilized oocytes with expression vectors containing the murine PrP promoter.

A member noted that the investigator included a Supplemental Form B for transgenic work; however, transgenic work is not described in the research summary. This needs to be clarified by the investigator.

The Committee discussed the investigator's autoclaving procedures. The investigator indicated that cages will be autoclaved at 132°C for 4.5 hours; however, the cages will not withstand repeated autoclaving under those conditions. The Committee requested that the investigator consult with the Centers for Disease Control (CDC) for the most recent recommendations regarding prion inactivation. If the investigator retains the current procedures in the protocol, he will have to work with [redacted] to discuss caging options.

The Committee discussed other issues that need to be addressed. The investigator needs to: check "Authorized Access Only" for BL3 practices; indicate safety glasses; explain post-treatment, otherwise remove reference; and describe the relevant qualifications of the individual responsible for oversight.

The Committee recommended approval after the noted issues are appropriately addressed.

Conditions:

1. A Supplemental Form B for the production of transgenic animals was provided. However, in Section IV, Summary of Research, production of transgenic animals was not described. The investigator needs to clarify if transgenic animals are being produced and if so, the investigator needs describe this work in Section IV.

2. In Section VII, question 5, the investigator needs to check "Authorized access only".

3. In Section VII, question 8, the investigator needs to check "Safety Glasses" and/or "Safety Goggles/Shield".

4. In Section VII, question 10, it is indicated that effective post exposure treatment is available. If this is correct, the investigator needs to provide details of the treatment available.

5. In Section VII, question 14, the investigator needs to describe Mark Ciaccio's qualifications with regard to working with biohazardous agents, microbiology and molecular biology techniques.

6. The protocol indicates that animal bedding and caging will be autoclaved at 132°C for 4.5 hours as recommended by the Biosafety in Microbiological and Biomedical Laboratories (BMBL), 4th Edition. The investigator was informed that the caging utilized by [redacted] may not be amenable to repeated autoclaving at this temperature and time. Therefore, the Committee recommends

consulting with the Centers for Disease Control (CDC) to verify the current guidelines for autoclaving prion waste. If the CDC recommendation continues to be 132°C for 4.5 hours, the investigator needs to consult with [redacted] regarding possible changes in caging that may be necessary.

596 Renewal/Malamy, Jocelyn/ *Approved* (9-0-0)

This research involves the study of molecular mechanisms that regulate root systems in plants and how these mechanisms incorporate environmental information. Arabidopsis thaliana will be used as a model system. The soil bacterium, Agrobacterium tumefaciens, will be used to introduce novel gene constructs into Arabidopsis to monitor gene expression.

The Committee had no issues with this protocol and recommended approval.

599 Renewal/Kossiakoff, Anthony/ *Approved* (9-0-0)

This research focuses on the biophysical and structural analysis of proteins of the growth hormone/prolactin protein signaling family. Protein function will be evaluated by introducing mutations into the amino acid sequence of human growth hormone; the human growth hormone receptor, prolactin; the prolactin receptor; and placental lactogen. Commercially available vectors, plasmids and helper phages will be used. Standard molecular biology techniques will be employed.

The Committee had no concerns with this protocol and recommended approval.

604 Renewal/Frank, Karen/ *Approved* (9-0-0)

This research involves the use of standard cloning techniques and common vectors to study nonhomologous endjoining. Wild-type and mutant genes will be propagated and modified in bacteria and yeast cells and then transiently and stably expressed in mammalian tissue cultured cells. In addition, a baculovirus system will be used to introduce and express genes in insect cells.

The Committee had no concerns with this protocol and recommended approval.

870 AD 01/Kalinichenko, Vladimir/ *Pending Conditions* (9-0-0)

This research involves the study of transcriptional targets of Foxf1 and the role of Foxm1b in endothelial proliferation, differentiation and migration. Studies will be conducted *in vitro* and *in vivo*. With this amendment, the investigator is including the use of an SPC-Foxm1 construct for the generation of transgenic mice.

The Committee recommended approval after the Institutional Animal Care and Use Committee (IACUC) reviews and approves the associated animal protocol.

Condition:

The Institutional Animal Care and Use Committee (IACUC) must review and approve the associated ACUP [redacted].

III. Old Business:

Protocol 897: Review of additional safety information regarding the use of PEG-based nanoparticles

At the 9/2/05 IBC meeting, the Committee discussed Dr. Kraig's response to the pending conditions letter of 8/5/05. The investigator submitted additional information regarding the use of polyethylene glycol (PEG)-based nanoparticles and requested that the animal biosafety level be reconsidered. The Committee determined that the information lacked sufficient data to support downgrading the protocol to ABSL1. After further discussion with Dr. Kraig, the IBC Chair was able to obtain additional safety data from an investigator in Greece who works with these nanoparticles. The investigator indicated that the particles are safe; however, the toxicity of the bioactive agent must be considered when determining the safety level. The investigator also indicated that animals injected with the particles would pose no additional risk to animal care workers as long as standard safety precautions were followed. Since Dr. Kraig plans to work with Enhanced Green Fluorescent Protein (EGFP), which it typically handled under ABSL1 conditions, the Committee determined that the animal biosafety level could be downgraded to ABSL1. The Committee noted, however, that the biosafety level would have to be reconsidered if the investigator decides to use additional recombinant DNAs.

The Committee recommended approval with the noted stipulations (9-0-0).

Stipulations:

1. The Committee has classified this protocol as Biosafety Level 1 with Biosafety Level 2 practices and determined that a biological safety cabinet must be used for all work involving the PEG-based nanoparticles (loading of cDNA into nanoparticles and inoculation of animals with nanoparticles).

2. The Animal Biosafety Level (ABSL) has been classified as ABSL1.

3. This protocol is only approved for the use of the PEG-based nanoparticles conjugated with enhanced green fluorescent protein (EGFP). Any change in the recombinant DNA conjugated to the PEG-based nanoparticles will require the review and approval of the IBC prior to initiation of the studies.

IV. New Business: New Submission Forms and Issues for Discussion

The Committee briefly discussed the proposed new submission forms and issues associated with the submission process. A detailed discussion of the forms and issues will take place at the November meeting.

V. Updates:

A. Safety and Environmental Affairs: Follow-up on Decontamination and Spill Procedures

In response to the Committee's requests at the last meeting, the Safety and Environmental Affairs Office presented a proposal for decontamination and spill procedures. Rather than implementing formal university policies, the Safety Office will refer investigators to the Health Canada website where they can find Material Safety Data Sheets (MSDS) for commonly used agents. These sheets provide methods of decontamination which are specific to each agent. A member noted that additional guidelines may be needed since the Health Canada site does not provide step-by-step procedures for spill containment and decontamination.

B. The Committee was provided with a reference article about bleach.

The University of Chicago

Institutional Biosafety Committee

5841 S. Maryland Avenue
AMB S-152 ♦ MC 1108
Chicago, IL 60637

Minutes of November 4, 2005 Meeting
1:45 PM in [redacted]

In attendance:

Voting Members

Gopal Thinakaran
Richard Hiipakka
Mark Abe
Malcolm Casadaban
George Daskal
Clara Gartner
Jean Greenberg
Tong-Chuan He
Mary Ellen Sheridan
James Mastrianni
Helena Mauceri
Lois Zitzow

Ex-Officio Members

Steve Beaudoin
Russell Herron
David Pitrak

Guest

John Bivona

Staff

Bill Pugh
Pamela Postlethwait
Jennifer Swanson

Absent:

Voting Members

Louis Philipson
Craig Wardrip

Ex-Officio Members

Markus Schaufele

Staff

None

I. **Minutes:** The minutes of the October 4, 2005 meeting were unanimously approved (11-0-0).

II. **Protocol Review:** The following protocols were reviewed at the meeting, with the disposition noted:

PR# Category/Investigator/Disposition

899 New/Birukov, Konstantin/Pending Conditions (12-0-0)

This research involves the use of E. coli, rDNA, human and bovine cell cultures and adenoviral vectors. The research goal is to understand the molecular mechanisms of cytoskeletal regulation of lung endothelial cell permeability by mechanical factors (stretching), barrier protective agonists (phospholipids, sphingosine) and edemagenic agents (thrombin, TNF alpha) as they relate to lung injury and inflammation. The research will involve exploration of signal transduction pathways pertaining to endothelial barrier regulation. This will be done by overexpressing or silencing genes that are related to focal adhesions, aherens junctions, and small GTPase-mediated signal transductions. Standard methods of DNA generation, mutation, and cell transfections will be used. Gene expression will be regulated by siRNA and dominant-negative inhibition. Several methods will be used to test the effects of these manipulations, including transendothelial electrical resistance of cells with gold microelectrodes; stretching and shearing the cells; or chemically stimulating them with oxidized phospholipids, HGF, TNF alpha, or thrombin.

The Committee discussed the adenoviral vectors. It appears that the investigator will be using the ADEasy 1 viral vector kits; however, it is unclear if the vectors will be prepared by the investigator or by an outside facility. The investigator needs to clarify who will be preparing the vectors and who will be testing the preparations for replication-competent virus. The investigator should also describe the methods that will be used to test the preparations. In addition, the Committee felt that more information was needed about how the vectors will be used in the research.

The reviewer noted the following issues that need to be addressed by the investigator: all genes must be properly described--the descriptions provided in the current version of the protocol are different from the previous version; all proteins to be expressed (corresponding to the 28 genes listed earlier in the protocol) must be listed; animal care and use should be deleted from the PI's responsibilities, as this research will not involve animals; safety goggles need to be indicated for face protection; hazards associated with the transgenes need to be described, especially with respect to cytoskeletal remodeling and cell adhesion; and more information is needed regarding qualifications of the individual who will be responsible for oversight.

The Committee recommended approval after the noted issues are appropriately addressed.

Pending Conditions

1. In Section II, under "Whole Animals," the investigator needs to de-select the checkbox ABL1, since he has indicated that the protocol does not involve animal work.

2. In Section III, question 3, some of the tag descriptions have changed since the original submission. For example, inserts 6-8 had the tag description "ras-related C3 botulinum toxin substrate 1," instead of the current "ras-related GTP-binding protein." The investigator needs to review, and if necessary revise, the following inserts/tags: 6-10, 14-17, and 27-28.

3. In Section III, question 4c, the investigator needs to specify who will be preparing the adenoviral vectors and who will be testing the viral preparations for replication-competence. In addition, the investigator needs to describe the methods that will be used to test for replication-competence. If 293

cells will not be used in the methods, the investigator needs to remove these references from this section. Also, the investigator needs to be informed that every batch must be tested.

4. In Section III, question 8, the investigator needs to de-select "BL1 w/BL2 practices," since this protocol will be conducted at BL2.

5. In Section III, question 9a, only one protein is listed; however, there are 28 genes listed in question 3. In 9a, the investigator needs to list all of the proteins that will be expressed during the course of this research.

6. In Section IV, the investigator needs to specify who will be producing the adenoviral vectors and describe the methods used to produce the vectors. In addition, the investigator needs to explain how the vectors will be used in this research.

7. In Section V, the PI's responsibilities still include "Animal Care and Use." Since animals will not be used in this research, the investigator needs to remove this reference to animal work.

8. In Section VII, question 4, the investigator needs to provide additional information regarding agent hazards. In particular, the investigator needs to describe the hazards associated with inhalation of the recombinant virus and expression of mutant genes or overexpression of genes in the lungs, especially with respect to cytoskeletal remodeling and cell adhesion.

9. In Section VII, question 5, next to PPE, the investigator needs to replace "face protection" with "face mask" and indicate "safety goggles."

10. In Section VII, question 8, the investigator needs to indicate "safety goggles/shield" instead of "safety glasses."

11. In Section VII, question 14, the investigator needs to provide relevant qualifications of A. Mikailyan. The Committee felt that "Research Professional Associate" did not adequately describe why this individual is qualified to oversee this project in the PI's absence.

904 New/ Daum, Robert /<u>Pending Conditions</u> (12-0-0)

This research involves the production of an animal model of community-acquired methicillin-resistant Staphylococcus aureus (CA-MRSA). The animal model will be used to study the role of Panton-Valentine leukocidin (PVL) in the pathogenesis of CA-MRSA severe sepsis. To create the model, CA-MRSA containing PVL will be administered to adult male rats by intratracheal inoculation. Rats will be euthanized when illness occurs and the carcasses will be used for histological analysis.

The Committee discussed several issues that need to be resolved. A member noted that the protocol includes some inaccurate information regarding consequences of exposure and communicability of the agent. In particular, pneumonia and septicemia should be listed as consequences of exposure. Also, in addition to clindamycin, the investigator should indicate acceptable alternatives.

The Committee noted the following additional issues that need to be addressed by the investigator: a type II biosafety cabinet must be used; safety goggles/shield should be used when working outside of a biosafety cabinet; in case of exposure, staff members need to contact UCOM rather than OSHA; and for spills, more information is needed about proper containment and decontamination procedures.

The Committee recommended approval after the noted issues are appropriately addressed.

Pending Conditions

1. The investigator needs to be informed that work with RG2/BL2 agents requires the use of a Class II Biosafety Cabinet. Therefore in Section VII, question 2, the investigator needs to indicate the use of either a IIa, IIb1, IIb2 or IIb3 Biosafety Cabinet.

2. In Section VII, question 4, the investigator needs to include pneumonia and septicemia as a potential consequence of exposure and include information regarding the communicability of the agent and mode of transmission. This information also needs to be included in the "Policies for Handling Staphylococcus aureus" manual.

3. In Section VII, question 5, under "Donning of PPE," the investigator needs to include safety goggles/shield when working outside of a biosafety cabinet. Additionally, in Section VII, question 8 and the "Policies for Handling Staphylococcus aureus" manual, the investigator needs to revise to make consistent with question 5.

