JOHNS HOPKINS
INSTITUTIONS

Institutional Biosafety Committee
Health, Safety & Environment
2024 East Monument Street, Suite B-200
Baltimore, MD 21205-2223
(410) 955-5918 / FAX (410) 955-5929

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

April 28, 2006

Dear Mr. Hammond:

Enclosed are the minutes of the Johns Hopkins Institutional Biosafety Committee (JHUIBC) meetings spanning the dates (May 1, 2003 to present) as requested in your FAX of March 15, 2006.

Please note that although the JHUIBC attempts to meet each month, meetings are scrubbed if we do not achieve a quorum. For this reason, you will not find minutes for November 2003, December 2003, or March 2004. You will also not find minutes for March or April 2006 because these have not been officially approved by the JHUIBC membership.

Johns Hopkins Institutional policy requires the JHUIBC to review research involving pathogens, infectious agents, and biological toxins in addition to the OBA/NIH-required review of research involving recombinant DNA. The JHUIBC also considers and discusses biosafety issues as they relate to JHU policies, construction and design, laboratory compliance, etc. I have noted on the Biosafety Listserve that some institutions are separating their OBA/NIH required review from their IBC's other duties in order to maintain a set of minutes that only contains recombinant DNA issues. JHU has not chosen to do this. Thus, you will note that the materials enclosed contain information not required to be shared by OBA/NIH.

You will also note that some information has been redacted from the enclosed documents. JHU redacts investigator and organizational/company names, select agents, and policy or other institutional issues/discussions held by the JHUIBC that do not involve recombinant DNA activities and are considered private for one reason or another.

You are welcome to contact me if you have further questions regarding the JHUIBC.

Regards,

Stephen C. Dahl, Ph.D., RBP
Biosafety Officer
Johns Hopkins Institutions

Johns Hopkins Institutional Biosafety Committee

Tuesday June 3, 2003
Room B-600, 2024 East Monument Street Building

Members Present: Dr. Hayward, Chair, Mr. Balog, Ms. Biedrzycki, Ms. MacAuley, Dr. Scott, Dr. Rade, Dr. Dahl, *ex-officio*

Members Absent: Dr. Adams, Ms. MacAuley, Dr. Margolick, Dr. McDevitt

Guests: Dr. [redacted], Dr. [redacted]

The meeting was called to order at 2:05 PM

I Minutes of February 25, 2003 meeting were unanimously approved without addition or correction.

II **Review of [redacted] protocol GT0306030101** "A Phase I Safety and Immunogenicity Trial of an Alphavirus replicon HIV Subtype C Gag Vaccine (AVX101, Alphavax, Inc.) in Healthy HIV-1 Uninfected Adult Volunteers"; Protocol # HVTN 040; version 2 FINAL; BBIND10171

The investigators presented an MS Powerpoint summary of the vaccine background and study design (attachment 1). The following is a record of IBC questions and the answers provided by the Principal Investigators.

The investigators responded to a query of whether or not the vector would persist, and for how long.

> "The vaccine is not infectious based on the deletion of the structural proteins of the VEE vector and the use of an attenuated Env gene in the helper segment. Two regions from the E1 promotor are deleted. The replicon is single-cycle, and non-replicating. Furthermore, only in vitro translated RNA not plasmid DNA is used to generate the virus preparation" Homologous recombination is possible, but only in the extreme. In this unlikely event, the result would be a replication incompetent virus due to the double deletion of E1 components necessary for infectivity."

The investigators were asked whether or not they had actually tested whether the vector persists post vaccination in animals and if so, for how long?
The investigators responded that data from pre-clinical animal experiments demonstrate the lack of persistence of the replicon in the experimental animals.

The investigators were asked why VEE was chosen rather than the more established alphavirus vectors such as sindbis. The investigators replied that although all target dendritic cells , the reason VEE was chosen was that there is already considerable experience with VEE vaccination in humans.

The investigators were also asked about the reasons for the previous FDA hold on the Alphavax product. The investigators responded that there had been two problems, initially a low level recombination event had been detected in a test of one lot, but that the assay used had been done at an excessively high concentration and only showed a problem after growth in cell culture. The second problem involved inadvertent

contamination with BHV4 from the bovine serum used in the culture medium and this has also now been resolved.

The investigators were asked if a shipping protocol has been established to comply with the regulations, and maintain the integrity of the study vaccine while in transit.
The investigators replied that the sponsor has a comprehensive plan to ensure the integrity of the product throughout the shipping process.

The investigators were asked about clinic waste handling and disposal.
The investigators replied that all clinic sites will be equipped with sharps containers for needles and syringes and other sharps. Other lab waste will be disposed of per JH policy.

The investigators were asked whether the EBV immortalization studies of PBMC collected from the volunteers would be done here at Hopkins, but The investigators responded that all of those tests would be done at the central study site laboratory facilities in North Carolina.

At the completion of the presentation, The investigators left the meeting..

The issue of long term follow up of study subjects was raised. The committee reviewed Section 11.3.3, page 25 of the IB specifications for quantity, storage and shipping of specimens obtained from study subjects. The committee deemed the plan appropriate, but agreed that all reviews of studies in the future should pay special attention to whether the investigators have made adequate plans on the issue of collection and long-term storage of patient specimens that would be suitable for future evaluation if new more sensitive tests are developed or if complications should arise.

There being no further questions, the Chair inquired if the committee was prepared to vote. The motion was made and seconded to vote on the protocol. Without dissent, IBC moved to vote. Results of IBC vote:

For Approval: 7
Disapproval: 0
Abstain: 0

Dr. Scott left the meeting at 3:25. His departure did not dissolve the quorum.

The Chair then turned over the meeting to Dr. Dahl for presentation of basic science laboratory recombinant DNA and Pathogen registrations for IBC review and vote.

The meeting adjourned at 4:10 PM

Institutional Biosafety Committee
June 3, 2003 Meeting
Registrations from 1/07/03 -- 4/04/03

Title	IBC#	BSL	Yes	No	Abstain
Structural Characterization of the Type III Secretion Machinery of Yersinia enterocolitica	DN0301280101	2	6	0	0
Structural Characterization of the Type III Secretion Machinery of Yersinia enterocolitica	P0301280101	2	6	0	0
Development of Ovarian Cancer Immunotherapy Using Serologically Identified Tumor Antigen	DN0301270201	1	6	0	0
Effect of Influenza Virus Infection on a Human Cell Line of Neural Origin	P0303210101	2	6	0	0
Sex Differences in rodent Models of Malaria	P0303310201	2	6	0	0
Development of Non-viral Gene Delivery Carriers	DN0303140101	2	6	0	0
Effects of Viral Inflammation on DNA Mutation Rates in the Mouse Prostate	P0303100101	2	6	0	0
Rickettsia in Dermacentor Ticks	P0302250101	2	6	0	0
Rickettsia in Dermacentor Ticks	P0302250201	2	6	0	0
Bertonella in Ticks	P0302250301	2	6	0	0
Molecular Mechanism for Oxidative Metabolism	DN0302280101	2	6	0	0
Molecular Mechanism for Oxidative Metabolism	P0302280101	2	6	0	0
Signal Transduction in Polycythemia Vera	DN0304030101	2	6	0	0

Role of Spinal Cord PSD-95 in Chronic Pain	DN0303130101	2	6	0	0
Effector and Memory CD8+ T cells Against Malaria Parasites	P0303310101	2	6	0	0

Johns Hopkins Institutional Biosafety Committee

Friday June 13, 2003
Room B-600, 2024 East Monument Street Building

Members Present: Dr. Hayward, Chair, Mr. Balog, Ms. Biedrzycki, Dr. Borrello, Ms. MacAuley, Dr. Scott, Dr. Dahl (*ex-officio)*

Members Absent: Dr. Hawley, Dr. Margolick, Dr. Rade

Guest: Dr. Bourgeois

The meeting was called to order at 10:10 AM

I Minutes of June 6, 2003 meeting were approved.

II a) **Review of [redacted] protocol GT0306130101**: "The Evaluation of the Pharmacokinetics of Rifaximin in Subjects with Shigellosis;" VTU032

The investigator presented a summary of the Vaccine Testing Unit (VTU) experience conducting trials involving infectious agents since 2000. He stated the VTU has conducted two previous studies involving *Shigella sp,* in collaboration with the General Clinical Research Center in the JHH and the Bayview Medical Center. The Center for Immunization Research and the GCRC discuss and coordinate safety components prior to initiation of new trial. Each of the previous trials concluded without incident to staff or study volunteers. The project overview (response to item 9 on the JH Pathogen Registration form) included suggestive rather than prescriptive language regarding safe work practices. He clarified that all staff will observe standard precautions when handling viable organisms, and patient specimens. Additionally, JH Epidemiology and Infection Control will arrange an in-service on contact precautions for the GCRC staff prior to initiation of this study.
The investigator indicated that the Research Pharmacy of the JHH has worked with VTU staff in the past and will observe manipulations of the *Shigella flexneri.*

The investigator was questioned regarding follow-up of patients for persistence of the organism. The protocol states that patients will be monitored for symptoms and their stool specimens screened prior to release from the GCRC will be screened. Additional follow-up will be scheduled on an out-patient basis 7 to 14 days after release from the GCRC.

Shigella flexneri (FDA BB MF 3908, a master file reference) produced under GMP conditions at the Walter Reed Army Institute of Research will be provided in lyophilized form to the VTU. The VTU will perform pre-study qualification testing by growing up the bacteria in culture and testing to ensure absence of contaminants, and to define the ratio of colony forming units (cfu) to Optical Density (OD) of culture. The investigator was asked about the JH laboratory where this process would take place (BSPH W 5603, W5608 & W5616).

At the conclusion of his presentation The investigator thanked the IBC for providing the opportunity to discuss the trial and left the meeting.

After the investigator's departure, the Chair instructed the Biosafety Officer to visit the BSPH laboratories involved with this study to ensure compliance with policy and to assess the secure storage of the test materials.

[The Biosafety Officer visited the laboratories in the afternoon of 6/13/03. No safety or security items were identified.]