4. In Section VII, question 9 and the "Policies for Handling Staphylococcus aureus" manual, the investigator needs to revise the spill procedures to indicate the following: In the event of a spill, personnel will leave the room for 30 minutes to allow aerosols to settle. Wearing the appropriate PPE, the spill will be covered with paper towels. Starting at the outer edges and working toward the center, a bleach solution (1:100) is applied for a contact time of 10 minutes. The surface will then be wiped with a 70% ethanol solution. All material is then placed in biohazard waste drum for pick-up by EVS. Please note that the Health Canada Material Safety Data Sheet (MSDS) for S. aureus recommends using a 1% hypochlorite solution (1:5 dilution of household bleach) for disinfecting.

5. The investigator needs to clarify if clindamycin is the only antibiotic available for treatment or are there acceptable alternatives. If so, the investigator needs to revise Section VII, question 10 accordingly.

6. In Supplemental Form B, Section VII, question 11, and the Form B narrative, under "What do I do if I am exposed?", the investigator also needs to indicate that individuals will report to the University of Chicago Office of Occupational Medicine (UCOM) in the event of an exposure.

908 New/ Chang, Eugene /Pending Conditions (12-0-0)

This research involves the preparation of conditioned media from Lactobacillus and Bifidobacteria species to test the anti-inflammatory and cytoprotective activity on intestinal structure and function in mouse models of colitis and ischemia/reperfusion injury.

The Committee had no concerns with this protocol and recommended approval after the noted issue has been resolved.

Pending Condition

In Supplemental Form B, Section IV, the investigator needs to indicate Animal Biosafety Level 1 (ABSL1).

598 Renewal/ Cohen, Ronald/Pending Conditions (12-0-0)

This research involves molecular biology techniques and mouse models to study the in vitro and in vivo mechanisms of nuclear hormone receptors (NHRs) and corepressors. In particular, the investigator will examine the role of nuclear receptor corepressor (NCoR) and silencing mediator of retinoid and thyroid hormone receptors (SMRT) in peroxisome-proliferated activated receptor (PPAR) and thyroid hormone receptor (TR) action. Standard plasmid vectors, cDNAs, E.coli and mammalian cell lines will be used.

The Committee noted the following issues that need to be addressed by the investigator: all genes should be specified, including genes that will be knocked down by RNA interference; administrative issues in section III need to be resolved; and one staff member's signature is still needed.

The Committee recommended approval after the noted issues are appropriately addressed.

Pending Conditions

1. In Section III, question 3, the investigator needs to remove "such as" or specify all the nuclear hormone receptors, transcription factors and cofactor proteins that will be studied in this project.

2. In Section III, question 4, it is indicated that shRNA constructs will be cloned into the pSIlencer vectors for RNA interference. Therefore, in Section IV, Summary of Research, the investigator needs to clarify which gene(s) will be knocked down in the RNA interference experiments.

3. In Section III, questions 4b and 4c, the investigator needs to indicate N/A.

4. In Section III, question 5, the investigator needs to indicate E. coli and mice as the host for the vectors.

5. In Section V, Staff Signatures, the investigator needs to have Christine Yu sign.

624 AD 04/Reardon-Alulis, Catherine/Pending Conditions (12-0-0)

The investigator has been studying the ability of apoproteins, lipid modifying proteins and lipoprotein receptors to influence lipid metabolism, lipoprotein profile and atherosclerosis using cultured cells and mouse models. This amendment is a request to change the animal biosafety level from ABSL2 to ABSL1 for injection of bone marrow or fetal liver cells transduced with ecotropic, replication-deficient retrovirus into mice.

The reviewer noted that a previous amendment was submitted to include the use of ecotropic, replication-deficient retrovirus. The retroviral vectors listed in the original amendment are MFG and pLXIN. Specific information regarding these vectors and the method used to verify that the retrovirus preparations remain replication-deficient were not requested in the original retroviral amendment. The investigator has now provided that information; however, some clarification is still needed. The investigator has indicated that RT-PCR will be used. Since the PCR method can result in false positives, the Committee recommended assaying

for replication competent virus when determining viral titer. Supernatant from the NIH 3T3 cells can be added to fresh cells to test for antibiotic resistance or transgene-derived protein. The Committee also requested that every batch of virus be tested.

The Committee requested the following additional changes: in the investigator's response to preliminary review, question 1, the term "recombination" needs to be changed to "packaging"; and in the section III of the protocol, more information is needed regarding the genes that will be studied.

The Committee recommended approval after the noted issues have been appropriately addressed.

Pending Conditions

1. In the PI Response Form sent 10/19/2005 to address reviewer's questions, under question 1, it is stated that "Recombination will occur in the GP2-293 cells that have the gag and pol genes stably integrated into the genome". As these cells will be used to package the virus, the investigator needs to revise to indicate "Packaging will occur in the GP2-293 cells that have the gag and pol genes stably integrated into the genome".

2. In Section III, question 3, the investigator needs to specify the genes being studied for each of the categories listed.

3. Prior to infecting the bone marrow or fetal livers cells, each preparation of retrovirus must be tested for the presence of replication competent virus (RCV). Rather than using PCR which could result in false positives, the Committee recommends assaying for RCVs when determining viral titer. Following infection of the NIH 3T3 cells, supernatant from these cells can be added to fresh cells and assayed for antibiotic resistance or expression of transgene-derived protein. The investigator needs to revise Section IV, Summary of Research and Supplemental Form B, Section VII, question 16 accordingly.

840 AD 02/ Li, Yan Chun /Pending Conditions (12-0-0)

This lab studies the roles of the vitamin D endocrine system. Adenoviral vectors are used to introduce genes of interest into mammalian cells and mice. With this amendment, the investigator is requesting to add the use of retroviral vectors (Moloney Murine Leukemia Virus). In addition, new staff members are being added.

The Committee discussed several issues that need to be resolved in the retroviral biosafety manual. It appears that the manual was created by copying the adenoviral manual, as there are several references to adenovirus instead of retrovirus. The investigator needs to ensure that the manual is specific to retrovirus. The investigator also needs to describe the hazards associated with the retrovirus itself (without the oncogenes) and the routes of exposure. In addition, a member requested that the term "should" be replace with "shall" so that staff members are aware that the PI must be contacted in all cases of exposure.

The investigator needs to address the following issues in the protocol: hazards associated with the retrovirus need to be described; full gene names are needed; "safety glasses" should be changed to "safety goggles"; and a staff member's signature is needed.

The Committee recommended approval after the noted issues are appropriately addressed.

Pending Conditions

1. The investigator needs to address the following issues in the "Biosafety Manual for Construction and Use of Recombinant Retrovirus."

   A. The Committee noted several instances where "adenovirus" was mentioned instead of "retrovirus." The investigator needs to search the document to ensure that "adenovirus" is replaced with "retrovirus."

   B. On page 1, f., the investigator needs to replace "should" with "shall." The investigator also needs to make this change in the biosafety manual for adenovirus.

   C. On page 1, "What disease could adenovirus [should be retrovirus] cause," the investigator also needs to describe the hazards associated with the retrovirus itself (without the oncogenes).

   D. On page 2, in "What is an exposure?" the investigator needs to use language that is similar to what was used in "How could I be exposed?" In particular, the investigator needs to replace "Direct contact with virus, direct inhalation of aerosols of virus or a needle stick" with "Direct contact with exposed skin, eyes, or mucosal membranes, ingestion, inhalation and injection."

2. The investigator needs to address the following issues in the Protocol Submission Form.

   A. In Section III of the protocol, question 3, the investigator needs to provide the full names for the gene acronyms.

   B. In Section VII, question 4, the investigator also needs to describe the hazards associated with integration of the retrovirus itself (without the oncogenes).

   C. In Section VII, questions 5 and 8, the investigator needs to indicate "safety goggles" instead of "safety glasses."

   D. In Section VII, question 14, the investigator needs to provide contact information for Dr. Kong.

897 AD 01/ Kraig, Richard/Pending Conditions (12-0-0)

This research involves the use of nanoparticles and plasmid DNA expressing green fluorescent protein (GFP). This amendment was submitted in order to clarify the location of procedures and correct an error in the original procedures. Plasmids with various promoters will be generated in the investigator's lab and will be transported to [redacted] where they will be incorporated into PEG-modified polylactic-polyglycolic acid nanoparticles. All work at [redacted] will be covered by that facility's IBC. Lyophilized nanoparticles will then be transported to University of Chicago. Nanoparticles will be reconstituted and introduced into cultured cells for studies of gene expression. Some of the cells will then be injected into animals. In addition, nanoparticles will be introduced into animals through intravenous or intranasal injections. Future work will involve intra-arterial injections that will require the use of stereotaxic equipment.

The reviewer noted that only the procedures carried out at this institution should be reviewed by this Committee. These include preparation of the plasmid DNA, reconstitution of the lyophilized nanoparticles, and in vitro and in vivo experiments.

The Committee discussed the location of work and noted that the location of the biosafety cabinet and the cabinet re-certification date need to be added to the protocol.

The Committee discussed the use of stereotaxic equipment. The investigator has indicated that future work involving intra-arterial injections will require stereotaxic equipment; however, the equipment cannot be used in a biosafety cabinet. After discussing some of the safety issues associated with working outside of the biosafety cabinet, the Committee decided to defer the issue until the investigator formally requests permission to carry out these procedures. Currently, only intravenous and intranasal injections are being performed. These injections do not require stereotaxic equipment and will be performed in the biosafety cabinet. The Committee had no further concerns with the current procedures.

The Committee recommended approval after the noted issues have been appropriately addressed.

Pending Conditions

1. In Section I, Project, the investigator needs to include [redacted] and [redacted] under "Location of Proposed Work/Experiments."

2. The investigator needs to provide the certification date for the biosafety cabinet in [redacted].

III. Old Business: None

IV. New Business:

A. Discussion of Proposed Changes to IBC Submission Forms
The Committee discussed the new protocol submission form and requested changes to some of the questions. The Committee also discussed the issue of human and non-human primate cell lines and whether investigators should complete the agent profile form to describe decontamination and disposal procedures for the cells. This issue, as well as review and discussion of the profile and amendment forms, were deferred until the next meeting.

B. Discussion of Issues Related to the Submission/Review Process
These issues were deferred until the next meeting.

V. Updates: None

The University of Chicago

Institutional Biosafety Committee

5841 S. Maryland Avenue
AMB S-152 ♦ MC 1108
Chicago, IL 60637

Minutes of December 2, 2005 Meeting
1:45 PM in [redacted]

In attendance:

Voting Members

Gopal Thinakaran
Richard Hiipakka
Mark Abe
Malcolm Casadaban
George Daskal
Jean Greenberg
Tong-Chuan He
Helena Mauceri
Craig Wardrip
Lois Zitzow

Ex-Officio Members

Steve Beaudoin
Russell Herron
David Pitrak
Markus Schaufele

Guests

None

Staff

Bill Pugh
Pamela Postlethwait
Jennifer Swanson

Absent:

Voting Members

Clara Gartner
Louis Philipson
James Mastrianni
Mary Ellen Sheridan

Ex-Officio Members

None

Staff

None

I. **Minutes:** The minutes of the November 4, 2005 meeting were unanimously approved (9-0-0).

II. **Protocol Review:** The following protocols were reviewed at the meeting, with the disposition noted:

PR# Category/Investigator/Disposition

912 New/Martinez, Juan/Approved (9-0-0)

This lab studies host cell signaling pathways and bacterial entry in Rickettsial infections. Genes for Rickettsial surface antigens will be cloned and expressed in *E. coli*. Standard gentamicin resistance assays will be conducted in mammalian cell lines to investigate the interactions between host cell and Rickettsial genes.

The reviewer noted that the agent used in this research is Risk Group 1; however, the protocol will be conducted under Biosafety Level 2. The investigator may have classified the research as BL2 because he plans to work with human and non-human primate cell lines. The reviewer questioned whether this protocol should have a separate biosafety manual for the BL2 practices. Typically, the IBC does not require a manual for RG1 agents. Also, since the research involves only genes from Rickettsial species and not whole organism, the Committee determined that a separate biosafety manual was not required for this protocol.

The Committee had no concerns with this protocol and recommended approval.

641 AD 03/Daum, Robert/Deferred (9-0-0)

This laboratory's goal is to determine possible antibiotic resistance mechanisms in *Staphylococcus aureus*. With this amendment, the investigator is adding new bacterial strains, including Vancomycin-resistant *S. aureus* and community-acquired Methicillin-resistant *S. aureus*. Some of the strains will be obtained from patient isolates and others will be obtained from the Centers for Disease Control (CDC). The investigator is also adding staff and rooms.

A member noted that the protocol includes a reference to effective post-exposure treatment; however, it lacks specific treatment options. The investigator should list the antibiotics that can be used to treat exposures.

The Committee discussed the surveillance plan for this protocol. The investigator has included the CDC guidelines for surveillance; however, since these guidelines were last approved in 2003, the investigator's surveillance plan may need to be revised. To ensure that the proper surveillance protocol is being followed, the Committee requested that the investigator meet with Steve Beaudoin, Director of Safety and Environmental Affairs. The Committee also requested that the final plan be incorporated into the protocol. In particular, the protocol should include the sampling method(s), sampling frequency, and procedures for documenting the sampling and results.

A member noted that the individual responsible for oversight is also the emergency contact. In addition, the individual has a phone number but not a pager number. For emergency purposes, the Committee requested that the investigator be added as an emergency contact and that alternate contact numbers be provided for both individuals.

The Committee felt that this protocol lacked sufficient information and deferred discussion until the noted issues have been appropriately addressed.

Reasons for Deferral:

1. In Section VII, question 10, it is indicated that effective post exposure treatment is available. The investigator needs to provide details regarding the post exposure treatment plan and specify the available antibiotics for treatment.

2. In Section VII, question 15, the investigator needs to include the Principal Investigator and provide a contact and alternate contact number for both individuals listed.

3. The investigator needs to work with Steve Beaudoin (4-1131), Director, University of Chicago Safety Office, to revise the surveillance protocol for these agents. The protocol should include the sampling method(s), sampling frequency, and procedures for documenting the sampling and results.

III. Old Business:

A. Discussion of Proposed Changes to IBC Submission Forms
The Committee discussed the new protocol submission forms and requested changes to some of the questions. Discussion of the new forms will continue at the next meeting.

B. Discussion of Issues Related to the Submission/Review Process
These issues were deferred until the next meeting.

IV. New Business: Delinquent Response to Annual Renewal Survey (Ferguson—739 and 741)

The Committee discussed the issue of Dr. Ferguson's delinquent response to several requests for submission of the annual renewal surveys. Dr. Ferguson was sent e-mail notifications from the IBC staff and Chairman. Responses to these e-mails were never received. The Committee felt that the investigator should be given a final one-week deadline to submit the renewal forms or the protocols will be terminated.

V. Updates: The Committee was provided with the IBC meeting schedule for 2006.

The University of Chicago

Institutional Biosafety Committee

5841 S. Maryland Avenue
AMB S-152 ♦ MC 1108
Chicago, IL 60637

Minutes of January 6, 2006 Meeting
1:45 PM in [redacted]

In attendance:

Voting Members

Gopal Thinakaran
Richard Hiipakka
Malcolm Casadaban
George Daskal
Clara Gartner
Tong-Chuan He
James Mastrianni
Helena Mauceri
Louis Philipson
Mary Ellen Sheridan
Lois Zitzow

Ex-Officio Members

Steve Beaudoin
Russell Herron
David Pitrak

Guests

John Bivona

Staff

Bill Pugh
Pamela Postlethwait
Jennifer Swanson

Absent:

Voting Members

Mark Abe
Jean Greenberg
Craig Wardrip

Ex-Officio Members

Markus Schaufele

Staff

None

I. **Minutes:** The minutes of the December 2, 2005 meeting were unanimously approved (9-0-0).

II. **Protocol Review:** The following protocols were reviewed at the meeting, with the disposition noted:

PR# Category/Investigator/Disposition

901 New/Tatyana Golovkina/Approved w/Comment (11-0-0)

This research will use a mouse model for resistance to leukemia to understand how enhanced responses of the immune system to tumors can lead to tumor suppression. The mouse model is based on mouse murine leukemia virus (MMLV), a retrovirus that causes leukemia in susceptible mice. Transgenic mice will be generated and infected with MMLV that has been isolated from sera of naturally infected mice. Infected mice will be aged and monitored for anti-virus antibody production. Susceptible and resistant (antibody producing) mice will be genotyped to map the resistant gene.

The Committee discussed the title of the protocol which makes reference to mammary tumors. It was unclear if the research would involve the use of mouse mammary tumor virus (MMTV), or just the genes from the virus. Since current literature suggests that MMTV is infectious to humans, the Committee requested that the investigator notify all staff members. A comment will be added to the letter.

The Committee recommended approval with a comment regarding the current literature on MMTV infection of human cells.

Comment:

The investigator should be advised that current literature indicates that the mouse mammary tumor virus (MMTV) is capable of infecting various human cells. The investigator needs to apprise staff members of this possibility and ensure that appropriate precautions are being taken when handling mice infected with MMTV. Also, the investigator should do not distribute mice infected with MMTV to other investigators in the facility.

911 New/Yoav Gilad/Pending Conditions (11-0-0)

This research involves the study of human and non-human primate putative promoters. Genes will be extracted from liver tissues of human, chimpanzee, orangutan and rhesus monkeys. Genes will be cloned in *E.coli* and transfected into commercial cell lines with a Luciferase reporter gene vector. Luciferase will be measured.

Since the protocol involves primate tissues, the Committee requested that the investigator complete and submit Section VII of the protocol. The biosafety level should also be changed to BL2. Prior to approval, the Committee requested that the Safety Office review the PI's response.

The Committee recommended approval after the noted issues have been addressed.

Condition:

Since this protocol involves the use of non-human primate tissues, the Committee requested that Section VII of the protocol be completed to describe hazards associated with non-human primate tissues and safety procedures (i.e., BL2 practices, Universal Precautions, procedures for needlesticks) that staff shall

use when handling these tissues. The investigator should refer to Appendix H of the CDC/NIH Biosafety in Microbiological and Biomedical Laboratories (BMBL) 4th Edition, http://www.cdc.gov/od/ohs/biosfty/bmbl4/bmbl4toc.htm for recommendations on the use of primate tissues. Pertinent information may also be found in the University's Bloodborne Pathogen Exposure Control Plan http://safety.uchicago.edu/3_2Frameset.html .

915 New/Eduardo Perozo/Pending Conditions (11-0-0)

The overall objective of this research is to understand the gating mechanisms for K+ channel activation. Genes of interest will be mutated, expressed in *E. coli*, purified and analyzed by spectroscopic techniques.

The Committee discussed two minor issues with the protocol. The PI indicated that antibiotic resistance genes will be used, but since the resistance genes he has listed are commonly used and not likely to compromise the use of drugs to treat disease, the question should be marked "No." In addition, the investigator's grant is still pending.

The Committee recommended approval after the noted issues have been appropriately addressed.

Conditions:

1. In Section III of the protocol, question 6, the investigator needs to change the response to "No." While this research will involve the use of antibiotic resistance genes, the genes listed are commonly used and will not compromise the use of drugs to control disease, as alternatives to these antibiotics are currently available.

2. At the time of submission, the external funding for this research was pending. The investigator needs to provide the funding agency and TRACS ID number/FAS account # upon receipt.

916 New/Alexander Chervonsky/Pending Conditions (11-0-0)

This protocol will involve administration of treated (boiled in water) and untreated *E. coli* to mice by gavage. Animals will be sacrificed and intestinal tissues will be harvested for analysis. The research will also include generation of T cell receptor transgenic mice. Diphtheria toxin will be used to ablate dendritic cells in the transgenic mice.

The PI has indicated that cages will be autoclaved; however, [redacted] does not routinely autoclave cages in the ABSL1 facility. If the cages must be autoclaved, then the animals will have to be moved to the ABSL2 facility. If not, the investigator needs to revise the form to remove the reference to autoclaving.

A member questioned whether the use of diphtheria toxin needed to be described on Form H and reviewed by the Safety Office. Review of this form would have gone through the IACUC and Safety. The administrative staff will look into this further to ensure that a proper review is being conducted.

The administrative staff informed the Committee that the removal and transport of animals was approved by IACUC. The Committee had no concerns and approved the transport of the animals as well.

The Committee discussed other minor issues that need to be addressed. In Section III of the protocol, question 5a, the investigator needs to indicate "RG1." In the Supplemental Form B for Recombinant DNA, Section II (Material Details) needs to be completed. In the Supplemental Form B for *E. coli*, Section III, question 1, the investigator needs to indicate "No." In Section VII, question 11, the investigator needs to describe the actions to be taken in response to an exposure from an animal bite.

The Committee recommended approval after the noted issues have been appropriately addressed.

Conditions:

1. In Section III, question 5a, the investigator needs to indicate "RG1".

2. In the Supplemental Form B for Recombinant DNA, Section II (Material Details),the investigator needs to specify the animal species, number of animals, dose, route of administration, volume, total number of doses, frequency and indicate the length of time considered hazardous.

3. In the Supplemental Form B for *E. coli*, the investigator needs to address the following:
   a. In Section III, question 1, the investigator needs to indicate "No".

   b. In Section VII, question 5, it is indicated that soiled cages need to be autoclaved; however, in question 4, it is indicated that for animal wastes and carcasses no special requirements are needed. As standard procedures in the barrier facility do not require autoclaving, the investigator needs to clarify if autoclaving of cages is necessary. If not, the investigator needs to indicate standard procedures for barrier facility.

   c. In Section VII, question 11, the investigator needs to describe the actions to be taken in response to an exposure from an animal bite.

917 New/Yimin Qin/Pending Conditions (11-0-0)

This protocol involves the use of adenoviral vectors to transduce mammalian cells for the study of proteins involved in apoptosis and mitochondrial dysfunction during ischemia/reperfusion injury.

The reviewer noted that the investigator will use HCT116 human colon cancer cell line to test his preparations for replication-competent virus. The Committee determined that this is a common cell line used for this type of work.

The Committee was unclear on the investigator's rationale for conducting this research. While the laboratory procedures were thoroughly discussed, the aim of the research was not apparent. The Committee requested that a rationale statement be added to the research summary.

The Committee discussed other minor issues that need to be corrected. In Section VII, question 5, the investigator needs to de-select items that do not apply to this agent. In addition, in questions 5 and 8, the investigator needs to indicate "Safety Goggles."

The Committee recommended approval after the noted issues have been appropriately addressed.

Conditions:

1. In Section IV of the protocol, a thorough description of laboratory procedures was provided; however, the overall objective of the research was not discussed. The Committee requested that a rationale statement be added to Section IV to clarify the investigator's interest in conducting this research.

2. In Section VII, question 5, the Committee noted that several boxes may have been checked unnecessarily (i.e. Immunization, Security Background Check), as the procedures may not apply to this particular agent or to BL2 practices. The investigator needs to revise this section accordingly. For information on BL2 recommendations, please refer to the CDC/NIH Biosafety in Microbiological and Biomedical Laboratories (4th edition), http://www.cdc.gov/od/ohs/biosfty/bmbl4/bmbl4toc.htm.

3. In Section VII, question 8, the investigator needs to check "safety goggles/shield," as the Committee requested that they be used when working with this agent. Additionally, for consistency, the investigator needs to include this information in question 5, "Donning of PPE."

918 New/David Boone/Pending Conditions (11-0-0)

The overall objective of this research is to understand the regulation of inflammation. Plasmid vectors will be used to introduce genes of interest and mutants into mammalian cell lines. The cells will be studied for their ability to mount an inflammatory signal in response to cytokines.

The investigator has indicated BL1 and BL2 for *E. coli*. While he will use BL2 practices, the investigator should indicate only BL1 for *E. coli*.

The Committee recommended approval after the noted issue has been appropriately addressed.

Condition:

In Section II of the protocol, under "Microorganisms," the investigator needs to de-select "BL2." While this protocol will be conducted at BL1 w/ BL2 practices, the biosafety level required for *E. coli* is BL1.

919 New/Jay Purdy/Pending Conditions (11-0-0)

This research will involve the characterization of regulatory elements involved in *Leishmania* gene expression. Contructs will be amplified in E. coli, isolated and then introduced into *Leishmania* by electroporation. In order to maintain virulence, *Leishmania* will be passaged in Syrian hamsters. Animals will be sacrificed and organs will be harvested and transported back to the lab for analysis. Animals will be injected with wild type *Leishmania* only and not recombinant organisms.

A member noted that the investigator has indicated the use of both a laminar flow hood and biosafety cabinet. For this type of work, a biosafety cabinet should be used. The Committee requested that the investigator revise the documents to reflect the use of only a biosafety cabinet. In addition, the biosafety cabinet needs to be re-certified.

The Committee discussed other issues that need to be addressed. In Section III of the protocol, question 8, the investigator needs to indicate only "BL2." In Supplemental Form B, the investigator needs to revise the decontamination and spill procedures to be consistent with standard practices in [redacted]. In the "Guidelines for Working with Leishmania in the Laboratory", the investigator needs to indicate that employees are to contact Occupational Medicine.

The corresponding animal care and use protocol (ACUP [redacted]) must be reviewed and approved by the Institutional Animal Care and Use Committee (IACUC).

The Committee recommended approval after the noted issues have been appropriately addressed.

Conditions:

1. In Section III, question 8, the investigator needs to indicate only "BL2".

2. Biosafety cabinets must be certified on an annual basis; therefore, in Section VII, question 2a, the investigator needs to provide the current certification date.

3. In Supplemental Form B, Section VI, question 1, it is indicated that post-mortem surgery and organ homogenization will be conducted in a laminar flow hood. A biosafety cabinet must be used for all manipulations involving the biohazardous agent; therefore, the investigator needs to revise accordingly. Also, in the "Guidelines for Working with *Leishmania* in the Laboratory," Section III.B, under item 6, please replace laminar flow hood with biosafety cabinet.

4. In Supplemental Form B, Section VI, question 1, it is indicated that hoods will be cleaned with 95% ethanol and spills will be decontaminated using either 70% ethanol or 5% bleach. The standard practice in [redacted] (ABSL2) is to decontaminate hoods and clean up spills with Clidox (chlorine dioxide). The investigator needs to revise accordingly.

5. In Supplemental Form B, Section VII, question 5, it is indicated that cages will be decontaminated with a disinfectant or chlorox. The standard practice in [redacted] is to autoclave the cages out of the facility. If autoclaving of cages is sufficient for decontamination, the investigator needs to revise accordingly.

6. In the "Guidelines for Working with *Leishmania* in the Laboratory", Section IV.A, under item 4, the investigator needs to include that employees are to contact the University of Chicago Office of Occupational Medicine (UCOM) in L-156 or at 2-6757. Also, the investigator needs to include this information in Section IV.B.

7. The corresponding animal care and use protocol (ACUP [redacted]) must be reviewed and approved by the Institutional Animal Care and Use Committee (IACUC).

920 New/John Kress/Pending Conditions (10-0-0)

This research involves the administration of *E.coli* to anesthetized rats to induce sepsis and investigate the interplay between sepsis and sedative induce physical immobility. E. coli H-:K- will be used. Rats will be sedated and injected intravenously with the agent. Sedation will continue for 0-7 days. Rats will be euthanized for tissue harvest. Sciatic nerves and tibialis muscles will be analyzed for histopathology.

The Committee discussed the particular strain of E. coli that will be used. There is no apparent hazard to humans.

The corresponding animal care and use protocol (ACUP [redacted]) is pending approval by the Institutional Animal Care and Use Committee (IACUC).