There being no further questions, The Chair asked for a motion to vote on the submission. The motion was made and seconded.
Without dissent, the IBC moved to a vote. Results of IBC vote:

For Approval: 7
Disapproval: 0
Abstain: 0

b) **Review of [redacted] Protocol GT0306130201** "A Multicenter, "Double-Blind, Placebo-Controlled, Phase II Study of Aerosolized tgAAVCFA Multicenter, Double-Blind, Placebo-Controlled, Phase II Study of Aerosolized tgAAVCF for the Treatment of Cystic Fibrosis"; RAC Protocol # 0301-569; BB5933, Targeted Genetics Corporation Protocol # 25E01 Amendment 1: 04/03/03

The Chair presented the protocol overview to the Committee. Members of the IBC agreed with Dr. Hayward's comment that an adequate animal model for Cystic Fibrosis (CF) does not exist. This presents a hurdle in developing and assessing the efficacy of the gene transfer event. Specimens are obtained from study subjects via "airway brushing" which yields few, if any, cells which can be tested for gene expression. This unfortunate reality negatively impacts the ability to accurately determine the success of the gene transfer event.

Concern was expressed that participation in this trial may preclude these patients from participating in future trials. The fatal progression of CF was noted, and that projecting patient participation in future studies may be more philosophical than practical.

It was commented that the adeno-associated viral vector (AAV) is not known to be disseminated beyond the organ or tissue administration site. It was also offered that this was not necessarily universally correct and that systemic expression was greatly influenced by the route of administration, either intravenously or intraperitoneally or intra-organ. Information obtained from a seminar was mentioned that AAV was recovered from sperm of a study subject.

The Committee noted the comment and agreed that the protocol in question which employs a nebulizer to administer the study compound, is not likely to result in systemic distribution of the vector.

There being no further questions, The Chair asked for a motion to vote on the submission. The motion was made and seconded.
Without dissent, the IBC moved to a vote. Results of IBC vote:

For Approval: 7
Disapproval: 0
Abstain: 0

Dr. Scott left the meeting at 11:20. His departure did not dissolve the quorum.

The Chair then turned over the meeting to Dr. Dahl for presentation of basic science laboratory recombinant DNA and Pathogen registrations for IBC review and vote.

The research registrations and the IBC vote is attached.

III New Business

Changes were initiated in the organization and meeting schedule of the IBC. In the interest of greater efficiency, Recombinant DNA Registrations, Pathogen Registrations and Human Subject Protocols will be pre-screened by sub-groups of the IBC to ensure application materials are complete prior to submission to the Full IBC for review and consideration for approval.

1. The rDNA / Pathogen Review subcommittee will meet on the second Tuesday of each month.

2. The human subject protocol review subcommittee will meet on the second Monday of each month. The time may vary in consideration of the availability of the Clinician members to participate.

3. The first working day of the month will be the submission deadline for receipt of protocols to be screened at the respective monthly subcommittee meeting.

4. The full IBC will convene on the third Monday of each month, beginning in July.

5. Members who have volunteered for the rDNA/Pathogen review subcommittee are Dr. Adams, Dr. Hayward, Dr. Scott, Dr. Dahl, & Mr. Balog.

6. Members who have volunteered for the human subjects protocol review subcommittee are; Dr. Rade, Dr. Borrello, Ms. Biedrzycki, Dr. Hayward, Dr. McDevitt, Dr. Margolick, Mr. Balog,.

7. The committee recommended that the deadlines and meeting date information be forwarded to the Joint Committee on Health, Safety & Environment and disseminated via usual campus means.

There being no further business, the meeting adjourned at 12:00 PM

Johns Hopkins Institutional Biosafety Committee

Institutional Biosafety Committee Registrations
June 13, 2003 Meeting
Registrations from 4/04/03 -- 5/31/03

Title	IBC#	BSL	Yes	No	Abstain
Mechanochemical Regulation of Pulmonary Vascular Permeability	DN0305300101	2	6	0	0
Adenovirus Meidated siRNA in Cultured Mammalian Cells	DN0305120101	2	6	0	0
Molecular Mechanism of Host Antiviral Gene Regulation by HIV-1	DN0304040101	2	6	0	0
Gene Transfer for Specific Immunotherapy of Myasthenia	P0304110101	2	6	0	0
Immunotherapy of Cancer Using Gene-modified Stem Cells	DN0305010201	2	6	0	0
Analysis of Plasmodium development in the mosquito	DN0305070101	1	6	0	0
Development of Gene Therapy for Chronic Pain	DN0305300201	2	6	0	0
Immunological Studies on Malarial Antigens	P0304140101	2	6	0	0
Immunological Studies on Malarial Antigens	P03041420201	2	6	0	0
Hypoxia Induced Mitogenic Factor in Lung Development in Mouse	DN0305130101	2	6	0	0
A p105-based NF-Kappa B Super Repressor and Skin Carcinomas	DN0305160101	2	6	0	0
Characterization of the role of ICAM1 in ischemia/reperfusion injury and chronic graft dysfunction	P0305220101	2	6	0	0

Johns Hopkins Institutional Biosafety Committee

Lysophospholipids in Lung Pathobiology	P0305270101	2	6	0	0
HIV Neuropathogenesis	P0305150301	2	6	0	0
West Nile Virus Testing of Chesapeake Bay Area Mosquitos	P0304150101	2	6	0	0
FAK and Src pattern pulmonary vascular injury response	DN0305150101	2	6	0	0
Preclinical Models of HIF-1α Gene Therapy	DN0304080101	2	6	0	0
Endothelial Cell Death and Inflammation in Emphysema	DN0305010101		6	0	0
Intravascular MRI - Enhanced Vascular Gene Transfer and Digital Optical Imaging of Vascular Gene Expression	P0305200101	2		Hold for more information	
Intravascular MRI - Enhanced Vascular Gene Transfer and Digital Optical Imaging of Vascular Gene Expression	P0305200201	2		Hold for more information	

Johns Hopkins Institutional Biosafety Committee

Monday July 21, 2003
Room B-600, 2024 East Monument Street Building

Members Present: Dr. Scott (Acting Chair), Dr. Adams, Mr. Balog, Ms. Biedrzycki (arrived after vote), Dr. Borrello, Dr. Dahl, Ms. MacAuley, Dr. McDevitt,

Members Absent: Dr. Hawley, Dr. Hayward, Dr. Margolick, Dr. Rade

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The meeting was called to order at 3:05PM

I Minutes of June 13, 2003 meeting were not ready and, thus, tabled.

II a) **Review of [redacted] Protocol GT0307210101**:
A WORLDWIDE, PHASE I DOSE-ESCALATING STUDY OF THE SAFETY, TOLERABILITY AND IMMUNOGENICITY OF A 3- DOSE REGIMEN OF THE MRKAd5 HIV-1 gag VACCINE IN HEALTHY ADULTS, HVTN 050/MERCK revision # 018

The IBC was presented with a summary of the information provided by the investigator. The concept of an HIV vaccine was first described in 1991, and the first DNA vaccine targeted influenza. Merck submitted an IND application for Adenovirus type 5 in 2000 and in 2001 Ad5 was used in vaccine trials for the first time. Merck has since abandoned its pursuit of HIV DNA vaccine research. In 2003 Merck initiates multi-center trials on several continents. The HVTN and Merck have partnered on several HIV vaccine trials. Only recently has the NIH Division of AIDS Research (DAIDS) initiated the requirement for IBC review of HIV vaccine trials funded by the NIH.

The safety components of this trial involve sera testing for Ad vector persistence, examination of the injection site for a reaction, monitoring participants for elevated temperature, fatigue, chill and myalgia.

Ad5 differs from MRKAd5 in that the former construct is E1and E3 deleted, and the latter has been found to be more efficient with merely an E1 deletion.

The JHIBC, through the Biosafety Officer has provided guidance to JH Investigators conducting gene transfer trials overseas. The JHIBC does not have the ability to provide IBC review as defined in the NIH Guidelines for studies conducted overseas.

The IBC then moved to a vote on protocol GT0307210101.

For Approval: 7
Disapproval: None
Abstain: None

The Acting Chair turned over the meeting to Dr. Dahl for presentation of basic science laboratory recombinant DNA and Pathogen registrations for IBC review and vote.

The research registrations and the IBC vote is attached.

There being no further business, the meeting adjourned at 3:50 PM

Institutional Biosafety Committee Registrations
July 21, 2003 Meeting
Registrations from 6/1/03 -- 6/30/03

Title	IBC#	BSL	Yes	No	Abstain
PTEN/tyrosine kinase interactions in gliomas	DN0306090101	2	7	0	0
Targeted Disruption of a Proliferation-associated SNF-2-like Gene (PASG) in Mice	DN0306300101	2	7	0	0
Nutrition in Apicomplexa	DN0307020101	2	7	0	0
Innate Immune Responses to Mycobacterium tuberculosis	P0306050101	3	7	0	0
A study of Telomeres in Mice	DN0306170101	2	7	0	0
Telomerase Deficiency in Leukemia and Lymphoma Murine Models	DN0306170201	2	7	0	0
Control of Stem Cell Fate in Drosophila Spermatogenesis	DN0306180101	1	7	0	0
Lipid Rafts as Cellular Targets for HIV Entry	P0306050201	3	7	0	0
rAAV-mediated transfection of BDNF, GFP, trkB or CNTF genes in rat glaucoma	DN0306160101	2	7	0	0
Transplantation of Mouse Insulinoma as a model of invitro and in vivo suicide gene expression	DN0306050101	2	7	0	0

Johns Hopkins Institutional Biosafety Committee

JHU IBC Minutes for Meeting of August 18, 2003
Room B-600 2024 E. Monument Street Building

Members Present: Dr. Hayward, Chair, Dr. Adams, Mr. Balog,, Dr. Borrello, Dr. Dahl, Ms. MacAuley, Dr. McDevitt, Dr. Margolick, Dr. Scott

Members Absent: Ms. Biedrzycki, Dr. Hawley, Dr. Rade

Guests: Dr. Kobrin, Ph.D., JHU Cell Processing and Gene Therapy Facility (CPGTF), Dr. [redacted].

The meeting was called to order at 3:08PM

I Dr. Kobrin, Ph.D. of the Cell Processing and Gene Therapy Facility at Johns Hopkins explained and discussed the capability, operation and facility design of the GMP Facility. The following is a summary of the presentation.

i. The Organization
Dr. Elizabeth Jaffee is the Medical Director of the Facility. Dr. Richard Jones is the Director of the Graft Engineering Lab (GEL). Product is produce according to established performance specifications. Product performance documentation is reviewed by Dr. Richard Jones of the GEL prior to release for patient use. Kathy Loper serves as the GMP Manager and GEL Manager. Dr. Kobrin serves as an Assistant Director.

ii. Facility Description & Capability
Dr. Kobrin stated the facility production capabilities are limited to Phase I and Phase II trials. A diagram depicting the physical layout of the facility was reviewed. The facility is a positively pressurized Class 10,000 clean room with room air comprised of 80 % outside air and 20% re-circulated air. Atlantic Technology provides contract cleaning and testing of the critical systems, and JHU Facilities Management services the HVAC system. The facility is constantly monitored for relative humidity, temperature and air supply.

iii. Operations
While the facility has the capability to simultaneously produce different products in each of the four rooms within the facility, only single production lots are produced at any given time. The production staff is trained in cell culture and GMP at the Maryland Biotech Institute on the 5th floor of Baltimore City Community College. The CPGTF staff do in-process environmental monitoring (touch plates) to validate aseptic technique was not compromised during production of the product. All equipment used in-process is on a managed serviced and calibration schedule. Any instance of equipment or system non-conformance is documented. Production may or may not be impacted by such instances of a non-conformance. The product is manufactured and tested in the confines of the GMP facility. Finished product is tested for conformance to the established specifications. Product deemed acceptable is transferred to the GEL for another level of review of the product performance and certificate of analysis prior to being released by the GEL for use in study patients.

The Chair inquired about GMP staff training frequency (on-going, at least annually), and facility cleaning (contractor and staff do cleaning).

II Minutes of June 13, 2003 and July 21, 2003 meetings were unanimously approved.

III **Review of [redacted] Protocol GT0308180101**:
"A PHASE I VACCINE SAFETY AND CHEMOTHERAPY DOSE-FINDING TRIAL OF AN ALLOGENEIC GM-CSF-SECRETING BREAST CANCER VACCINE GIVEN IN A SPECIFICALLY TIMED SEQUENCE WITH IMMUNOMODULATORY DOSES OF CYCLOPHOSPHAMIDE AND DOXORUBICIN"
OBA RAC Human Gene Transfer Protocol # 0304-578

No concerns were expressed by members of the IBC after a summary presentation presented by the investigator. The Chair presented a summary of the protocol. He stated that the product is manufactured using 2 ATCC-derived cell-lines. The study will enroll Stage IV breast cancer patients. The protocol is to administer 10^8 cells via dermal injection into 3 of the patient's limbs during a single outpatient session. The immunomodulatory dose of the chemotherapeutic agents varies. It was noted that there is a lifetime exposure tolerance for doxorubicin (350mg/m^3) and Stage IV breast cancer patients are a heavily-treated population. It was further stated that discovery of the most effective immunomodulatory dose (which enhances the product activity *in-vivo*) is a goal for subsequent trials. The Chair stated the FDA has not raised any issues about the JHU GMP facility, and has issued an IND number for the product.

It was noted that, to date, autoimmune disease has not been observed in human tumor vaccine studies.

For the record, Dr. Rade submitted his recommendation for approval by email.

The IBC then moved to a vote on protocol GT0308190101.
For Approval: 9
Disapproval: 0
Abstain: 0

V The Chair turned over proceedings to Dr. Dahl for presentation of laboratory based recombinant DNA and Pathogen registrations for IBC review and vote.

The research registrations and the IBC vote are attached.

There being no further business, the meeting adjourned at 3:50 PM

Johns Hopkins Institutional Biosafety Committee

Institutional Biosafety Committee Registrations
August 18, 2003 Meeting
Registrations from 7/3/03 -- 8/6/03

Title	IBC#	BSL	Yes	No	Abstain
Nutrition in Apicomplexia	P0307220101	2	9	0	0
Nutrition in Apicomplexia	P0307220201	2	9	0	0
Role of TFII-1 in Endothelial Cell Biology	DN 0308010101	2	9	0	0
EBV and HHV-8 interactions in primary effusion lymphomas	P0307230101	2	8	0	1
Lentiviral gene transfer to express cDNA in tissue culture cells and laboratory animals	DN0308060101	2	9	0	0
Antimalarial thymidylate synthase inhibitors in mammalian systems	P0307310101	2	9	0	0
Antimalarial thymidylate synthase inhibitors in mammalian systems	P0307310201	2	9	0	0

Johns Hopkins Institutional Biosafety Committee

JHU IBC Minutes for Meeting of September 15, 2003
Room B-600 2024 E. Monument Street Building

Members Present: Dr. Hayward, Chair, Mr. Balog,, Dr. Borrello, Ms. Biedrzycki, Dr. Dahl, Ms. MacAuley, Dr. Margolick, Dr. McDevitt, Dr. Rade, Dr. Scott

Members Absent: Dr. Adams, Dr. Hawley

The meeting was called to order at 3:15PM

I Minutes of August 18, 2003 meeting were unanimously approved.

II **Review of [redacted] Protocol GT0309150101:**

"A PHASE I/II CLINICAL TRIAL OF Pngvl-4a-Sig/E7(detox)/HSP70 FOR THE TREATMENT OF PATIENTS HPV16+ CERVICAL INTRAEPITHELIAL NEOPLASIA 2/3 (CIN2/3)"
OBA RAC Human Gene Transfer Protocol # 0307-595
FDA IND: BB-IND 11116

Members of the JHIBC met on 8 September to hear a summary presentation by the investigator. In attendance were Dr. Hayward, Ms. Biedrzycki, Mr. Balog, Dr. McDevitt, Dr. Rade, and Dr. Dahl. One IBC member remarked that the presentation was well organized, concise, and well presented. This member had no questions or concerns about the study.

The Chair noted that to date, the Committee is unaware of patient-related problems with exposure to "naked-DNA" vaccines. He remarked that integration is not suspected and the DNA is not expected to persist for an extended period post-vaccination. Finally, it was noted for the record that the IRB recommended extending patient monitoring post-vaccination monitoring.

One IBC member asked if the Committee had concerns about the lack of experimental documentation of the inactivation of the E7 binding to RB? There were no concerns expressed by the membership. The Chair agreed that more data would have been helpful, but stated that with this particular protocol, the strategy was based on established, well documented information and that therefore the supporting publications are not strictly required to be submitted to the IBC for this protocol. However, in the future, such claims must be substantiated by brief explanations and citations from the literature should be clearly referenced in the protocol narrative (as they were in this case).

The IBC then moved to a vote on protocol GT0309150101.
For Approval: 9
Disapproval: 0
Abstain: 1

Subsequent discussion resulted in the Chair directing IBC submission of Human gene transfer and vaccination protocols should be simultaneous with IRB submission. This is necessary to ensure that any subcommittee recommendations for protocol revisions may be implemented in a timely manner. The revised protocol would then be re-reviewed by the IBC prior to a vote.

III The Chair turned over proceeding to Dr. Dahl for presentation of laboratory based recombinant DNA and Pathogen registrations for the IBC to review and vote on the seven registrations received during the past month. The IBC approved the biosafety level assessment and the recommendation to approve each of the seven registrations.

The research registrations and the IBC vote are attached below.

The IBC discussed and decided to assign Animal Biosafety Levels (ABSL) for registrations involving infectious agents and pathogens in whole animals. Currently the IBC assigns BSL for the laboratory manipulation of infectious agents and pathogens.

IV Old Business:

The IBC was informed to expect a new protocol submission for the October meeting.

New Business:

Dr. Glass, Dr. Zavala, and Mr. Kempner of the BSPH Malaria Research Institute will discuss safe work practices when handling mosquitoes, malaria parasites, and related arboviruses or recombinant DNA, decontamination, and containment in an insectary. Mr. Kempner will present design strategy to promote safe work practices. These presentations and discussion of insect containment levels will be scheduled for the October 19 meeting, if feasible.

There being no further business, the meeting adjourned at 4:20 PM

Institutional Biosafety Committee Registrations
September 15, 2003 Meeting
Registrations from 8/08/03 -- 9/04/03

Title	IBC#	BSL	Yes	No	Abstain
Studying the transport of adenoviruses to improve gene delivery efficiency	**P0308290101**	**2**	**10**	**0**	**0**
EBV and HHV-8 Interactions in Primary Effusion Lymphomas	**DN0308150101** *P0307230101*	**2**	**9**	**0**	**1**
Targeting of the SARS coronavirus envelope proteins	**DN0309040101** *P0308250101*	**2**	**10**	**0**	**0**
Adenoviral vectors for gene transfer in mammalian cells	**P0309040101**	**2**	**10**	**0**	**0**
Retroviral vectors for gene transfer in mammalian cells	**P0309040201**	**2**	**10**	**0**	**0**

Johns Hopkins Institutional Biosafety Committee

Center for inflammatory disorders	**P0308200101**	**2**	**10**	**0**	**0**
Design of a neural chip to study growth and development of primary mammalian neurons	**DN0308270101** *P0308270101* *P0308270201* *P0308270301*	**2**	**10**	**0**	**0**

Johns Hopkins Institutional Biosafety Committee

JHU IBC Minutes for October 20, 2003
Room B-600, 2024 E. Monument Street Building

Members Present:	Dr. Hayward, Chair; Dr. Adams, Mr. Balog, Ms. Biedrzycki, Dr. Dahl, Ms. MacAuley, Dr. Margolick, Dr. Scott
Members Absent:	Dr. Borrello, Dr. Hawley, Dr. McDevitt, Dr. Rade
Guests:	Dr. Dimopoulos, Dr. Jacobs-Lorena, Dr. Kumar, Dr. Norris, Dr. Zavala

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The meeting was called to order at 3:10 PM.

Copies of the Arthropod Containment Guidelines (version 3.1) published by the American Committee of Medical Entomology of the American Society of Tropical Medicine and Hygiene were handed out to IBC members. The Chair acknowledged the presence of guests who are members of the School of Public Health involved in the development of the new insectary…a presentation of which was to follow approval of minutes and human gene transfer votes.

Approval of September Minutes
The Chair asked for a vote regarding the approval of the September minutes.
The IBC moved to vote:
For Approval: 8
Disapproval: 0
Abstain: 0

Human Subjects Gene Transfer/Pathogen Protocols
One protocol was reviewed by the human subjects sub-group for presentation to the IBC.