The Committee recommended approval after the noted issue has been appropriately addressed.

Condition:

The corresponding animal care and use protocol (ACUP [redacted]) must be reviewed and approved by the Institutional Animal Care and Use Committee (IACUC).

921 New/Ralph Weichselbaum/Pending Conditions (10-0-0)

The research involves studies in cell culture to evaluate targeting, delivery and uptake of nanoparticles with encapsulated genetic constructs. PGLA nanoparticles will be loaded with assorted plasmids including CMV and egr driven TNFalpha expressing vectors as well as plasmids capable of expressing luciferase, lacz (beta-gal), and EGFP. Nanoparticles will be coated/conjugated with FVIIai (tissue factor receptor inhibitor) which targets nanoparticles to tumor cells and tumor vasculature/endothelial cells. Nanoparticles will be prepared in a chemical fume hood and then filter-sterilized. Nanoparticles will be injected 2-10 times IP, IV and intratumorally. Mice will be irradiated. Studies in mice will be used to evaluate the efficiency of localized and systemic delivery to enhance the anti-tumor effects of radio-inducible/chemo-inducible gene therapy.

The Committee discussed issues that need to be addressed. In Section III of the protocol, question 3a, the investigator needs to indicate only "No." In addition, the amendment to the corresponding animal protocol is pending.

The Committee recommended approval after the noted issues have been appropriately addressed.

Conditions:

1. In Section III, question 3a, the investigator needs to indicate only "No".
2. The amendment to the corresponding animal care and use protocol (ACUP [redacted]) must be reviewed and approved by the Institutional Animal Care and Use Committee (IACUC).

600 Renewal/Judy Cho/Pending Conditions (11-0-0)

This lab studies Inflammatory Bowel Disease through the use of cDNAs, plasmid vectors and standard molecular biology techniques. NOD2 will be transfected into HEK 293 cells for studies of transcription factor activation and cytokine expression. Human blood samples will also be collected for studies of NOD2 gene expression and expression of cytokines regulated by NOD2/CARD15.

The reviewer noted that the investigator plans to use mutations of genes; however, this is not indicated in Section III of the protocol. The investigator needs to check "Yes" in question 3a and describe the mutations.

The reviewer also asked the Committee if the biosafety level was appropriate for this research. The Committee agreed that BL1 with BL2 practices is acceptable.

The Committee recommended approval after the noted issue is appropriately addressed.

Condition:

In Section III, question 3a, the investigator needs to change the response to "Yes" and describe the Nod2 mutations that were indicated in Section IV.

595 AD 01/ John Crispino/Pending Conditions (11-0-0)

The research laboratory investigates the mechanisms of blood cell development using *in vivo* and *in vitro* techniques. The investigator is amending to include the generation of transgenic mice by [redacted] and ACUP [redacted].

Administrative staff noted that the corresponding animal protocol is pending.

The Committee recommended approval after the noted issue is resolved.

Condition:

The corresponding animal care and use protocol (ACUP [redacted]) must be reviewed and approved by the Institutional Animal Care and Use Committee (IACUC).

752 AD 14/ Olaf Schneewind/Pending Conditions (11-0-0)

This research focuses on characterizing the mechanisms of substrate recognition and regulation of Type III transport in Yersinia pestis KIM D-27. Transposon mutagenesis will be used to identify and characterize the Yersinia Type III regulon. A mouse model will be used to study the role of Type III secretion in the establishment of infection. The investigator is amending the protocol to include the identified proteins and the purification of these proteins.

The Committee discussed issues that need to be addressed. In the protocol and Supplemental Form B, the investigator needs to indicate that the PI and supervisor need to be notified in the event of an exposure. Additionally, the investigator needs to indicate methods of decontamination: bleach, autoclave and clidox.

The Committee recommended approval after the noted issues are appropriately addressed.

Conditions:

1. In Section VII, question 10, the investigator needs to indicate that the Principal Investigator will be notified in the event of an exposure.

2. In Section VII, question 12, the investigator also needs to include autoclaving at 250°F for 30 minutes and bleach (0.5 to 1%) as methods for decontamination.

3. In the Supplemental Form B, Section VII, question 11, the investigator also needs to include that in the event of an exposure, staff shall notify their immediate supervisor and the Principal Investigator.

776 AD 04/ Chyung-Ru Wang/Pending Conditions (11-0-0)

MHC Class Ib deficient mice and MHC Class Ib transgenic mice will be infected with *Mycobacterium tuberculosis* to study the impact of MHC Class Ib-restricted response in acquired resistance to this pathogen. Class Ib-restricted T cell lines will be derived from *M. tuberculosis* infected mice and the lipid antigen requirement for presentation by Class Ib molecules will be studied. The investigator is amending the protocol to include the use of *Mycobacterium bovis* (BCG vaccine strain).

A member questioned whether it was appropriate for the investigator to work with the animals under ABSL2 conditions, as there is a risk of inhalation from the bedding. During the discussion of the original submission, it was clarified that ABSL2 is appropriate for this agent. There were no further comments regarding this issue.

A member noted that the investigator needs to check "respirator" in Section VII of the protocol.

The Committee recommended approval after the noted issue is corrected.

Condition:

As it is indicated that staff will wear an N-95 mask or a PAPR (Powered Air Protection Respirator), in Section VII, question 8, the investigator needs to check "Respirator".

828 AD 03/ James Madara/Pending Conditions (10-0-0)

The research study involves the use of *Salmonella typhimurium* to explore the nature and consequences of interactions between intestinal epithelial cells and polymorphonuclear leukocytes (neutrophils) as well as epithelial responses to *Salmonella*. With this amendment, the PI is requesting to use the agent in a streptomycin treated mouse model system. Mice will be pre-treated with streptomycin to lower endogenous microflora to enhance colonization by *S. typhimurium*, which will be administered by gavage. Six hours after infection, mice will be euthanized and tissues will be harvested for analysis. Tissues will be formalin-fixed and used for histochemistry or immunohistochemistry. Non-fixed samples will undergo cell lysis and be used for immunoprecipitation and immunoblot analysis.

A member questioned whether cell lysates could contain active agents. If so, the lysates should be handled under BL2 conditions. The Committee requested that the investigator clarify whether the mild conditions of cell lysis would effectively inactive the agent. If not, the investigator needs to inform staff that the lysates must take the necessary precautions when handling the lysates.

Administrative staff indicated that the corresponding animal protocol is pending.

The Committee recommended approval after the noted issues have been appropriately addressed.

Conditions:

1. Section IV (Research Summary) and Supplemental Form B, Section VI, question 1, describe immunoprecipitation experiments using intestinal tissue lysates from animals gavaged with *S. typhimurium*. Although other proposed experiments use fixed tissues, these immunoprecipitation experiments do not and the Committee was concerned there may be live *S. typhimurium* in these lysates. While subsequent steps in the analysis, such as boiling in SDS-containing buffers, should inactivate the bacteria, it was not clear whether the mild conditions of cell lysis alone would sufficiently decontaminate the lysates. The investigator needs to clarify if the *S. typhimurium* will be inactivated at cell lysis. If not, the investigator needs to indicate in these sections that these samples will need to be handled under BL2 conditions.

2. The corresponding animal care and use protocol (ACUP [redacted]) must be reviewed and approved by the Institutional Animal Care and Use Committee (IACUC).

869 AD 01/ Maciej Lesniak/Deferred (11-0-0)

The work involves construction and use of replication-competent adenoviral vector. With this amendment, the investigator proposes to use the agent in primate tissues.

The Committee discussed issues regarding the use of primary non-human primate cells and replication competent adenovirus in facilities that will be shared with other investigators. The Committee requested that the investigator work with the Safety Office to ensure that the biosafety manual contains the appropriate precautions for work with these tissues and that the facilities are acceptable for this type of work. In addition, the Committee requested that the investigator and Safety meet with the other investigators to discuss any concerns they may have regarding the work.

The Committee felt that more information was needed in Section VII of the protocol regarding the use of non-human primate tissues. The investigator needs to include the potential hazards of working with this material, the possible consequences of an exposure as well as the possible routes of exposure (i.e. contact, needlestick, etc.).

The investigator needs to add all laboratory rooms to the protocol and explain the procedures to be conducted in each room.

The Committee requested that all staff read and sign the revised protocol.

The Committee recommended that the protocol be deferred until all issues have been appropriately resolved.

Reason(s) for Deferral:

1. The Committee has several concerns regarding the use of primary non-human primate cells and replication competent adenovirus in [redacted] and [redacted] which are shared research facilities. Therefore, the Committee requests that the investigator work with Steve Beaudoin (4-1131) from the University Safety Office in order to address the following issues:
   - The investigator needs to revise the Biosafety Manual to incorporate the procedures and practices to be followed when working with non-human primate tissue or cells.
   - It is not clear whether other investigators utilizing these facilities are aware of the experiments involving the replication competent virus and non-human primate tissues and/or cells and whether they have any concerns regarding the use of these agents. Therefore, the Committee requests that the investigator and Steve Beaudoin meet with these investigators to address any concerns they may have regarding agent hazards and practices for handling the agents. The investigator needs to revise the protocol and Biosafety Manual to incorporate any changes to procedures or practices that may result as a consequence of this meeting.
   - During an inspection of [redacted], University Safety noted that the following issues require correction: 1) eyewash stations must be tested and results logged weekly; 2) the biohazard bin is overfilled; and 3) the microwave and two refrigerators need to be labeled with "No Food or Drink" signs.
   - During an inspection of [redacted], University Safety noted that the clean bench expired in July 2001. This needs to be recertified.

2. In Section I, under "Location of Proposed Work/Experiments", the investigator also needs to include [redacted].

3. In Section IV, Research Summary, the investigator needs to clearly delineate the procedures to be performed in each of the laboratories listed (i.e. [redacted]).

4. Non-human primate tissue and/or cells may harbor potential hazards such as viral pathogens (i.e. hepatitis and herpes). Therefore, in Section VII, question 4, for the non-human primate cells, the investigator needs to include the potential hazards of working with this material, the possible consequences of an exposure as well as the possible routes of exposure (i.e. contact, needlestick, etc.).

5. Once revisions to the protocol submission form and Biosafety Manual have been reviewed and found to be acceptable by University Safety, the investigator needs to have all staff members review the protocol and sign Section V.

III. Old Business:
Time did not allow for review of the new IBC Forms; therefore, discussions will resume at the next IBC meeting.

IV. New Business:
None

V. Updates:
The Chairman updated the Committee on Dr. Ferguson's delinquent renewals that were discussed at the last meeting. Dr. Ferguson was given a 1-week deadline to submit his annual renewal surveys for protocols 739 and 741; however, he did not comply with this request. IBC protocols 739 and 741 were terminated due to lack of compliance to University policies. The PI, his Department Chair and the grants department were notified of these terminations.

The University of Chicago

Institutional Biosafety Committee

5841 S. Maryland Avenue
AMB S-152 ♦ MC 1108
Chicago, IL 60637

Minutes of February 3, 2006 Meeting
1:45 PM in [redacted]

In attendance:

Voting Members

Gopal Thinakaran
Richard Hiipakka
Mark Abe
Malcolm Casadaban
George Daskal
Clara Gartner
Jean Greenberg
James Mastrianni
Helena Mauceri
Craig Wardrip
Lois Zitzow

Ex-Officio Members

Steve Beaudoin
David Pitrak
Markus Schaufele

Guests

None

Staff

Bill Pugh
Pamela Postlethwait
Jennifer Swanson

Absent:

Voting Members

Tong-Chuan He
Louis Philipson
Mary Ellen Sheridan

Ex-Officio Members

Russell Herron

Staff

None

I. **Minutes:** The minutes of the January 6, 2006 meeting were unanimously approved (11-0-0), pending confirmation of the autoclaving time for protocol 752. The administrative staff will confirm if autoclaving should be done for 30 minutes or 40 minutes.

II. Protocol Review: The following protocols were reviewed at the meeting, with the disposition noted:

PR# Category/Investigator/Disposition

641 AD 03 Revised Deferral/Robert Daum/Approved (11-0-0)

This laboratory's goal is to determine possible antibiotic resistance mechanisms in *Staphylococcus aureus*. With this amendment, the investigator is adding new bacterial strains, including Vancomycin-resistant *S. aureus* and community-acquired Methicillin-resistant *S. aureus*. Some of the strains will be obtained from patient isolates and others will be obtained from the Centers for Disease Control (CDC). The investigator is also adding staff and rooms.

At the 12/2/05 IBC meeting, this amendment was deferred by the Committee due to concerns regarding the surveillance plan. The investigator conferred with the Safety Office and submitted a revised protocol and biosafety manual to address the Committee's concerns.

The Committee felt that all outstanding issues were appropriately addressed and recommended approval of the amendment. Prior to the final approval, however, the Committee requested that the Safety Office discuss the protocol with University Occupational Medicine (UCOM).

869 AD 01 Revised Deferral/Maciej Lesniak/Pending Conditions (11-0-0)

The work involves construction and use of replication-competent adenoviral vector. With this amendment, the investigator proposes to use the agent in primate tissues.

At the 1/6/06 IBC meeting, this amendment was deferred due to concerns regarding shared facilities and hazards associated with use of non-human primate tissues. The investigator conferred with the Safety Office and submitted a revised protocol and biosafety manual to address the Committee's concerns. In addition, the investigator and Safety met with other individuals who use the shared facilities to discuss concerns they may have with the work. All concerns were addressed and none of the individuals had objections to the work moving forward.

The Committee discussed the facilities and had concerns about how the investigator will safeguard the rooms while conducting this work. The Committee requested that the door be locked and proper signage be displayed to alert individuals who have access to the facility that the work is in progress.

The Committee discussed the use of non-human primate tissues. While the investigator and his staff will not be working with the animals, the Committee felt that the needlestick and eyewash procedures should be consistent with the University policy for Herpes B exposure. The Committee requested that the Herpes B protocol should be referenced or summarized in this protocol.