1) [redacted] **Protocol GT0310200101,** K562/GM-CSF vaccination in combination with imatinib mesylate for chronic myeloid leukemia. OBA RAC human gene transfer protocol #0309-602, FDA IND: BB-IND 11284.

Discussion centered on the presentation given earlier by the investigator. It was noted that the protocol involved the introduction of an inactivated transformed human cell line into immuno-compromised patients. It was asked if there were concerns regarding proof of inactivation prior to use. The members felt the irradiation proposed was sufficient for cell inactivation and a standard treatment as this cell line has been used previously in human patients. Appendix M was complete and found to be acceptable.

The IBC moved to vote on protocol GT0310200101:
For Approval: 7
Disapproval: 0
Abstain: 1

The Chair suggested a change in the agenda to allow the guests to do their presentation next instead of waiting for the completion of IBC business. All members were in agreement.

BSPH Malaria Research Unit Presentation

The facility will include a BSL2 cell culture facility, a BSL 3 facility for handling human pathogens, multiple walk-in prep incubators for housing mosquitos and ticks, and several prep rooms. All walls will be of a light color (white) to facilitate identification of any escaped insects. Electronic insect traps will be stationed throughout the facility. The facility will maintain negative pressure in comparison to the surrounding environment.

Much of the work will occur on rodent-specific malaria. Most mosquitos to be used in the insectary will not be infected, rather, they will be raising stock. Plasmodium berghei and yoelii are rodent specific. They do not infect humans or primates. Berghei and yoelii do not exist in the Baltimore area. They are temperature restricted--only infect at 19° C. --so mouse to mouse transmission is not possible. Mice injected with plasmodium will not be "infectious" because they will not have a chance of "seeing" a mosquito.

Some work will focus on human malaria. Rbcs from volunteers will be used to maintain the plasmodium in culture. This work will be performed in the BL2 cell culture of the proposed facility. Infections will be performed in the BSL3 facility.

The IBC thanked the guests for their presentation and commenced IBC business after the guests departed.

Recombinant DNA/Pathogen Research Registrations
Ten research registrations were presented for IBC consideration. Eight were approved unanimously, two were held for further information (see attached list).

The meeting ended with Mr. Balog saying goodbye and thanking the members for their support and participation. Mr. Balog has resigned his position as Biosafety Officer of Johns Hopkins Institutions in order to assume the Biosafety Officer role at an institution in the southwest. The IBC members wished him well in his new position. Dr. Dahl, the Associate Biosafety Officer will assume Mr. Balog's duties on November 10, 2003.

The meeting was adjourned at 5:15 PM

Institutional Biosafety Committee Registrations
October 20, 2003 Meeting
Registrations from 9/05/03 -- 10/06/03

Title	IBC#	BSL	ABSL	Yes	No	Abstain
Chromagar, MRSA clinical evaluation for detection of methacillin resistant Staph. aureus from surveillance cultures	P0309300301	2	na	8	0	0
Motor Neuron Differentiation	DN0309170101 *P0309170201*	2	na	8	0	0
Role of Sphingosine 1 Phosphate in Acute Lung Injury	P0309150101	2	2	8	0	0
HIV-Drug Resistance During HAART in Adolescents	P0309080101	2	na	8	0	0
FAK in E. coli Pathogenesis	P0309170101	2	na	Unanimous vote to hold for more information		
Molecular and Cellular Mechanisms Regulating Adult Neural Stem Cells	DN0309160101 *P0309160101* *P0309160201*	2	2	8	0	0
Determination of Methylation of HHV-8 Infected Endothelial Cells HHV-8 infected endothelial cells will be processed for DNA extraction and methylation scan.	P0309050101	2	na	8	0	0
Development of virus-like particle based SARS virus vaccine	DN0309300101	2	na	Unanimous vote to hold for more information		
RNA interference in beta amyloid mouse models	DN0309230101 *P0309230101*	2	2	8	0	0
Evaluation of HIV-1 DNA Vaccine and Human Immunodeficiency Virus-like Particle Vaccine	DN0310060301	2	1	8	0	0

Johns Hopkins Institutional Biosafety Committee

JHU IBC Minutes for January 20, 2004
Room B-600, 2024 E. Monument Street Building

Members Present: Dr. Hayward, Chair; Dr. Adams, Ms. Biedrzycki, Dr. Borrello, Dr. Dahl, Ms. MacAuley, Dr. McDevitt, Dr. Scott

Members Absent: Dr. Hawley, Dr. Margolick, Dr. Rade

Guests: None

The meeting was called to order at 3:07 PM in the mail facility conference room due to scheduling conflicts and MLK holiday.

The latest CDC guidance (January 8, 2004) on the handling of SARS virus was handed out as was the WHO guidelines for handling SARS specimens. A policy forum from the journal, Science, titled "A sound rationale needed for phase III HIV-1 vaccine trials." was distributed.

Human Subjects Gene Transfer/Pathogen Protocols
Five protocols were reviewed by the human subjects sub-group for presentation to the IBC, two of which were follow-ups.

1) [redacted] **Protocol GT0401200201**, A phase II, multi-center, single arm evaluation of preoperative chemoradiation plus TNFerade biologic prior to esophagectomy for locally advanced respectable esophageal cancer.

Approval had been held for this protocol pending clarification on the training of physicians involved in the delivery of the agent. Additional information provided by the investigator was discussed and found to be satisfactory.

The IBC moved to vote on protocol GT0401200201:

For Approval: 8
Disapproval: 0
Abstain: 0

2) [redacted] **Protocol GT0401200301**, A phase I/II clinical trial of pNGVL4a-Sig/E7(detox)/HSP70 for the treatment of patients with HPV16 + cervical intraepithelial neoplasia 2/3 (CIN2/3)

Changes had been received in this previously approved protocol. None had biosafety implications.

The IBC moved to vote on protocol GT0401200301:

For Approval: 7
Disapproval: 0
Abstain: 1

3. [redacted] **Protocol GT0311170101,** A phase II, randomized, double-blind, placebo-controlled, parallel group, efficacy and safety study of different doses and schedules of administration of NV1FGF in patients with severe peripheral artery occlusive disease. Sponsor's protocol number NV1FGF-PM202, version 4.0, including amendment no. 1, 2 and 3, dated December 2002.

An appendix M had been requested of this investigator at a prior IBC meeting. IBC review found the document to be acceptable, but questions were raised regarding changes that may have been made to this protocol since it was first approved. It was decided that approval would be held pending receipt of the final IRB version.

The IBC moved to table the evaluation of protocol GT0311170101 pending receipt of requested documentation:

For: 8
Against: 0
Abstain: 0

4. [redacted] **Protocol GT0401200101,** A Phase IB Clinical Trial to Evaluate the Safety and Immunogenicity of a Multiclade HIV-1 DNA Plasmid Vaccine, VRC-HIVDNA009-00-VP, Administered at 2 Different Dosing Schedules, in HIV-1 Uninfected Adult Participants (HVTN 052, Version 1)" CHR #H.22.03.09.23.A2

This protocol presented a multivalent HIV vaccine similar to other protocols approved for the investigator.

The IBC moved to vote on protocol:

For Approval: 8
Disapproval: 0
Abstain: 0

Following this vote, a there was a brief discussion concerning the respective roles of the IBC and the IRB. Points that were made included:

1) The IBC should consider safety implications for other people involved in the project such as staff such as those who are administering the drug whom the IRB may not be concerned with. The IBC should focus on both the patient's AND the provider's safety

2) The IBC should see all product-related severe adverse events documentation.

3) The IBC should see adverse events for administering staff--for example, needlesticks w/virus to be administered.

4) The Animal Care and Use Committee requires investigators to provide an annual research status report. The IBC should request some sort of an annual review letter as well.

5) Investigators should provide documentation of training for involved staff.

6) There should be a form that states if the project has been started/is active.

5. [redacted] **Protocol GT0401200401,** Phase I study of the safety and immunogenicity of rDEN2/4 Δ 30 (ME), a live attenuated virus vaccine candidate for the prevention of dengue serotype 2.

The principal investigator presented the project and answered questions regarding the protocol and future projects. The Chair summarized the protocol noting it used an attenuated Dengue virus with Dengue 2 in a Dengue 4 background for testing in adults. Dengue transmission is by mosquito, and infection with one variant makes the patient more susceptible to other Dengue viruses.

The following requests were made of the investigator:

1) Documentation of the company's QC procedure for confirming the integrity of the recombinant construct.

2) Documentation of FDA approval for this reagent and any comments that may have been made by the FDA, IRB, and study group.

3) An assessment of viremia and the potential for transmissibility and attenuation of the double mutant.

4) Information regarding the evaluation of patient viremia and asymptomatic viremia. Patient screening should allow for patients that might get the disease if something unexpected happens due to mixing of serotypes--2/4, 1/4, 3/4. It was noted that maximum viremia is reported to be seen in a few days.

5) An education program for subjects regarding Dengue and increased susceptibility to other variants

6) Consider performing the protocol in the winter. If not feasible, educate patients on how to avoid getting bitten by mosquitos during the viremic stage.

The IBC decided it should register the people who will handle the vaccine. The IBC moved to table the evaluation of protocol GT0401200401 pending receipt of requested documentation:

For:	8
Against:	0
Abstain:	0

Recombinant DNA/Pathogen Research Registrations
Fifteen research registrations were presented for IBC consideration; seven of which were held over from the cancelled November meeting (no meeting was scheduled in December). Ten were approved unanimously, five were held for further information (see attached list).

The meeting ended with a discussion of BSL3 space on campus and the housing of investigators who wish to work with SARS virus. It was suggested that the Jefferson BSL3 was vacated by an investigator moving to the new BRB building and that one could talk to the Dean of Research about this space.

The IBC will conduct an inspection survey of all BSL3 spaces on campus prior to considering any work with live SARS virus.

Institutional Biosafety Committee Registrations
January 20, 2004 Meeting
Registrations from 10/07/03 -- 1/08/04

Includes items from cancelled November meeting

Title	IBC#	BSL	ABSL	Yes	No	Abstain
Cellular signaling pathways in carcinogenesis and organogenesis	DN0310160101	2	na	8	0	0
Phase I study of the safety and immunogenicity of tick-borne Langat/Dengue 4 chimera virus	P0311050301	2	na	Unanimous vote to hold for more information		
Bone sialoproteins and tumor progression	DN0311040101 *P0311040101*	2	na	8	0	0
Myocardial regeneration by bone-marrow derived stem cells in old versus young Wistar rats	P0311050201	2	2	8	0	0
Characterization of the role of ICAM-1 in ischemia/reperfusion injury and chronic graft dysfunction	P0311050101	2	2	8	0	0
Generation of defective SARS-Cov pseudovirus	DN0311040201 *P0311040201*	3	na	Unanimous vote to hold for more information		
Enzyme-linked Immunosorbent Assays for Detection of Antibodies to SARS Coronavirus	P0310160101	2	na	Unanimous vote to hold for more information		
January Protocols						
Molecular Genetics of HSV-1 Virion	DN0312310101 *P0312310101*	2	na	8	0	0
Comparison of Various Plasmids to Enhance Wound Healing	P0312310201	2	na	8	0	0

PDE5 in the pulmonary circulation: modulator of function in chronic hypoxia	**DN0312260101**	**2**	**2**	**8**	**0**	**0**
Hedgehog signalling in epithelial regeneration and cancer in the digestive tract	**DN0312240101**	**2**	**1**	**8**	**0**	**0**
Assessment of fluconazole-resistance of candida recovered from blood cultures at the Johns Hopkins Hospital	**P0312220101**	**2**	**na**	**8**	**0**	**0**
Roles of HHV-8 genes in viral replication	**DN0312290101** *P0312290101* *P0312290201* *P0312290301*	**2**	**na**	**8**	**0**	**0**
SARS Neutralization Assays	**P0401080101**	**3**	**na**	**Unanimous vote to hold for more information**		
DNA Vaccines for SARS	**DN0401060101**	**2**	**2**	**Unanimous vote to hold for more information**		

Johns Hopkins Institutional Biosafety Committee

JHU IBC Minutes for February 16, 2004
Room B-600, 2024 E. Monument Street Building

Members Present: Dr. Hayward, Chair; Dr. Adams, Ms. Biedrzycki, Dr. Borrello, Dr. Dahl, Ms. MacAuley, Dr. McDevitt, Dr. Norris, Dr. Rade, Dr. Scott

Members Absent: Dr. Hawley, Dr. Margolick,

Guests: None

The meeting was called to order at 3:15 PM.

The principal investigator for protocol **GT0401200401** ([redacted]) was scheduled to give a presentation, however, due to administrative error regarding the location for the meeting this will have to be rescheduled.

Dr. Norris was introduced and welcomed as a new member of the IBC.

Human Subjects Gene Transfer/Pathogen Protocols
Three protocols were reviewed by the human subjects sub-group for presentation to the IBC.

1) [redacted] **Protocol GT0402160101,** A phase I clinical trial to evaluate the safety and immunogenicity of a CTL multi-epitope peptide HIV vaccine formulated with RC529-SE, with or without GM-CSF in healthy, HIV-1 uninfected adult participants, HVTN 056, version 1.

This HIV vaccination protocol uses various peptide epitopes to elicit CTL responses. There is no recombinant DNA component in this particular protocol. Recombinant *protein* GMCSF is used. No virus, no vector, no DNA. A previous study using a different adjuvant was closed due to adjuvant reactivity. This adjuvant is supposed to take care of that issue.

A second phase will require study enrollees from above to get a plasmid expressing IL12 so, in effect, this is a two-step protocol. The second phase will require IBC approval. Although the current protocol under consideration does not require IBC review, given the nature of the second phase, the IBC decided to vote on this submission for the record.

Approval of this does not mean phase 2 gets to be approved.

The IBC moved to approve protocol GT0402160101 conditional on proof of IND submission.

For Approval: 10
Disapproval: 0
Abstain: 0

2) [redacted] **Protocol GT0402160201,** A phase I/II clinical trial to evaluate the safety and immunogenicity of LIPO-5 alone, ALVAC-HIV (vCP1452) alone, and ALVAC HIV prime/LIPO-5 boost in healthy, HIV-1 uninfected adult participants: HVTN 042/ANRS VAC19, version 1.

This is a Canary Pox vaccine derived from an attenuated strain. Canary specific—no other avians get it. Virus was passed 200 times in chick cells to attenuate. Genetically modified—wild-type B + gag + pieces of pol and nef as epitopes. E3L + K3L from vaccinia are also included.
Virulence is down 10^5 compared to vaccinia in nude mice. Greater than 600 human subjects have received a similar canary pox background.

The IBC moved to approve protocol GT0402160201 conditional on proof of IND submission:

For Approval: 10
Disapproval: 0
Abstain: 0

3. [redacted] **Protocol GT0402160301,** A phase 1/II trial of intraprostatic injection of CG7870 followed by three-dimensional conformal radiation therapy (3D-CRT) in patients with clinically localized intermediate risk prostate cancer.

This is a human gene transfer protocol that uses adenovirus to deliver the recombinant.
It will be used to treat intermediate risk prostate cancer. Treatment with radiation alone leads to side effects. The investigators are looking for some synergistic effect from the construct.
The vector/recombinant, GC7870, is a tissue specific, replication deficient adenovirus.
Virus is detectable after one month with high titer (They will use $1/10^{th}$ of the virus used)

1) Pathogen needs registration with biosafety.

2) FDA had issue with first virus. Request information regarding the previous construct.

3) Request we receive letters from the PI stipulating PPE (eye protection, gowns, and gloves) that will be used by those administering the agent.

4) Request information regarding how the investigator will modify the protocol as done in Seattle to what will be done at Johns Hopkins? Brochure, consent forms, Appendix M should be tailored to JHU. A cover letter specific to the Appendix M would be sufficient.

5) Request clarification regarding the number of patients expected in the JHU arm of the study.

The IBC moved to table the evaluation of protocol GT0402160301 pending receipt of requested documentation:

For: 10
Against: 0
Abstain: 0

Recombinant DNA/Pathogen Research Registrations

Nine research registrations were presented for IBC consideration

Institutional Biosafety Committee Registrations
February 16, 2004 Meeting
Registrations from 1/09/04 -- 2/04/04

Title	IBC#	BSL	ABSL	Yes	No	Abstain
Silent Infarct Transfusion (SIT) Clinical Trial Repository	P0402030101	1	na	10	0	0
The factors effecting endothelial barrier function	DN0402020101	2	2	10	0	0
Presence of Babesia microti in ticks in Maryland	P0402040101	2	na	10	0	0
Pharmacokinetics and pharmacodynamics of new anti-tuberculosis compounds in the mouse	P0401160101	3	2-3	Unanimous vote to hold for more information - BSL 3 SOP		
Genetic and functional programs in dendritic cells induced by infection with viruses	P0401270101	2	na	10	0	0
Genetic and functional programs in dendritic cells induced by infection with viruses	P0401270201	2	na	Unanimous vote to hold for more information - VSV transfer permit		
Genetic and functional programs in dendritic cells induced by infection with viruses	P0401270301	2	na	10	0	0
Genetic and functional programs in dendritic cells induced by infection with viruses	P0401270401	2	na	10	0	0
Rapid identification of Staphylococcus aureus	P0401160201	2	2	10	0	0

Johns Hopkins Institutional Biosafety Committee

JHU IBC Minutes for April 19, 2004
Room B-600, 2024 E. Monument Street Building

Members Present: Dr. Hayward, Chair; Dr. Adams, Ms. Biedrzycki, Dr. Borrello, Dr. Dahl, Ms. MacAuley, Dr. Margolick,

Members Absent: Dr. Hawley, Dr. McDevitt, Dr. Norris, Dr. Rade, Dr. Scott

Guests: None

The meeting was called to order at 3:45 PM.

Approval of Minutes
For clarity, it was decided that PI names would be retained on the minutes destined to be used within the IBC committee. The official public minutes would have the PI names redacted.

For Approval: 7
Disapproval: 0
Abstain: 0

OLD BUSINESS

Human Subjects Gene Transfer/Pathogen Protocols
Three protocols were reviewed by the human subjects sub-group for presentation to the IBC.

1) [redacted] **Protocol GT0311170101.** "A phase II, randomized, double-blind, placebo-controlled, parallel group, efficacy and safety study of different doses and schedules of administration of NV1FGF in patients with severe peripheral artery occlusive disease. Sponsor's protocol number NV1FGF-PM202, version 4.0, including amendment no. 1, 2 and 3, dated December 2002"

This protocol was originally approved in 2001. It has many amendments since then which is why it keeps reappearing in the IBC. There have been 2 adverse event reports that may have been product related. The protocol now excludes all patients who have had cancer. Two patients have been enrolled as of 2/18/04.

Adverse events were:
a) 73 year old man with 4mg of material had a merkle cell carcinoma most likely due to study medication (blinding code was broken to find this out).
b) Severe macular degeneration resulting in blindness due to neovascularization in the eye.

Only one was in the IRB report from her. She reported 3 adverse events from Hopkins.

1) The IBC moved to provide update copies to all members.

2) Request a letter detailing PPE used with protocol

3) Request Hopkins-specific Appendix M

The IBC moved to table protocol GT0311170101 until requested material has been reviewed:

For: 7
Against: 0
Abstain: 0

2) [redacted] **Protocol GT0402160201,** "A phase I/II clinical trial to evaluate the safety and immunogenicity of LIPO-5 alone, ALVAC-HIV (vCP1452) alone, and ALVAC HIV prime/LIPO-5 boost in healthy, HIV-1 uninfected adult participants: HVTN 042/ANRS VAC19, version 1"

This protocol is approved pending information on IND status. Vote held for requested information.

For: 7
Against: 0
Abstain: 0

3. [redacted] **Protocol GT0402160301,** "A phase I/II trial of intraprostatic injection of CG7870 followed by three-dimensional conformal radiation therapy (3D-CRT) in patients with clinically localized intermediate risk prostate cancer."

Investigator has not provided a list of associated personnel.

IBC previously requested additional information regarding the first-generation of the virus. Investigator reports that the reagent had some replication-competent adenovirus so FDA rejected the lot. Information regarding PPE was received as was a pathogen registration form.

Additional information is requested

1) Investigator should submit an amendment to the Appendix M pages 15-18 that reflects Hopkins specific information regarding patient numbers and personnel involved.

The IBC can not approve until this is received.