The following additional changes were requested by the Committee: references to work with non-human primates need to be removed from the protocol and biosafety manual, as this research involves only the tissue from the animals; the current biosafety cabinet certification date needs to be added to Section VII; and procedures for spills and needlestick exposures need to be harmonized in the protocol and biosafety manual.

The Committee recommended approval after the noted issues have been appropriately addressed.

Conditions:

1. In Section VII, question 2a, the investigator needs to update the form to include the current certification date for the biosafety cabinet.

2. When experiments are in progress involving the non-human primate cells and the replication competent adenoviral vector, the Committee requests that the laboratory door be locked throughout the duration of the experiments and a hazard warning sign identifying the biohazardous agents be posted on the door. The investigator needs to revise the following sections to reflect this information:
   - Section IV (Summary of Research)
   - Section VII, Question 5
   - Biosafety Manual under Special Practices for the BL2/3 Facility

3. The investigator needs to review the information in Section VII of the protocol submission form and the Biosafety Manual to ensure that these sections are consistent. Specifically, the investigator needs to ensure the following are addressed:
   - In Section VII, question 9, the spill procedures indicate the use of 20% bleach while the Biosafety Manual indicates 10%. The Committee determined that the use of 10% bleach is adequate for this agent.
   - The measures to be taken in the event of a needlestick as outlined in the Biosafety Manual need to be incorporated into Section VII, question 10.

4. Staff members that will be handling non-human primate tissue need to undergo a Herpes B orientation. This can be accomplished by contacting Dr. Craig Wardrip at 2-9361. Staff members also need to be aware that exposure to non-human primate tissue must be treated as an exposure to Herpes B Virus. Accordingly, an exposure must be reported and managed as outlined in the attached University of Chicago Hospitals Policy "First Aid Procedures for Personnel Working with Primates." The investigator needs to revise the protocol submission and Biosafety Manual to incorporate this information.

5. As the investigator is not working directly with non-human primates but rather tissues and cells, he needs to revise the Biosafety Manual, under "Rules for Working with Non-Human Primate Tissue or Cells," to remove references to working with animals and working in the animal facility.

910 New/Alexander Verin/ Pending Conditions (11-0-0)

This protocol involves the study of signaling pathways and cytoskeletal rearrangements involved in vascular barrier function. Replication-defective adenoviral vectors will be used to introduce cDNAs for candidate proteins into cultured endothelial cells.

The Committee requested the following minor revisions: PPE needs to be consistent in the research summary and Section VII; contact information is needed for the oversight person; and the investigator needs to be added to the staff group.

The Committee recommended approval after the noted issues have been appropriately addressed.

Conditions:

1. In Section IV, under Adenovirus, line 8, the PPE listed needs to be harmonized with Section VII, questions 5 and 8. Therefore, in all of these sections, the investigator needs to indicate the use of lab coats, gloves, masks and safety goggles/shield.

2. In Section V, the investigator needs to include himself as a staff member, list his responsibilities and sign the page.

3. In Section VII, question 14, the investigator needs to provide contact information for Dr. Kolosova.

607 Renewal/Elizabeth Grove/ Approved (11-0-0)

The investigator studies neuronal differentiation and patterning in the embryonic mouse brain. *In utero* electroporation will be utilized to study the roles of candidate neuronal patterning genes on development of the cerebral cortex. The investigator will perform laparatomies on pregnant mice and, with the aid of fiberoptics, will inject DNA into embryonic neural tubes and use electroporation to facilitate gene transfection. The investigator plans to perform these procedures in her lab and then transfer the mice to the animal facility.

The Committee had no concerns with this protocol and recommended approval.

609 Renewal/Michael Nishimura/ Pending Conditions (11-0-0)

This protocol involves the use of commercially available plasmid and retroviral vector kits to study T cell receptor genes in human and murine cells.

The Committee noted that the investigator has provided rationale for not testing viral preparations for replication competent virus. Since the investigator will be generating stable producer cell lines, the Committee requested that the preparations be tested. Therefore, the investigator needs to describe his testing methodology and frequency.

A member noted that the investigator provided descriptions for the classes of genes that will be studied, but did not include a complete list of the specific genes. In order to fully assess the level of risk, the Committee requested that the investigator list all genes that will be expressed in this project.

The Committee recommended approval after the noted issues have been appropriately addressed.

Conditions:

1. In Section III, question 3, the investigator has provided general descriptions of the four classes of genes that will be studied. The Committee requested that the investigator also include a list of the specific genes that will be expressed in this research.

2. In Section III, question 4c, the investigator has provided rationale for not testing the preparations for replication competent virus. However, due to the production of stable producer cell lines, the Committee requests that routine batch testing be performed. Therefore, the investigator needs to revise this section to describe your methods for testing the preparations for replication competent virus and indicate the frequency of testing.

583 AD 01/Chyung-Ru Wang/ Pending Conditions (11-0-0)

This protocol involves the use of class Ib-deficient mice and transgenic mice to examine the contribution of MHC class Ib-restricted response during primary and secondary infection by *Listeria monocytogenes*. With this amendment, the investigator would like to include administration of *L. monocytogenes* to mice by oral gavage.

A member noted that the investigator plans to ask staff members if they are immunocompromised or pregnant before allowing them to work with the agent. Since employers cannot inquire about a staff member's health status, the Committee requested that the protocol be revised to describe the increased risk to those who are immunocompromised or pregnant and indicate that staff members are allowed to choose whether or not they will work with the agent.

A member questioned whether exposure prophylaxis is typically given for this agent. A member clarified that prophylaxis is not given; however, if infection develops, antibiotics should be offered. The protocol should be revised to reflect this information.

The Committee also requested the following revisions: the staff signature page needs to be updated to include all staff; decontamination procedures and emergency contact information need to be harmonized in the protocol and biosafety manual; and the amendment to the corresponding animal protocol needs to be approved.

The Committee recommended approval after the noted issues have been appropriately addressed.

Conditions:

1. In Section V, Staff Group, the investigator needs to clarify the individuals that are involved with this protocol. Julie Mach was added by amendment to the protocol in November 2005 but was not included in the staff group. Additionally, Hahn Nguyen is listed as primary contact and designee in the PI's absence but was not included in the staff group.

2. As inquiring about personal health information is prohibited, in Section VII, question 4, the investigator needs to remove the last statement that references determining an individual's HIV status or asking if they are immunocompromised. Staff must be allowed to determine whether or not they wish to work with an agent based on the associated risk. Therefore, the investigator needs to specify that individuals who are immunosuppressed because of medication or underlying medical conditions may be at a higher risk for infection and that those individuals are encouraged to discuss the matter with their personal physician or with UCOM before beginning work with the agent.

3. In Section VII, question 9, the bleach concentration is indicated as 10% while question 12 indicates 20% bleach. Additionally, in the Biosafety Manual, Section 7 indicates undiluted household bleach. The investigator needs to reconcile the bleach concentration. The Committee determined that 10% bleach is adequate for this agent.

4. In Section VII, question 10, under "Effective Post Exposure Treatment," rather than stating that "antibiotics are available to be applied to the wound," the investigator needs to revise to indicate that individuals must report to UCOM for determination of antibiotic therapy. The investigator also needs to revise the Supplemental Form B Narrative (What do I do if I am exposed?) and the Biosafety Manual, Section 9 accordingly.

5. In Section VII, question 14, the investigator needs to provide contact information (e.g. lab phone, home phone, pager) for the individual listed as assuming day-to-day oversight in the absence of the PI. Also, while Hahn Nguyen is listed as the oversight individual, Hahn is not listed as staff on this protocol. Additionally, the Biosafety Manual indicates that Mike Zimmer is the designee in the PI's absence. The investigator needs to reconcile these issues.

6. In addition to the University contact information for the PI provided in Section VII, question 15, the investigator needs to provide contact information when she is off campus such as home phone, cell phone or pager.

7. The corresponding amendment to ACUP [redacted] must be reviewed and approved by the Institutional Animal Care and Use Committee (IACUC).

630 AD 06/Yimin Zou/ Pending Conditions (11-0-0)

This research team uses recombinant DNA technology to study proteins that are involved in the nervous system. Specifically, proteins are used to study molecular mechanisms of axon guidance. With this amendment, the investigator would like to include the generation of transgenic mice (ACUP [redacted]) by [redacted]

The Committee had no concerns with this protocol and recommended approval after the corresponding animal protocol is approved.

Conditions:

The corresponding amendment to ACUP [redacted] must be reviewed and approved by the Institutional Animal Care and Use Committee (IACUC).

III. Old Business:
The Committee discussed the new IBC submission forms. The Committee approved the new forms pending minor revisions that were requested at the meeting.

IV. New Business:
None

V. Updates:
A member updated the Committee on the newest edition of the BMBL which should be out by the end of the year.

Institutional Biosafety Committee

5841 S. Maryland Avenue
AMB S-152 ♦ MC 1108
Chicago, IL 60637

Minutes of April 7, 2006 Meeting
1:45 PM in [redacted]

In attendance:

Voting Members

Gopal Thinakaran
Richard Hiipakka
Mark Abe
Malcolm Casadaban
George Daskal
Clara Gartner
Jean Greenberg
Tong-Chuan He
Helena Mauceri
Louis Philipson
Mary Ellen Sheridan
Craig Wardrip
Lois Zitzow

Ex-Officio Members

Steve Beaudoin
Markus Schaufele

Guests

Lorinda Baker
John Bivona

Staff

Pamela Postlethwait
Bill Pugh

Absent:

Voting Members

James Mastrianni

Ex-Officio Members

Russell Herron
David Pitrak

Staff

None

I. **Minutes:** The minutes of the March 3, 2006 meeting were unanimously approved (12-0-0) with a minor correction to Section V.B.

II. **Protocol Review:** The following protocols were reviewed at the meeting, with the disposition noted:

PR# Category/Investigator/*Disposition*

616 Revised Deferral/Kathleen Millen/*Approved w/Comment* (12-0-0)

The research laboratory is interested in studying the genetics of central nervous system (CNS) development using mammalian cell culture techniques, transgenic mice and chick embryos. Genes suspected of playing a role in CNS development will be over-expressed or knocked down in mouse and/or human cell lines. Transgenic mice will be generated through the University of Chicago [redacted] In ovo electroporation of genes of interest will also be performed and developing chick embryos less than E10 will be studied. Mutant forms of the target genes will also be generated and studied.

This protocol was deferred at the April meeting due to the lack of information regarding the RCASA virus needed to evaluate the biosafety issues. The investigator has since submitted a revised protocol for Committee review.

The Committee felt that all outstanding issues had been appropriately addressed and recommended approval of the protocol. However, since the protocol involved screening for genes expressed during development, it was recommended that at the time of annual review, the investigator submit a brief report detailing the genes identified and characterized during the past year.

Comment:

1. As the protocol involves a screen for genes expressed during development of the brain, the Committee requests a report be submitted with the annual renewal survey that briefly describes genes that have been identified and characterized during the past year.

922 New/Eric Svensson/*Pending Conditions* (13-0-0)

The research interest is in the mechanisms regulating cardiovascular development. The protocol involves the use of replication defective adenoviral vectors to introduce the genes of interest into cultured cardiomyocytes.

The Committee noted that the use of safety goggles/shield needed to be included as personal protective equipment. Following a brief discussion, the Committee determined that it was not necessary for laboratory staff to use N95 respirators when working with this agent and requested all references to the use of N95 respirators be removed.

The Committee recommended approval after the noted issues are appropriately addressed.

Conditions:

1. In Section VII, question 5, under "Donning of PPE", the investigator needs to also include "safety goggles/shield".

2. The Committee determined that the use of an N95 respirator is not necessary. The investigator needs to remove references to the N95 respirator in Section VII, questions 8 and 9 and the Biosafety Manual.

928 New/Sean Crosson/*Pending Condition* (12-0-0)

The research focus is the growth and development of *Vibrio cholerae*. The mechanisms by which the two chromosomes segregate during bacterial cell division and the ability to change morphology in response to environmental conditions will be investigated using fluorescence microscopy.

The Committee had no concerns with this protocol and recommended approval after the noted issue has been resolved.

Condition:

1. In Section VII, question 9 indicates the use of 1% sodium hypochlorite while questions 12 and 13 indicate the use of 1% bleach. The investigator needs to reconcile this discrepancy. Please note that the Committee recommends the addition of bleach to a final concentration of 10%.

929 New/Sean Crosson/*Pending Condition* (12-0-0)

The research interest centers on how chemical and physical signals are received, processed, and integrated by a bacterial cell to generate an appropriate biological response. Environmental sensor genes from *Caulobacter crescentus* will be cloned, expressed and purified from *Escherichia coli*. The purified proteins will be used to study how structure and dynamics relate to function.

The Committee had no concerns with this protocol and recommended approval after the noted issue has been resolved.

Condition:

1. The signatures provided in Section V (Staff Group) are not clearly decipherable. The investigator needs to have staff members sign a new signature page for submission to the Committee.

930 New/Sean Crosson/*Pending Condition* (12-0-0)

The research interest centers on how chemical and physical signals are received, processed, and integrated by a bacterial cell to generate an appropriate biological response. Strains of *C. crescentus* will be generated in which the gene of interest has been deleted in order to elucidate the function.

The Committee had no concerns with this protocol and recommended approval after the noted issue has been resolved.

Condition:

1. The signatures provided in Section V (Staff Group) are not clearly decipherable. The investigator needs to have staff members sign a new signature page for submission to the Committee.

931 New/Viswanathan Natarajan/*Pending Conditions* (12-0-0)

The research interest is in the mechanisms of airway inflammation. Replication defective, self-inactivating lentiviral vectors will be used to transduce human bronchial epithelial and pulmonary artery endothelial cells to investigate the role of acylglycerol kinase, ceramide kinase, Nox2 and Nox4 in pro- and anti-inflammatory responses and physiological responses such as motility and chemotaxis.