The IBC moved to table the evaluation of protocol GT0402160301 pending receipt of requested documentation:

For: 7
Against: 0
Abstain: 0

4. [redacted] **Protocol GT0401200401,** "Phase I study of the safety and immunogenicity of rDEN2/4 Δ 30 (ME), a live attenuated virus vaccine candidate for the prevention of dengue serotype 2"

A letter detailing the OBA's opinions on the recombinant virus detailed in this protocol was received from the investigator on April 16, 2004. The letter was electronically distributed to IBC members for review. Additional materials were also distributed electronically that Dr. [redacted] provided including "a summary of human experience with live attenuated dengue serotype 2 vaccines" and "a summary of human experience with live attenuated tick-borne encephalitis (TBE) vaccines."

Research Protocols

[redacted] **Protocol: Prion-infected Brain Tissue**

The protocol will be presented at the next IBC meeting with emphasis on the safety aspects of approving the research protocol.

Approval of Protocols on Hold

A number of protocols have been on hold from previous IBC meetings. Most required additional information from the investigators or other sources. Three protocols have been on hold waiting for a decision from CDC regarding the shipment of SARS cDNAs from overseas. A letter from the CDC regarding this question was received by the Biosafety Office stating that "Genomic material that does not encode for infectious and/or replication competent forms of an etiologic agent of human disease do not require a U.S. PHS permit." Since the cDNAs in question represented fragments of the total SARS genome, the IBC moved to release the hold and approve the applicable protocols: [redacted] DN0309300101 and [redacted] DN0401060101

For: 7
Against: 0
Abstain: 0

Lentiviral accident

Dr. Dahl discussed the lentiviral vector accident that occurred in Dr. [redacted] laboratory in March.

A post-doctoral fellow, [redacted], was aspirating media from cells previously transduced with a lentiviral vector. The glass dispo-pipette was broken after the procedure and in the course of picking up the broken pieces, the investigator suffered a cut from the broken glass. Since the pipette had previously been exposed to the potentially lentivirus-containing media, an exposure was possible.

The investigator reported to the ER and subsequently to Occupational Health where the investigator was put on a course of antiviral therapy similar to what one would undertake after a needle stick on an AIDS patient.

[redacted] was not registered with the Biosafety Office or approved by the IBC for possessing lentivirus as required by JHU policy.

Following Dr. Dahl's presentation, the IBC discussed possible responses to the incident including:
1) Request for a written report
2) Requesting the appearance of the PI at the next IBC meeting for discussion of the incident.
3) Suspension of lentivirus use by the laboratory.

The Chair stated that he would draft letters to both the investigator and the investigator's Department Chairman requesting immediate filing of required documents and suspension of any lentiviral activity in the laboratory until the matter is resolved.

Recombinant DNA/Pathogen Research Registrations
Twenty five research registrations were presented for IBC consideration:

Institutional Biosafety Committee Registrations
April 19, 2004 Meeting
Registrations from 2/05/04 – 4/07/04

Title	IBC#	BSL	ABSL	Yes	No	Abstain
March Registrations (from 2/5/04 -- 3/4/04)						
MR tracking of magnetically labelled cells	DN0402060101	2	1	7	0	0
Role of Heat Shock Proteins in Vessicle Trafficking	P0402110101	2	na	7	0	0
Dissection of Anopheles Response	P0402230101	2	1	7	0	0
Dissection of Anopheles Response	P0402230201	2	1	7	0	0
Modeling in vivo EBV gene expression	P0403010101	2	2	7	0	0
Role of oncogenes in phenotype of prostate and breast cancer	P0403020101	2	na	7	0	0
Epithelium and Chronic rhinosinusitis	P0402040101	2	na	Hold for recombinant DNA form and investigator statement that only the corona viruses listed in the protocol will be used		
Epithelium and Chronic rhinosinusitis	P0402040201	2	na	Hold for recombinant DNA form and investigator statement that only the corona viruses listed in the protocol will be used		
Efficacy of CPE in the treatment of primary breast cancer and metastasis	T0402130101	2	1	7	0	0
Isolation of genomic DNA from bacteria	P0402260101	1	na	7	0	0

Isolation of genomic DNA from bacteria	**P0402260201**	**2**	**na**	**7**	**0**	**0**
Mechanisms of signal transduction in the immune system	**DN0402160101** *P0402160101* *P0402160201* *B0402160101*	**2**	**na**	**7**	**0**	**0**
Innate immune responses to infection with Nippostrongylus brazilliensis in mus musculus	**P0402250101**	**2**	**2**	**7**	**0**	**0**

April Registrations (from 3/5/04 -- 4/7/04)

Models of neurodegeneration	**DN0403100101** *P0403100101* *B0403100101*	**2**	**na**	**7**	**0**	**0**
Cell specification in developing retina and hypothalamus	**DN0403260101** *P0403260101* *B0403260101*	**2**	**2**	**7**	**0**	**0**
Study of colonization of mice by non-pathogenic Escherichia coli	**DN0403150101** *P0403150101*	**2**	**1**	**7**	**0**	**0**
Molecular Analysis of Pediatric Brain Tumors	**DN0403070101** *P0403070101*	**2**	**na**	**7**	**0**	**0**
Analysis of Plasmodium development in the mosquito	**P0404070101**	**2**	**2**	**7**	**0**	**0**
Genetic alterations in pancreatic cancer	**P0403230101**	**2**	**na**	**7**	**0**	**0**
Genetic alterations in pancreatic cancer	**P0403230201**	**2**	**na**	**7**	**0**	**0**
Functional analysis of CFTR	**P0403290101**	**1**	**na**	**7**	**0**	**0**

Molecular Biology and Frog Transgenesis	**DN0403120101**	**1**	**1**	**7**	**0**	**0**
Safety and efficacy of a topical retroviral vector bearing a mutant cyclin G1 gene for the prevention...	**DN0404050101** *P0404050101*	**2**	**2**	**7**	**0**	**0**
Role of HuR in allergic inflammation	**P0404060101**	**2**	**2**	**7**	**0**	**0**
Activation of brain endothelium by HIV and entry into brain	**P0403240101**	**2**	**na**	**7**	**0**	**0**

Johns Hopkins Institutional Biosafety Committee

JHU IBC Minutes for May 17, 2004
Room B-600, 2024 E. Monument Street Building

Members Present:	Gary Hayward, Chair; Robert Adams, Barbara Biedrzycki, Stephen Dahl, Claudia MacAuley, Djikolgnar Maouyo, Michael McDevitt, Alan Scott
Members Absent:	Ivan Borrello, Joseph Margolick, Douglas Norris, Jeffrey Rade,
Guests:	John Schaefer, Associate Director Health, Safety and Environment

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The meeting was called to order at 3:15

Special Presentation, Hazardous Waste Disposal

Mr. Schaefer was introduced as an invited speaker who would present a brief summary of Hazardous Waste disposal on campus.

Potentially biohazardous waste on campus is termed special medical waste which constitutes waste from humans or animals that is considered "potentially infectious". Anything from a laboratory that is not chem waste or rad waste is handles as special medical waste. Originally the material was incinerated in Ross. No longer. Now that incinerator is used to burn multiple half-decayed (cold) rad and animal carcases. JHU uses Stericycle. JHH uses Phoenix. Both are DOT certified and trained in handling hazardous and spilled materials. State of Maryland requires incinerated and sterilized and then rendered non-recognizable.

An IBC member asked to confirm that the material is incinerated. The member also noted that waste can be specified incinerate only if so desired. For example, if a company's incinerator were experiencing downtime, the company might just autoclave. For prion work, the waste should be marked "incinerate only".

[redacted]

An IBC member asked if the ABSL3 material could be incinerated on campus. The IBC was told that the rate limiting step is how much material can be fed per minute into the Ross incinerator. The incinerator was just recertified so it is up and running. The incinerator is supervised by Radiation Safety and they would be the ones to consult if such incineration were requested.

With no further questions for the speaker, the IBC Chair thanked Mr. Schaefer for the presentation and Mr. Schaefer excused himself from the meeting.

Approval of Minutes
The minutes for the February 20 IBC meeting were approved.

For:	8
Against:	0
Abstain:	0

Human Subjects Gene Transfer/Pathogen Protocols
Four protocols were reviewed by the human subjects sub-group for presentation to the IBC, four of which ([redacted]-GT0401200401, [redacted]-GT0402160101, [redacted]-GT0402160301, and [redacted]-GT0302250201) were follow-ups.

1) [redacted] **Protocol, GT0405170101,**

This is a Phase I study of an HIV vaccine. The investigator would like to participate in Part B of the study. The study involves 10 patients (healthy, uninfected volunteers) who will receive IM HIV vaccine at 0, 3, and 9 months injected into the deltoid muscle. Two plasmids (up to 1000ug) will be injected that express the HIV-1 gag and HIV-1 env genes. The patients will be boosted with GP140 protein (up to 100ug). Appendix M is not needed because they are testing for immune response.

The IBC moved to approve GT0405170101 upon receipt of IND documentation and copies of IRB comments.

For Approval:	7
Disapproval:	0
Abstain:	1

2) **Follow-up for** [redacted] **protocols GT0401200401,** Phase I study of the safety and immunogenicity of rDEN2/4 Δ 30 (ME), a live attenuated virus vaccine candidate for the prevention of dengue serotype 2 **and GT0402160101,** Langat/Dengue 4 Chimera Virus (LGT(TP21)/DEN4), Live Attenuated Vaccine for Tick-Borne Encephalitis

A letter addressed to Dr. Thomas Shih of the NIH RAC was sent by Dr. Hayward requesting guidance on the RAC review for the protocols. No answer has been received to date.

3) **Follow-up for** [redacted] **protocol GT0402160301,** A phase I/II trial of intraprostatic injection of CG7870 followed by three-dimensional conformal radiation therapy (3D-CRT) in patients with clinically localized intermediate risk prostate cancer.

Approval had been held for this protocol pending receipt of Hopkins-specific Appendix M information. The information provided by the investigator was discussed and found to be satisfactory.

The IBC then moved to vote on protocol GT0402160301:

For Approval: 7
Disapproval: 0
Abstain: 1

4) **Follow-up for [redacted] protocol GT0302250201,** "Phase II, Multi—Center Single Arm Evaluation of Preoperative Chemoradiation Plus TNFerade®. Biologic (ADGVEGR.TNF.11D) Prior to Esophagectomy for Locally Advanced Resectable Esophageal Cancer"

This protocol was approved by the IBC at the February 25, 2003 Meeting. The investigator has filed an amendment that includes a requested increase in maximum dose from $4x10^{10}$ to $4x10^{11}$ particle units.