The Committee discussed whether the method provided by the investigator for testing viral preparations for replication competent virus was acceptable. The Committee also noted that the investigator needed to correct a typographical error in the Research Summary and revise Section VII, question 5.

The Committee recommended approval following satisfactory resolution of the noted issues.

Conditions:

1. In Section IV, Research Summary, in the very last sentence, the investigator needs to change "soups" to "supernatants".

2. The investigator needs to remove the "No" from Section VII, question 5, under "Specific Training, Please Indicate".

3. The Committee determined that sera banking/testing were not necessary; therefore, Section VII, question 11 needs to be revised to indicate that no surveillance is required.

932 New/Kenneth Alexander/*Pending Conditions* (12-0-0)

This protocol is for the growth of a tissue culture adapted, murine adapted laboratory reference strain of influenza (H1N1 A/Puerto Rico/8/34) for use in an in vivo mouse model by other investigators.

While the Committee had no major issues with this protocol, it was noted that this agent would require an import permit from the U.S. Department of Agriculture (USDA) or Animal and Plant Health Inspection Service (APHIS).

The Committee recommended approval following resolution of the noted issues.

Conditions:

1. In Section III, the investigator needs to answer question 6.

2. Confirmation that an import permit for influenza virus has been approved by the U.S. Department of Agriculture (USDA)/Animal and Plant Health Inspection Service (APHIS) needs to be provided by the investigator.

934 New/Marcelo Nobrega/*Pending Condition* (12-0-0)

This protocol is for the production of transgenic mice to investigate the role of the TBX20 gene in heart development and congenital cardiac malformations. The DNA of interest will be cloned in *E. coli*, purified and provided to [redacted] for generation of transgenic mice.

The Committee noted the investigator needed to further elaborate on the generation of the transgenic animals and the procedures that will these animals will be involved in.

The Committee recommended approval after this issue is appropriately addressed.

Condition:

1. In Section IV, Research Summary, the investigator needs to briefly describe the transgenic animals that will be constructed, clarify who will generate the transgenic animals (the laboratory or [redacted]) and the experiments involving the transgenic animals.

935 New/Kenneth Alexander/*Pending Conditions* (12-0-0)

This proposal will investigate the human papillomavirus E6 mediated activation of NF-kappaB expression. It is thought that this activation results from the association of E6 protein with cylindromatosis tumor suppressor (CYLD), a negative regulator of NF-kappaB expression. NF-kappaB expression as a function of E6 will be evaluated in cultured cells, the structural aspects of the E6:CYLD association will be elucidated and how E6 affects the regulatory activities of CYLD will be determined.

The Committee requested the investigator clarify the source of the recombinant DNA. Additionally, the use of human cell lines in this project was discussed. As the Committee determined that protocols utilizing human cell lines are Biosafety Level 2 (BL2) protocols, it was questioned whether the investigator would be using a biosafety cabinet for this work. The Committee requested confirmation of access to a biosafety cabinet and the certification date.

The Committee recommended approval following appropriate resolution of the following issues.

Conditions:

1. In Section III, question 2 indicates that expression vectors containing the CYLD gene sequences were obtained from other investigators. The investigator needs to specify these investigators or provide literature citations.

2. The Biosafety in Microbiological and Biomedical Laboratories (BMBL) recommends that all work involving human cell lines be performed in a biosafety cabinet. The investigator needs to confirm that there is a biosafety cabinet in the laboratory and provide the certification date. Please note that biosafety cabinets must be certified annually. This information needs to be incorporated in Section IV, Research Summary.

936 New/Erin Adams/*Pending Condition* (12-0-0)

This protocol will utilize recombinant DNA technology, mammalian cell cultures and the baculoviral expression system to express proteins of interest for biochemical characterization and structural determination.

The Committee noted that human cell lines would be utilized in this project and requested confirmation of access to a biosafety cabinet and the certification date.

The Committee recommended approval after the noted issue has been resolved.

Condition:

1. The Biosafety in Microbiological and Biomedical Laboratories (BMBL) recommends that all work involving human cell lines be performed in a biosafety cabinet. The investigator needs to confirm that there is a biosafety cabinet in the laboratory and provide the certification date. Please note that biosafety cabinets must be certified annually. This information needs to be incorporated in Section IV, Research Summary.

938 New/Wanqing Liu/*Pending Conditions* (12-0-0)

The research will focus on a list of drug targets, drug metabolism genes and regulatory genes to investigate how expression and function are altered as well as the role of these genes in drug metabolism and drug response. Genes of interest will be cloned into a luciferase reporter vector, amplified in *E. coli*, transfected into cultured cells and the luciferase signal measured.

The Committee noted that human cell lines would be utilized in this project and requested confirmation of access to a biosafety cabinet and the certification date.

The Committee recommended approval after the noted issue has been resolved.

Conditions:

1. In Section III, question 5b, please remove "human" and indicate "N/A".

2. The Biosafety in Microbiological and Biomedical Laboratories (BMBL) recommends that all work involving human cell lines be performed in a biosafety cabinet. Please confirm that there is a biosafety cabinet in the laboratory and provide the certification date. Please note that biosafety cabinets must be certified annually. Please incorporate this information in Section IV, Research Summary.

939 New/Stephanie Dulawa/*Pending Condition* (12-0-0)

Using a mouse model, the investigator will evaluate the role of receptors and transporters of monoaminergic systems (serotonin, dopamine, noradrenaline) in behavioral phenotypes such as prepulse inhibition and locomotor stereotypy. The DNA of interest will be cloned in *E. coli*, purified and provided to [redacted] for generation of knockin, knockout and transgenic mice.

The Committee recommended approval after the associated animal protocol is reviewed and approved by the Institutional Animal Care and Use Committee (IACUC).

Condition:

1. The corresponding animal care and use protocol (ACUP [redacted]) must be reviewed and approved by the Institutional Animal Care and Use Committee (IACUC).

940 New/Frederico Innocenti/*Pending Conditions* (12-0-0)

The goal of the research is to determine the effect of single nucleotide polymorphisms (SNPs) on the expression of vascular endothelial growth factor receptor-2 (KDR). KDR variants will be cloned into a luciferase expression vector and the effect on gene transcriptional efficiency evaluated by luciferase assay in human cell lines. Additionally, a baculoviral system will be used for the expression and purification of KDR variants for protein activity studies.

The Committee noted that human cell lines would be utilized in this project and requested the investigator specify the lines to be used. Additionally, confirmation of access to a biosafety cabinet and the certification date was requested.

The Committee recommended approval after satisfactorily resolution of the noted issues.

Conditions:

1. In Section IV, Research Summary, the investigator needs to specify the human cell lines that will be utilized in this project.

2. The Biosafety in Microbiological and Biomedical Laboratories (BMBL) recommends that all work involving human cell lines be performed in a biosafety cabinet. The investigator needs to confirm that there is a biosafety cabinet in the laboratory and provide the certification date. Please note that biosafety cabinets must be certified annually. This information needs to be incorporated in Section IV, Research Summary.

941 New/Ming Xu/*Pending Conditions* (12-0-0)

This proposal is for the generation of transgenic mice to be utilized in determining the molecular mechanisms of brain development and function. The DNA of interest will be cloned in *E. coli*, purified and provided to [redacted] for generation of transgenic mice.

The Committee noted that as the investigative staff has yet to arrive on campus, contact information, information regarding work locations and signatures could not be obtained. Additionally, the IACUC must review and approve the associated animal care and use protocol.

The Committee recommended approval after these issues have been satisfactorily addressed.

Conditions:

1. Upon arrival at the University of Chicago, the investigator needs to submit a revised protocol submission form and Supplemental Form B that includes contact information, location of work and original signatures.

2. The corresponding animal care and use protocol (ACUP [redacted]) must be reviewed and approved by the Institutional Animal Care and Use Committee (IACUC).

942 New/Jiajun Chen/*Approved* (12-0-0)

The research focus is the role of peptidyl arginine deiminase type IV (PADI4), regulator of G-protein signaling 2 (RGS2), chaperonin containing TCP1 subunit 8 (CCT8) and solute carrier family 35 member A4 (SLC35A4) in leukemia pathogenesis. Replication defective retroviral vectors will be used to over-express genes of interest in cell cultures. Additionally, retroviral vectors expressing short-hairpin RNAs (shRNAs) will be used to silence genes of interest.

The Committee had no concerns with this protocol and recommended approval.

943 New/Ralph Weichselbaum/*Approved* (12-0-0)

The research focus is on evaluating the functional role of nine select Stat1-associated/radioresistane signature genes previously identified as conferring radioresistance and chemoresistance in two target carcinoma cell lines, SCC61 and MDA-MB-231. The genes of interest will be transduced into these cell lines using replication defective, amphotropic retrovirus.

The Committee had no concerns with this protocol and recommended approval.

945 New/Edwin Ferguson/*Approved w/Comment* (12-0-0)

The research objective is to identify and characterize the molecular mechanisms of a newly discovered intracellular positive feedback pathway active in the dorsal-ventral patterning process. Transgenic Drosophila that express wild-type or mutant versions of genes involved in either the bone morphogenetic protein signaling pathway or genes involved in receptor-mediated endocytosis will be generated and phenotypes evaluated. Additionally, the effects of microinjection of mRNA encoding these same components into the early embryo will be evaluated.

The Committee had no concerns with this protocol and recommended approval.

Comment:
1. IBC protocols are approved for 5 years and are subject to annual review.

946 New/Edwin Ferguson/*Approved w/Comment* (12-0-0)

The focus of the research is the mechanisms involved in the asymmetric, self-renewal divisions of the Drosophila germ line stem cells (GSCs). Experiments will involve the use of transgenic Drosophila in which wild-type or mutant versions of the genes required to establish or maintain cellular polarity are specifically expressed in the GSC. Transgenic Drosophila in which wild-type or mutant components of the bone morphogenetic signaling pathway are expressed in the GSC and its immediate descendants will be evaluated. Also, classical genetic screens will be used to identify additional genes required for GSC maintenance.

The Committee had no concerns with this protocol and recommended approval.

Comment:
1. IBC protocols are approved for 5 years and are subject to annual review.

709 AD 02/Nancy Schwartz/*Pending Condition* (12-0-0)

The research objective is to identify and investigate mechanisms that regulate proteoglycan synthesis. DNAs encoding structural/regulatory proteins (aggrecan, CIRP) and enzymes (PAPSS1 and PAPSS2) will be employed. Normal and mutated chick aggrecan promoter constructs will be used in transient transfection experiments in cultured cells and chick embryos. Mammalian expression constructs will also be used to transfect cultured cells. Mutated versions of the PAPS synthetases will be expressed in bacteria to produce protein for analysis. PAPSS and CIRP proteins will also be produced for use in TAT-mediated transfection experiments. The investigator is amending the protocol to include the generation of transgenic mice by [redacted] that over-express either the PAPSS1, PAPSS2 or aggrecan proteins under the control of the collagen II promoter.

The Committee recommended approval after the associated animal protocol is reviewed and approved by the Institutional Animal Care and Use Committee (IACUC).

Condition:
1. The corresponding amendment to the animal care and use protocol (ACUP [redacted]) must be reviewed and approved by the Institutional Animal Care and Use Committee (IACUC).

737 **AD 05/Rima McLeod/*Pending Condition & Stipulation* (12-0-0)**

The research goals are to better understand the pathogenesis and protection in apicomplexan, specifically *Toxoplasmosis gondii*, infections and to develop better ways to prevent and treat these infections. *T. gondii* will be passaged in both tissue culture and mice. Genes of interest will be mutated or deleted to study structure-function relationships. In this amendment, the investigator is requesting to image cells and mice infected with *T. gondii* using the Xenogen camera in [redacted]

The Committee discussed the biosafety issues related to the investigator's proposal for imaging cells and mice inoculated with *T. gondii*. The investigator contends that the luciferin must be administered within seconds of imaging and therefore proposes to transport the animals in an airtight box from [redacted] to a room contiguous with the camera facility for either topical or intraperitoneal administration of luciferin. Cells would also be transported in sealed containers to this room for administration of luciferin prior to imaging. It was noted that the space available next to the imaging facility was not appropriate for manipulations involving Biosafety Level 2 agents.

The Committee determined that the investigator did not demonstrate a need to administer luciferin outside of [redacted]. Therefore, all procedures involving handling of the mice must be performed within [redacted]. The Committee also recommended the use of injectable anesthetics for anesthetize mice prior to imaging. Additionally, the Committee determined that there was no risk, with proper procedures, in returning mice to [redacted].

The Committee recommended approval of this amendment following satisfactorily resolution of the noted condition and adherence to the noted stipulations.

Condition:

1. A revised amendment and protocol must be submitted to incorporate all the stipulations noted below and no other details about animal use. All references to the use of a laminar flow hood, BSC (outside [redacted] or the investigator's laboratory), caging, and water bottles must be removed from this protocol.

Stipulations:

1. All procedures involving the handling of mice outside the airtight box must be performed in [redacted] The box must not be opened to reposition mice outside of [redacted] It is recommended that injectable anesthetics be used to anesthetize mice.

2. All mice must be immediately returned to [redacted] after imaging.

3. This protocol is not approved for tissue culture work outside the investigator's laboratory.

822 **AD 04/Lucy Godley/*Pending Conditions* (12-0-0)**

The research focus is on understanding the molecular mechanisms through which DNA methylation is established and maintained in cancer cells. Procedures involve the cloning of DNMT3B cDNAs from established human cancer cell lines and from primary acute myeloid leukemia cells to characterize aberrant mRNA splice forms. Various DNMT3B forms will be expressed in cultured cells to study the effects on DNA methylation, growth and chromosomal stability. Replication defective retroviral vectors will be used to transduce mouse cells for in vitro and in vivo analysis. The investigator is amending the protocol to include the production of small interfering RNAs (siRNAs) for altering DNMT3B transcript levels to determine effect on DNA methylation.

Additionally, 293 cells expressing a truncated DNMT3B protein will be injected into the rear flanks of nude mice to determine if these cells have acquired the ability to form tumors.

The Committee discussed the investigator's method for testing viral preparations for replication competent viruses. It was not clear from the information provided what the investigator would be testing for to determine the presence of replication competent viruses and how often this testing would be performed. The investigator also needs to correct in Section VII the concentration of bleach and clarify if decontaminated liquids will be disposed of down the drains.

The Committee recommended approval of the amendment following satisfactorily resolution of the noted issues.

Conditions:

1. In Section III, question 4c, viral preparations will be tested for replication competent viruses by taking supernatant from infected cells and trying to infect fresh cells. The investigator needs to clarify what will be tested for (i.e. gene expression, antibiotic resistance, etc) to determine whether replication competent virus have been generated. Also, how often testing for replication competent virus will be done needs to be clarified. The Committee recommends that each viral preparation be tested.

2. In Section VII, question 9 indicates the use of a bleach solution (one part bleach to one hundred parts water) while question 12 indicates a 1:10 bleach solution. The investigator needs to reconcile this discrepancy. Please note that the Committee recommends the addition of bleach to a final concentration of 10%.

3. If liquids will be decontaminated with bleach and disposed of down the drains, then the investigator needs to check "General Waste and Sanitary Sewer" in Section VII, question 13.

854 AD 02/Jian Zhang/*Pending Condition* (12-0-0)

The laboratory will investigate the role of Cbl-b in T cell activation and CD40-mediated B cell activation as well as the effect of IL-4 on T cell apoptosis in autoimmune arthritis. Electroporation and lipofectamine techniques will be employed to transfect Jurkat T cells and mouse B cell line with pCEFL containing different Cbl-b cDNAs with a C-terminal HA-tag and His6-tagged ubiquitin vector to determine the structural requirements for Cbl-b ubiquitination. Replication defective retroviral vectors will be used to transduce primary mouse T and B cells to determine the structural requirement of Cbl-b in the formation of immunological synapse. The protocol is being amended to include e of Jurkat T cells with vectors expressing caspase-9 and mutants, PKC-theta and mutants, Bcl 10 and mutants by electroporation to determine their role in T cell activation and immune response.

The Committee had no concerns with this amendment and recommended approval after the noted issue has been resolved.

Condition:

1. In Section VII, the investigator needs to make the information in question 8 consistent with that provided in question 5 under "Donning of PPE".

869 AD 02/Maciej Lesniak/*Pending Conditions* (12-0-0)

This proposal involves the construction of a replication competent adenoviral vector that has been retargeted to bind αvβ3/5 integrins to deliver human IL-2, murine GM-CSF, murine IL-12, murine TNFα and luciferase to malignant gliomas. Procedures will involve stereotaxic injection of the viral vector into mice and harvesting of tissue 7, 14 and 21 days after viral injection for immunohistochemistry analysis. Additionally, non-human primate primary cell cultures will be established for infection with adenoviral vectors expressing luciferase and 48 hours later a luciferase assay will be performed. With this amendment, the investigator is requesting to use Syrian hamsters to study the toxicology of the adenoviral vector.

The Committee had no major issues with this protocol; however it was requested that the Supplemental Form B revised as a result of IACUC review process be submitted to the IBC.

The Committee recommended approval of the amendment after review and approval of the associated animal care and use protocol by the IACUC.

Conditions:

1. The associated animal care and use protocol (ACUP [redacted]) must be reviewed and approved by the Institutional Animal Care and Use Committee (IACUC).

2. The investigator needs to submit the revised Supplemental Form B that was submitted to the IACUC on April 4, 2006 that also includes the following revisions:

   a. The Committee determined the use of disposable wrap around gowns rather than Tyvek suits were sufficient for working in [redacted]. The investigator needs revise Section VII, question 7 accordingly.

   b. In Section VII, question 11, notification of an [redacted] veterinarian is required in the event of a bite needs to be included.

878 AD 01/James Brorson/*Pending Conditions* (12-0-0)

The protocol involves the use of replication-defective adenoviral vectors to transfect mouse neurons with wild-type genes of interest (human SOD1, SOD2, catalase and CMVCre) in order to determine the effects of targeted proteins on neuronal activity. The protocol is being amended to include new adenoviral constructs expressing either hypoxia inducible factor1 alpha$^{PP\rightarrow AG}$ (HIF-1$\alpha^{PP\rightarrow AG}$), HIF-1$\alpha^{PP\rightarrow AG}$ fused to enhanced green fluorescent protein or HRE-luciferase from a collaborator.

The Committee noted the investigator needed to list the proteins to be expressed and the current certification date for the biosafety cabinet.

The Committee recommended approval following resolution of these issues.

Conditions:

1. In Section III, question 9, the investigator needs to include the proteins that will be expressed from the new adenoviral vector constructs.

2. In Section VII, question 2a, the investigator needs to provide the current certification date for the biosafety cabinet.

906 **AD 01/Manami Hara/*Approved* (12-0-0)**
Using genetic approaches, the investigator will characterize genes involved in the formation and function of endocrine and exocrine tissue of the pancreas. Genes will be cloned and inserted into *E. coli* or *S. cerevisiae* for in vitro studied. With this amendment, the investigator is requesting production of transgenic mice by [redacted].

The Committee had no concerns with this amendment and recommended approval.

918 **AD 01/David Boone/*Pending Condition* (12-0-0)**

The overall objective of this research is to understand the regulation of inflammation. Plasmid vectors will be used to introduce genes of interest and mutants into mammalian cell lines. The cells will be studied for their ability to mount an inflammatory signal in response to cytokines. With this amendment, the investigator is requesting production of transgenic mice by [redacted]

The Committee had no concerns with this amendment and recommended approval after the noted issue has been resolved.

Condition:
1. In Section II, question 1, the investigator needs to deselect "Yes".

III. Old Business: None

IV. New Business:

A. Chair Signature. Currently, all internally funded IBC proposals must be signed by the Departmental Chair. The Committee discussed whether Departmental Chair signatures were needed and unanimously agreed (12-0-0) that this was not a necessary requirement. The Committee instructed administrative staff to remove the Departmental Chair signature section from the new IBC forms.

V. Updates: None

Institutional Biosafety Committee

5841 S. Maryland Avenue
AMB S-152 ♦ MC 1108
Chicago, IL 60637

Revised Minutes of May 5, 2006 Meeting
1:45 PM in [redacted]

In attendance:

Voting Members

Gopal Thinakaran
Richard Hiipakka
Malcolm Casadaban
George Daskal
Clara Gartner
Jean Greenberg
Tong-Chuan He
Helena Mauceri
Louis Philipson
Craig Wardrip
Lois Zitzow

Ex-Officio Members

Steve Beaudoin
Russell Herron
David Pitrak
Markus Schaufele

Guests

John Bivona

Staff

Lorinda Baker
Pamela Postlethwait
Bill Pugh

Absent:

Voting Members

Mark Abe
James Mastrianni
Mary Ellen Sheridan

Ex-Officio Members

None

Staff

None

I. **Minutes:** The minutes of the April 7, 2006 meeting were unanimously approved (11-0-0) with no corrections or deletions.

II. Protocol Review: The following protocols were reviewed at the meeting, with the disposition noted:

PR# Category/Investigator/*Disposition*

924 New/Anita Chong/*Pending Conditions* (11-0-0)

The research objective is to investigate whether bacterial infections can prevent and reverse allograft tolerance. Mice that have been transplanted with an allogenic heart and treated with immunosuppressive agents to prevent rejection and induce tolerance will be infected with live or heat-killed *Listeria monocytogenes* either by oral or intraperitoneal routes. The dose of *L. monocytogenes* required to prevent and reverse tolerance will be determined and used to investigate the molecular mechanisms responsible for this effect.

As the protocol was discussed, it was not clear to the Committee whether the investigative staff or a colleague would be preparing the bacterial culture. The investigator was requested to clarify who would be preparing the bacterial culture, where the preparation would take place and how the agent would be transported to [redacted] The Committee recommended reminding the investigator that the agent as well as harvested tissue would need to be triple packaged for transport.

The Committee also discussed the necessary personal protective equipment needed when working with this agent. The reviewer expressed concerns that the investigator had not consistently indicated throughout the protocol the need for eye protection (safety goggles or face shield) when working with this agent. Also, the Committee noted the investigator did not adequately describe the possible routes of exposure or outline the procedures to be performed in the event of accidental exposure by ingestion or splashing of the eye or mucous membranes.

The Committee recommended approval following successful resolution of the noted issues.

Conditions:

1. In Section IV, Research Summary, the investigator needs to address the following:
   - Clarify who will be preparing the *Listeria* cultures.
   - Clarify where this work will be performed.
   - Clarify if mice will be inoculated with the agent in [redacted] and if so, describe how *Listeria* cultures will be transported to this facility. The agent must be triple packaged for transport.
   - It is appropriate to necropsy and harvest tissue in a biosafety cabinet in [redacted] however tissue transported out of the facility must be appropriately triple packaged. The investigator needs to clarify where the tissues will be taken for analysis.

2. In Section VII, the investigator needs to address the following issues:
   a. In question 4, exposure to *Listeria* could result in fever, gastroenteritis and in rare cases, meningitis needs to be included.
   b. In question 10, the investigator needs to describe the measures to be take in the event of accidental ingestion and mucosal or eye splash. Splashes to the eyes need to be flushed with water for 15 minutes.

c. In question 11, it indicates there is "currently no surveillance or serologic testing" available for Listeria infections, yet the following paragraph states that "infections can be followed using serological testing". The investigator needs to reconcile this discrepancy.

d. In question 13, the investigator needs to also check "Potentially infectious waste is placed in a biohazard waste drum and picked-up and shipped by EVS" and "Sharps container pick-up and shipped by EVS".

3. In the Biosafety Manual, under "Mode of Transmission", the investigator needs to also include that individuals may be exposed to the agent in the laboratory or through an infected laboratory animal.

4. When manipulating the agent outside of a biosafety cabinet or when administering the agent to animals, safety goggles or face shield must be worn. The investigator needs to ensure that this is clearly and consistently indicated in the appropriate sections of the protocol submission – Section VII, Biosafety Manual, Supplemental Form B and Supplemental Form B narrative.

926 New/Anita Chong/*Pending Conditions* (10-0-0)

The research objective is to investigate whether bacterial infections can prevent and reverse allograft tolerance. Mice that have been transplanted with an allogenic heart and treated with immunosuppressive agents to prevent rejection and induce tolerance will be infected with live or heat-killed *Escherichia coli* either by oral or intraperitoneal routes. The dose of *E. coli* required to prevent and reverse tolerance will be determined and used to investigate the molecular mechanisms responsible for this effect.

During review, it was noted that the investigator proposes to use the O16:K1:H6 strain of *E. coli*. While information regarding the pathogenicity of various classes of enterovirulent *E. coli* was provided, specific information regarding the pathogenicity of this particular strain was not. In order to properly address accidental exposures to this agent, the Committee requested the investigator elaborate on the pathogenicity of the O16:K1:H6 strain.

It was not clear to the Committee whether the investigative staff or a colleague would be preparing the bacterial culture. The investigator was requested to clarify who would be preparing the bacterial culture, where the preparation would take place and how the agent would be transported to [redacted] The Committee recommended reminding the investigator that the agent as well as harvested tissues would need to be triple packaged for transport.

The Committee also discussed the necessary personal protective equipment needed when working with this agent. The reviewer expressed concerns that the investigator had not consistently indicated throughout the protocol the need for eye protection (safety goggles or face shield) when working with this agent. Also, the Committee noted the investigator did not adequately describe the possible routes of exposure or outline the procedures to be performed in the event of accidental exposure by ingestion or splashing of the eye or mucous membranes.

Conditions:

1. Although general information has been provided regarding the various classes of enterovirulent *E. coli*, the investigator needs to provide information regarding pathogenicity specific to the *E. coli* O16:K1:H6 strain that will be utilized in this project. The appropriate sections of the protocol submission and supplemental forms need to be revised accordingly.

2. In Section IV, Research Summary, the investigator needs to address the following:
   - Clarify who will be preparing the *E. coli* cultures.
   - Clarify where this work will be performed.
   - Clarify if mice will be inoculated with the agent in [redacted] and if so, please describe how *E. coli* cultures will be transported to this facility. Please note that the agent must be triple packaged for transport.
   - It is appropriate to necropsy and harvest tissue in a biosafety cabinet in [redacted] however tissue transported out of the facility must be appropriately triple packaged. The investigator needs to clarify where the tissues will be taken for analysis.
3. In Section VII, the investigator needs to address the following issues:
   a. In question 10, the measures to be take in the event of accidental ingestion and mucosal or eye splash need to be described. Splashes to the eyes need to be flushed with water for 15 minutes.
   b. In question 13, the investigator needs to also check "Potentially infectious waste is placed in a biohazard waste drum and picked-up and shipped by EVS" and "Sharps container pick-up and shipped by EVS".
4. In the Biosafety Manual, Section II, under "Mode of Transmission", the investigator needs to also include that individuals may be exposed to the agent in the laboratory or through an infected laboratory animal.
5. When manipulating the agent outside of a biosafety cabinet or when administering the agent to animals, safety goggles or face shield must be worn. The investigator needs to ensure that this is clearly and consistently indicated in the appropriate sections of the protocol submission – Section VII, Biosafety Manual, Supplemental Form B and Supplemental Form B narrative.

927 New/Anita Chong/*Pending Conditions* (10-0-0)

The research objective is to investigate whether bacterial infections can prevent and reverse allograft tolerance. Mice that have been transplanted with an allogenic heart and treated with immunosuppressive agents to prevent rejection and induce tolerance will be infected with live or heat-killed *Staphylococcus aureus* either by intranasal or intraperitoneal routes. The dose of *S. aureus* required to prevent and reverse tolerance will be determined and used to investigate the molecular mechanisms responsible for this effect.