The increased dosage was discussed and determined to be reasonable in comparison to other studies.

The IBC then moved to vote on the amendment to protocol GT0302250201:

For Approval: 8
Disapproval: 0
Abstain: 0

Old Business

Prion Protocol of Dr. [redacted]:

The IBC discussed the potential biohazard issues associated with this protocol. Specifically, the difficult nature of prion decontamination was discussed. It was decided that the investigator should register the project with a Pathogen Registration form and that the investigator or a representative should appear before the IBC to discuss the research and answer questions. The potential for the investigator to use an outside facility such as the prion research labs at the University of Maryland was also raised.

March Lentiviral Vector Incident:

Written responses and registrations were received from the investigator and chair. The potential that other members in this group were also using the vector withour proper JHU registration was discussed and it was decided the Biosafety Officer would investigate.

New Business

Animal Services ABSL2 Request
Dr. Dahl reported that a request had been received from the Animal Services group regarding the ABSL ratings of animal rooms. Animal Services was asking if projects involving replication-defective viral vectors such as the popular adenoviral and lentiviral agents could be step-rated. In other words, be assigned ABSL2 for the first few weeks and then step down to ABSL1. It was noted that the Animal Services Group essentially works at ABSL2 practices including gowns, masks and gloves. The main deficiency associated with ABSL2 rating of animal space has been the requirement for a hand washing sink located within the room as described in the BMBL.

The IBC discussed the request and noted that viral revertants were always a possibility. It was stated that the presence of a sink was always preferable. It was also noted, however, that sinks are available nearby--outside specific animal rooms, but still within the animal facilities. The IBC decided that rather than a step-rated system, a better solution would be to allow for the use of hand sanitizing stations in animal rooms that lacked sinks with the understanding that personnel would then procede directly to a sink for further cleansing.

The IBC then moved to vote on the use of hand sanitizing stations in animal rooms that lacked plumbed sinks:

For Approval: 8
Disapproval: 0
Abstain: 0

Bag-in/Bag-out Survey and Maintenance Program:
Dr. Dahl reported that he had been working with Mr. Joseph Zolenas of School of Medicine (SOM) facilites to inspect the Bag-in/Bag-out filters owned by SOM and devise a maintenance plan that enlisted the services of the Biosafety Cabinet Certification Team that works with the Biosafety Office

IBC Roster List
Dr. Dahl passed out a copy of the current IBC Roster list and asked for corrections in title, spelling, address or other contact information.

Recombinant DNA/Pathogen Research Registrations
12 research registrations were presented for IBC consideration. 8 were approved, 4 were held for further information (see attached list).

The meeting was adjourned at 5:30

Institutional Biosafety Committee Registrations
May 17, 2004 Meeting
Registrations from 4/8/04 -- 5/3/04

Title	IBC#	BSL	ABSL	Yes	No	Abstain
Development of novel therapeutic methods for cancer in mouse models Genes coloned into plasmid vectors will be expressed in cell culture or in mice. DN--Uses recombinant DNA directly in mice or transfected into cells that are transplanted into mice *Supporting Document-Human Tissue Registration--Research*	DN0404260101 *B0404260101*	2	1	7	0	0
Microarray Analysis of the action of B-sulfonylacetamides on M. tuberculosis	P0404140101	3	na	Hold for BSL3 SOP		

M. tb will be extracted for RNA and subsequent microarray analysis *Pathogen registration for Mycobacterium tuberculosis*						
Validation of methods for the identification of [redacted] Strains of [redacted] will be used to evaluate and validate identification assay systems *Pathogen registration for [redacted]*	**P0404140201**	**3**	**na**	**Hold for more information**		
Glycoconjugates in Development and Immunity Adenovirus will be used to express O-GlcNAcase in mammalian cell lines *Pathogen registration for Adenoviral vectors*	**P0404120101**	**2**	**na**	**7**	**0**	**0**
Modeling in vivo EBV gene expression Lentiviral vectors will be used to study EBV promotor sequences *Pathogen registration for Lentiviral vectors*	**P0404190101**	**2**	**2**	**6**	**0**	**1**
Role of HuR in allergic inflammation Adenoviral vectors will be used to transduce mice with the RNA binding factor HuR *Pathogen registration for Adenoviral vectors*	**P0405030101**	**2**	**2**	**7**	**0**	**0**
Effect of [redacted] on signal transduction in endothelial cells [redacted] will be used to study effects on endothelial cells *Toxin registration for [redacted]*	**T0404080101**	**2**	**na**	**Hold for Policy letter**		
Transgenic analysis of disease gene regulation Regulatory sequences will be cloned and expressed in cell lines and mice to make transgenics DN--Uses plasmid-based recombinant DNA transfected in cell lines and mice	**DN0405040101**	**2**	**1**	**7**	**0**	**0**
Network vasomotor response to tissue adenosine [redacted] will be used to block/inactivate K-ATP channels in hamsters *Toxin registration for [redacted]*	**T0404280101**	**2**	**1**	**Hold for Policy letter**		
Lyn Kinase Regulation of Allergic Inflammation Upgrade of DE0112190102 registration to add viral vector DN--Uses recombinant DNA and MMLV *Supporting Document-Pathogen registration for MMLV*	**DN0112190102** *P0404200101*	**2**	**na**	**7**	**0**	**0**
Lyn Kinase Regulation of Allergic Inflammation Moloney Murine Leukemia Virus will be used to transduce cell lines *Pathogen registration for Moloney Murine Leukemia viral vector to support upgraded protocol DN0112190102*	**P0404200101**	**2**	**2**	**7**	**0**	**0**

The biology of organ-specific metastasis from renal cell carcinoma, breast carcinoma, and osteosarcoma **Growth factor receptors will be transfected into carcinoma cell lines and transplanted into nude mice.** **DN--Uses recombinant DNA transfected into cells that are transplanted into mice**	**DN0404210101**	**2**	**1**	**7**	**0**	**0**
Supporting Document-Human Tissue Registration--Research	*B0404210101*					

Johns Hopkins Institutional Biosafety Committee

JHU IBC Minutes for June 21, 2004
Room B-600, 2024 E. Monument Street Building

Members Present: Dr. Hayward, Chair; Dr. Adams, Ms. Biedrzycki, Dr. Dahl, Ms. MacAuley, Dr. Maouyo, Dr. McDevitt, Dr. Norris, Dr. Rade, Dr. Scott

Members Absent: Dr. Borrello, Dr. Margolick,

Guests: Dr. [redacted]

The meeting was called to order at 3:20 upon the arrival of Dr. [redacted].

Special Presentation, Prion Project

Dr. [redacted] was introduced as an invited speaker who is a collaborator with the [redacted] laboratory that has submitted the prion project.

Dr. [redacted] gave a basic background on prion-based disease noting that they are thought to be transferred human to human and animal to human though human to human tissue transmission has not been rigorously proven.

The laboratory wants to conduct experiments with tissues derived from Creutzfeld/Jakob (CJD) afflicted patients. The laboratory they intend to use is rated at BSL2, however, there is a BSL3 laboratory available to them. Dr. [redacted] admits that there may be reluctance to work in a laboratory handling prion-infected tissues and this may limit their ability to obtain permission to work in another investigator's BSL3 facility. A BSL3 facility on Meyer 6 was one option which is managed by [redacted].

An IBC member noted that decontamination would require autoclaving at 134° C. for 1 hour, but confirmed that CJD is a BSL2 agent.

It was suggested the investigators would need CJD dedicated incubators, bench space, and Biosafety Cabinet noting that decontamination of this cabinet would be very problematic and could require the entire unit be autoclaved.

It was also suggested that the investigators look into collaborating with the University of Maryland Prion Group.

With no further questions or comments for the speaker, the IBC Chair thanked Dr. [redacted] for the presentation and Dr. [redacted] excused himself from the meeting.

Approval of Minutes
The minutes for the April 19, 2004 IBC meeting were approved.

For: 10
Against: 0
Abstain: 0

Human Subjects Gene Transfer/Pathogen Protocols
Three protocols were reviewed by the human subjects sub-group for presentation to the IBC, one of which ([redacted] GT0311170101) was a follow-up.

1) [redacted] **Protocol, GT0406210101,** A Phase III Randomized, Open-label Study of CG1940 and CG8711 Versus Docetaxel and Prednisone in Patients with Metastatic Hormone-refractory Prostate Cancer who are Chemotherapy-naïve (CGI G-0029)

The investigator intends to use adeno-associated virus expressing GM-CSF as an allogeneic vaccine for prostate cancer.

It was noted that this project is similar to others the IBC has approved but uses an adeno-associated viral vector whereas others have used adenoviral vectors. The project documentation was found to be complete except that the Appendix M lacked Hopkins-specific information. The IBC moved to approve the protocol pending receipt of Hopkins-specific Appendix M information.

The IBC moved to approve GT0406210101 upon receipt of Hopkins-specific Appendix M information.

For Approval: 9
Disapproval: 0
Abstain: 1

2) [redacted] **protocol GT0406210201,** An Open-label Phase One Study of the Safety and Immunogenicity of Repeated Vaccination with NGVL4a-HPV16Sig/E7(detox)/HSP70 in Patients with Stage III or IV HPV 16-positive Head and Neck Squamous Cell Carcinoma (HNSCC)

The investigator intends to inject patients with plasmid DNA designed to express the tumor specific antigen HPV16 E7. The induction of immune response will be evaluated.

The IBC found the extensive and thorough documentation to be in order and moved to approve pending receipt of RAC approval.

For Approval: 10
Disapproval: 0
Abstain: 0

3) **Follow-up for** [redacted] **protocol GT0311170101,** A phase II, randomized, double-blind, placebo-controlled, parallel group, efficacy and safety study of different doses and schedules of administration of

NV1FGF in patients with severe peripheral artery occlusive disease. Sponsor's protocol number NV1FGF-PM202, version 4.0, including amendment no. 1, 2 and 3, dated December 2002

It was noted that the IBC had received the requested information from this investigator, but, as is often the case, the Appendix M lacked Hopkins-specific information. The IBC moved to approve the protocol pending receipt of Hopkins-specific Appendix M information. In addition, the investigator should be reminded to report all significant adverse events to the IBC.