During review, it was noted that the investigator needed to provide information regarding the source, strain and antibiotic resistance of the *S. aureus* to be utilized in this protocol. Additionally, it was requested the appropriate treatment for exposure to this agent be clarified.

It was not clear to the Committee whether the investigative staff or a colleague would be preparing the bacterial cultures. The investigator was requested to clarify who would be preparing the bacterial culture, where the preparation would take place and how the agent would be transported to [redacted]

[redacted] The Committee recommended reminding the investigator that the agent as well as harvested tissues would need to be triple packaged for transport.

The Committee also discussed the necessary personal protective equipment needed when working with this agent. The reviewer expressed concerns that the investigator had not consistently indicated throughout the protocol the need for eye protection (safety goggles or face shield) when working with this agent. Also, the Committee noted the investigator did not adequately describe the possible routes of exposure or outline the procedures to be performed in the event of accidental exposure by ingestion or splashing of mucus membranes or the eye.

Conditions:

1. The investigator needs to provide information regarding the specific strain, source and antibiotic resistance of the *Staphylococcus aureus* that will be utilized in this project and the appropriate treatment for exposures to this agent. The appropriate sections of the protocol submission and supplemental forms need to be revised accordingly.

2. In Section IV, Research Summary, the investigator needs to address the following:
   - Clarify who will be preparing the *S. aureus* cultures.
   - Clarify where this work will be performed.
   - Clarify if mice will be inoculated with the agent in [redacted] and if so, please describe how *S. aureus* cultures will be transported to this facility. The agent must be triple packaged for transport.
   - It is appropriate to necropsy and harvest tissue in a biosafety cabinet in [redacted] however tissue transported out of the facility must be appropriately triple packaged. The investigator needs to clarify where the tissues will be taken for analysis.

3. In Section VII, the investigator needs to address the following issues:
   a. In question 10, the measures to be take in the event of accidental ingestion and mucosal or eye splash need to be described. Splashes to the eyes need to be flushed with water for 15 minutes.
   b. In question 13, the investigator needs to also check "Potentially infectious waste is placed in a biohazard waste drum and picked-up and shipped by EVS" and "Sharps container pick-up and shipped by EVS".

4. In the Biosafety Manual, Section II, under "Mode of Transmission", the investigator needs to also include that individuals may be exposed to the agent in the laboratory or through an infected laboratory animal.

5. When manipulating the agent outside of a biosafety cabinet or when administering the agent to animals, safety goggles or face shield must be worn. The investigator needs to ensure that this is clearly and consistently indicated in the appropriate sections of the protocol submission – Section VII, Biosafety Manual, Supplemental Form B and Supplemental Form B narrative.

937 New/Andy Minn/*Pending Condition* (11-0-0)

To assess the effect of various genes implicated in metastasis as well as chemotherapy and radiation resistance, the research laboratory will employ retroviral vectors to over-express or knock down these genes in cultured cells. Functional assays such as cell survival assays, transcription factor activity and growth curves will be performed.

The Committee had no concerns with this protocol and recommended approval after the noted issue has been resolved.

Condition:

1. In Section VII (directly beneath the header), the principal investigator, the lab room number(s) and the phone number needs to be listed.

948 New/H. Rosie Xing/*Pending Conditions* (11-0-0)

The laboratory will investigate whether kinase suppressor of Ras1 (KSR1), a newly identified modifier of gain-of-function Ras signaling, might serve as a mediator of tumorigenesis, progression and response to ionizing radiation treatment. The generation and maintenance of KSR1 knockouts and the use of relevant human xenografts models will be used to facilitate studies of the biological function of KSR1 and mechanisms of signaling through KSR1. Additionally, the relationship between KSR1 function and cellular, tumor and tissue sensitivity to radiation treatment will be investigated.

During review of the protocol, it was questioned as to whether this protocol was necessary as the transduced cell lines had been previously generated by the investigator at another institution. The Committee determined that as these cell lines are expressing recombinant DNA and would be utilized in animal experiments, the experimental procedures needed to be reviewed. The investigator was requested to further elaborate on the use of these cells in animals.

Also, the Committee requested clarification regarding the location of procedures, location of and transport to the irradiator, indicating the animals are not hazardous and correction of typographical errors.

The Committee recommended approval following successful resolution of the noted issues.

Conditions:

1. In Section I, under "Department", correct to "Pathology".
2. In Section I, under "Location", correct to "[redacted]".
3. In Section IV, Research Summary, the investigator needs to briefly describe the experiments involving the use of the transduced A431 cell line in mice.
4. In Supplemental Form B, the investigator needs to address the following issues:
   a. In Section II, Material Details, under "Indicate the length of time the animal is considered hazardous", not hazardous needs to be indicated.
   b. In Section VI, question 2 indicates the use of the [redacted] surgical suite. As the [redacted] does not have a surgical suite therefore clarify if the investigator means the [redacted] procedural room.

c. In Section VI, question 3 indicates that animals will be transported for tumor irradiation. Where the irradiator is and how the animals will be transported to this facility needs to be clarified.

613 Renewal/Aaron Fox/*Pending Conditions* (11-0-0)

The research laboratory studies calcium channels and synaptic proteins and their role in transmitter release. Cell cultures will be transfected with plasmids containing the gene of interest for evaluation of function. Additionally, shRNA constructs will be used to knock down specific proteins.

The Committee had no concerns with this protocol and recommended approval after the noted issue has been resolved.

Condition:

1. In Section II, question 2, under "Microorganisms", the investigator needs to indicate *E. coli* and check Biosafety Level 1 (BL1).

620 Renewal/Chyung-Ru Wang/*Pending Conditions* (9-0-0)

The research objective is to study the expression, gene regulation and immunological function of several MHC Class Ib molecules. To examine the effects of immunological stimuli on expression and analyze the structure function relationship of TCR recognition, cDNAs of the genes of interest will be cloned and expressed in drosophila cell lines. How these molecules present antigens to T cells will be investigated by expressing in mammalian cell lines and performing immunological assays. Transcriptional regulation will be investigated by cloning promoter regions and evaluating using luciferase assays.

The Committee noted the investigator needed to further elaborate on the specific genes that would be investigated in this project.

The Committee recommended approval after the noted issues have been appropriately addressed.

Conditions:

1. Section III, question 3 indicates the project will utilize genomic and cDNA encoding MHC Class I Molecules. The investigator needs to clarify how many of these MHC Class I Molecule genes are being studied and provide their names.

2. In Section III, question 4e, "Risk Group 1" needs to be unchecked as there is no viral agent being utilized.

631 Renewal/Eric Beyer/*Pending Conditions* (8-0-0)

The research centers on intercellular communication as mediated by gap junctions, specifically the role of cell-to-cell communication and the subunit proteins that form gap junctions in various tissues including the heart, lens and blood vessels. The AdEasy system will be utilized to generate connexin adenoviral recombinants to evaluate gene expression and function in cultured cells. Using a mouse

model, adenoviral vectors expressing connexin 37 will be used to investigate the effect on tumor angiogenesis.

As the Committee discussed the experimental procedures, it was not clear where the adenoviral vector injections of the animals would be performed. The investigator indicated that these procedures would be performed in the surgery room of [redacted]; however this facility does not have a surgery room. It was noted that if the procedure is performed outside of [redacted] then the investigator will need to describe how this area will be decontaminated and how the animals will be contained and transported to [redacted].

The Committee recommended approval after the noted issues have been appropriately resolved.

Conditions:

1. In Section I, under "Location of Proposed Work/Experiments", the building and room number(s) where the animal experiments will be performed needs to be included.

2. In Section II, question 2, under "Microorganisms", *E. coli* needs to be included.

3. In Section VII, question 5, the investigator needs to also check "Infectious specimen packages opened in biosafety cabinet only".

4. In Section VII, question 6, under item #2, the investigator needs to revise to indicate that "Laboratory coats and *safety goggles/shield* for face protection (when splashes or sprays of infectious materials are anticipated) are worn while in the laboratory".

5. In Section VII, question 14, the relevant qualifications of the individual designated as having day-to-day oversight and supervision of the laboratory in the principal investigator's absence needs to be described.

6. In Supplemental Form B, Section VI, question 1 indicates that tail vein injections will be performed in the surgery room in the [redacted]. As it is not clear to the Committee which room is being referenced, the investigator needs to clarify the room number. If these procedures will be performed in an area outside of [redacted], then the containment and transport of the animals and how the area will be decontaminated must be described.

640 Renewal/Matthew Brady/*Approved* (8-0-0)

The research focus is on understanding the function of protein phasphatase-1 glycogen-targeting subunits. The targeting subunits will be cloned into expression vectors for production of recombinant proteins and analyzed by enzymatic assays and immunoblotting.

The Committee had no concerns with this protocol and recommended approval.

687 AD 05/Ralph Weichselbaum/*Pending Condition* (10-0-0)

The research examines the effects of combining anti-tumor and anti-angiogenic therapies with radiotherapy. HSV-1 vectors are used in conjunction with ionizing radiation to achieve tumor control and cure. With this amendment, the investigator is requesting to image tumors growing in the hind

limb of nude mice to evaluate the distribution of gene therapy vectors. Tumor bearing mice will be injected with HSV-I-GCluc 24 hours prior to imaging.

The Committee discussed the procedures proposed by the investigator for imaging animals inoculated with HSV vectors. On the day of imaging, animals will be anesthetized in [redacted], placed in Ziploc bags with small holes cut in the tips, placed in a plastic box and hand carried to the imaging facility. The animals will remain in the plastic bags for imaging and once completed, will be placed in the plastic box for return to [redacted].

Committee members were in agreement that the investigator had appropriately addressed the biosafety concerns regarding imaging of animals inoculated with HSV vectors. However, it was requested that written confirmation be obtained from [redacted] to confirm that this facility has reviewed and approved the procedures as outlined by the investigator.

The Committee recommended approval after the following issue is appropriately addressed.

Condition:

1. A letter from Dr. Jeffrey Souris, Technical Director of [redacted] confirming that [redacted] has reviewed and approved the procedures to be used for imaging mice inoculated with HSV I vector needs to be provided.

806 AD 05/Dominique Missiakas/*Pending Conditions* (9-0-0)

Based on database searches of the *Bacillus anthracis* genome, the investigator postulates that protein translocation across the phospholipid bilayer will be similar to that described for *E. coli*. In order to explore this hypothesis, the investigator will isolate mutants of the *B. anthracis* Sterne strain that fail to secrete protective antigen (PA), edema factor (EF), and lethal factor (LF) and characterize the corresponding genes. Additionally the genes identified will be examined for their role in *B. anthracis* virulence. With this amendment, the investigator is requesting a change in title, clarification of staff, addition of procedures involving allelic exchange and new resistance markers for use in plasmid or mutation selection strategies and experiments involving the use of mice.

During review of the amendment, the reviewer brought to the Committee's attention that during the review process, the investigator made revisions to Risk Management section of the protocol that was not included in the amendment nor requested during the review process. While the revisions were found to be appropriate, the Committee agreed the investigator needed to detail these changes in the amendment form. Additionally, the investigator was requested to indicate that staff would need to report to UCOM or Mitchell ER as appropriate in the event of an accidental exposure.

It also questioned whether the use of chloroamphenical resistance as a selection marker in the Stern strain would require review by either the Center for Disease Control (CDC) or the Office of Biotechnology Activities (OBA) at the National Institutes of Health (NIH).

The Committee noted that the CDC excludes the Sterne strain from the select agent regulations as it has been determined to be $10^5 - 10^7$-fold less virulent, used to vaccinate both humans and animals and thus does not pose a severe threat to the public health and safety. Therefore, as an excluded strain, the introduction of antibiotic resistance markers would not require submission to the CDC for review and approval. However, as OBA does not appear to distinguish between pathogenic and non-pathogenic strains, the Committee must determine whether the investigator's use of chloroamphenicol as a selection marker would require submission to OBA for review and approval.

A Committee member was of the strong opinion that OBA should be contacted to determine if chloroamphenicol could in fact be utilized as a selection marker in the Sterne strain. The NIH Guidelines state that deliberate transfer of a drug resistance trait to microorganisms that are not known to acquire the trait naturally and if such acquisition could compromise the use of the drug to control disease agents in humans, veterinary medicine or agriculture, it would need to be reviewed by the Recombinant DNA Advisory Committee (RAC).

In determining whether to contact to OBA, the Committee thoroughly discussed the pathogenicity of the Sterne strain and the antibiotics used to treat *B. anthracis* infections. It was noted that the Sterne strain is not considered to be a disease causing agent as it is missing a plasmid necessary for virulence and is in fact used as a vaccine in humans and animals. Additionally, while chloroamphenicol may have been previously used to treat *B. anthracis* infections, it is not an antibiotic that would currently be used to treat an infection. Therefore, the Committee did not believe the use of chloroamphenicol as a selection marker met the criteria set forth by the NIH Guidelines and concluded (9-0-1) submission to OBA was not warranted.

Conditions:

1. During review of the amendment, it was noted that several changes were made in the protocol to Section VII, Risk Management, and to Supplemental Form B that were not detailed in the amendment form. These changes included autoclaving for one hour, using 1:10 hypochlorite solution for disinfection, using 70% ethyl alcohol to disinfect skin and spraying the hood with sporocidal for 5 minutes and then wiping down. The amendment form needs to be revised to indicate that these changes have also been made to the protocol.

2. In Section VII, question 4, under item #3, the investigator needs to also indicate that staff must report to UCOM (University of Chicago Office of Occupational Medicine) in L-156 during regular hours or Mitchell ER during off hours in the event of a needlestick, animal bite or contamination of a wound.

III. Old Business: None

IV. New Business: None

V. Updates: None