The IBC then moved to approve GT upon receipt of Hopkins-specific Appendix M information:

For Approval: 9
Disapproval: 0
Abstain: 1

Old Business

[redacted] **Protocols GT0401200401** (rDEN2/4 Δ 30) **and GT0402160101** (Langat/Dengue 4)**:**

The IBC discussed plans for external review of these protocols. The RAC refused to review given the "vaccine" status of the protocols. The RAC letter did suggest external reviewers if the IBC wished to do so. The IBC decided to have Dr. Norris contact the outside reviewers and that Dr. Hayward would give the investigator the right of refusal if some of the reviewers were deemed objectionable.

March Lentiviral Vector Incident:

Additional registrations were received from the investigator. A copy of the "self-report" requested from the post-doc by the Biosafety Officer was supplied to the IBC. There was discussion and a difference of opinion regarding whether the nature of the incident constituted a "reportable event".

New Business

Animal work in Church Home Building-comments?
Dr. Dahl reported that an inquiry had been received regarding the handling of animal tissues in the Church Home building. Dr. Dahl noted that the building currently houses the Hopkins Daycare on the first and second floors and JHMI Human Resources and JHI Occupational Health on the third floor. The investigator is scheduled to be housed on the third floor and will only perform necropsy on previously healthy animals. Dr. Dahl also noted that the current assessment by HSE suggested that extensive renovation would be required to improve air handling from partial recirculation to 100% exhaust and that HSE was opposed to the plan. Dr. Dahl invited comments from IBC members and suggested emailed comments would be forwarded to the Associate Director of HSE.

Recombinant DNA/Pathogen Research Registrations
18 research registrations were presented for IBC consideration. 12 were approved unanimously, 6 were held for further information (see attached list).

The meeting was adjourned at 5:30

Institutional Biosafety Committee Registrations
June 21, 2004 Meeting
Registrations from 5/4/04 – 6/9/04

Title	IBC#	BSL	ABSL	Yes	No	Abstain
Nude Mouse Studies to Assess Tumorogenicity of Differentiated Tumors Adenovirus will be used to transduce cells *Pathogen registration for Adenoviral vectors*	**P0405240101**	**2**	**na**	**10**	**0**	**0**
Critical role of Nrf2 in the protection of lungs against oxidative stress Adenoviral and Lentiviral vectors will be used to transduce cells and mice DN--Uses recombinant DNA and viral vectors in mice *Supporting Document - Pathogen registration for Adenoviral vectors* *Supporting Document - Pathogen registration for Lentiviral vectors*	**DN0406090201** *P0405180101* *P0405180201*	**2**	**2**	**10**	**0**	**0**
Regulation of interferon response genes in HIV infected macrophages Moloney Murine Leukemia Viral vectors will be used to transduce cultured cells *Pathogen registration for MoMLV*	**P0405250101**	**2**	**na**	**10**	**0**	**0**
Molecular Physiology of Ion Channels Ion channels will be cloned and mutagenized for expression studies through transfection or transduction of cells DN--Uses cells or guinea pigs transduced or transfected to express recombinant DNA	**DN0405190101**	**2**	**2**	**Hold for SA policy letter**		
Molecular Physiology of Ion Channels [redacted] will be used to study ion channels *Toxin registration for* [redacted]	**T0405190101**	**2**	**2**	**Hold for SA policy letter**		
Molecular Physiology of Ion Channels [redacted] will be used to study ion channels *Toxin registration for* [redacted]	**T0405190201**	**2**	**2**	**Hold for SA policy letter**		

Molecular Physiology of Ion Channels [redacted] will be used to study ion channels *Toxin registration for* [redacted]	**T0405190301**	**2**	**2**	**Hold for SA policy letter**		
Regulation of NOS2 Adenoviral vectors will be used to transduce cells *Pathogen registration for Adenoviral vectors*	**P0405200101**	**2**	**na**	**Hold for SA policy letter from last month**		
Functional analysis of stem cell transplantation and ion channels by somatic gene transfer Viral vectors will be used to generate genetically-modified stem cells which will then be used for in vivo transplantation studies **DN**--Uses cells transduced or transfected to express recombinant DNA that are then transplanted into animals *Supporting Document - Pathogen registration for Lentiviral vectors*	**DN0405120101** *P0405120101*	**2**	**2**	**10**	**0**	**0**
Analysis of the in vivo growth characteristics of genes identified by SAGE transcriptional profiling in medulloblastoma Brain tumor cells will be transduced with retrovirus vectors (MoMLV) or transfected with plasmids and introduced into mice. **DN**--Uses cells transduced or transfected to express recombinant DNA that are then transplanted into mice *Supporting Document-Pathogen registration for MoMLV*	**DN0405140101** *P0405260101*	**2**	**2**	**10**	**0**	**0**
Functional analysis of brain cancer associated genes Cell lines will be transduced with retroviral vector MoMLV **DN**--Uses cells transduced with retrovirus *Supporting Document-Pathogen registration for MoMLV*	**DN0405140201** *P0405260101*	**2**	**na**	**10**	**0**	**0**
Immunotoxic effects of mercury compounds Plasmodium yoelii will be used to liver stage malaria disease and the effects of mercury treatment on the disease. *Pathogen registration for Plasmodium yoelii*	**P0405100101**	**2**	**2**	**10**	**0**	**0**

Immunotoxic effects of mercury compounds The effects of mercury will be tested on mice infected with Coxsackie virus B3 *Pathogen registration for Coxsackie virus*	**P0405110201**	**2**	**2**	**10**	**0**	**0**
Immune based therapies Hematopoietic stem cells will be transduced to express genes to study immune response **DN--Uses cells transduced with viral vectors and transplanted into mice** *Supporting Document - Pathogen registration for Lentiviral vectors* *Supporting Document - Pathogen registration for vaccinia vectors* *Supporting Document - Human Tissue Registration--Laboratory*	**DN0405270101** *P0405270101* *P0405270201* *B0405270101*	**2**	**2**	**Hold for Vaccinia policy letter**		

Previously Held Protocols, Now Complete

Epithelium and Chronic rhinosinusitis Human rhinovirus will be used to study inflammatory response in cultured cells. *Pathogen registration for Rhinovirus*	**P0402040101**	**2**	**na**	**10**	**0**	**0**
Epithelium and Chronic rhinosinusitis Human corona virus will be used to study inflammatory response in cultured cells. *Pathogen registration for Corona virus*	**P0402040201**	**2**	**na**	**10**	**0**	**0**
Genetic alterations in pancreatic cancer Adenoviral vectors will be used to transduce cells *Pathogen registration for adenoviral vectors*	**P0403230101**	**2**	**na**	**10**	**0**	**0**
Genetic alterations in pancreatic cancer MMLV retroviral vectors will be used to transduce cells *Pathogen registration for MMLV retroviral vectors*	**P0403230201**	**2**	**na**	**10**	**0**	**0**

Johns Hopkins Institutional Biosafety Committee

JHU IBC Minutes for July 19, 2004
Room B-600, 2024 E. Monument Street Building

Members Present: Dr. Hayward, Chair; Dr. Adams, Ms. Biedrzycki, Dr. Dahl, Ms. MacAuley, Dr. Margolick, Dr. Norris, Dr. Pan, Dr. Rade,

Members Absent: Dr. Borrello, Dr. Maouyo, Dr. McDevitt, Dr. Scott

Guests: None

The meeting was called to order at 3:15.

Human Subjects Gene Transfer/Pathogen Protocols
Six protocols were presented to the IBC, four of which ([redacted] GT0401200401 and GT0402160101, [redacted] GT0311170101, and [redacted] GT0406210201) were follow-ups.

1) [redacted] **Protocols GT0407190101** (rDEN1delta30), **GT0401200401** (rDEN2/4 Δ 30) **and GT0402160101** (Langat/Dengue 4):

The IBC approved unanimously protocol **GT0407190101**.

The IBC then reviewed the current state of the decision:

a) Original RAC review was for Δ 30 only. The IBC requested reconsideration of rDEN2/4 Δ 30 and Langat/Dengue 4.
b) There is a lack of quantitative data in the proposals as they now stand. Issues to consider include whether the recombinants will be more transmissible in humans than they have been in cell culture studies.
c) Data exists suggesting that new serotypes of Dengue fever that lead to hemorrhagic fever in those with partial immunity may be more pathogenic in south Asians due to prior exposure to other strains. Will WHO approve this protocol's approach?
d) If patients are con-infected with live virus Δ 30 could be spliced right out of the recombinant virus.
e) It is important to determine from external reviewers if the investigators involved with this protocol are taking the precautions necessary to ensure a safe trial.
f) It is important to note that mosquitos populations of concern are present in the Baltimore area until the first freeze.

2) **Follow-up for** [redacted] **protocol GT0311170101,** A phase II, randomized, double-blind, placebo-controlled, parallel group, efficacy and safety study of different doses and schedules of administration of NV1FGF in patients with severe peripheral artery occlusive disease. Sponsor's protocol number NV1FGF-PM202, version 4.0, including amendment no. 1, 2 and 3, dated December 2002

It was noted that the IBC's request for a Hopkins-specific Appendix M had yet to be fulfilled. Thus, due to the conditional approval given at last month's IBC meeting, the protocol continues to stand as unapproved until receipt of this document.

3) [redacted] **protocol GT0406210201,** An Open-label Phase One Study of the Safety and Immunogenicity of Repeated Vaccination with NGVL4a-HPV16Sig/E7(detox)/HSP70 in Patients with Stage III or IV HPV 16-positive Head and Neck Squamous Cell Carcinoma (HNSCC)

The IBC received the RAC response letter for this protocol and an IND approval letter from the FDA. The FDA noted the presence of the β-lactamase Amp R element in the plasmid submitted for review and recommended that the sequence be removed, especially if a protein product is expressed from the open reading frame. It was noted that the FDA did not require removal, however, and stated that the "study may proceed".

The IBC then moved to approve protocol GT0406210201:

For Approval: 9
Disapproval: 0
Abstain: 0

4) [redacted] **protocol GT04071900201,** A Phase I/II Dose Escalation Trial of Intravenous CG7870 I Combination with Docetaxel in Chemotherapy-Naïve Patients with Metastatic Hormone-Refractory Prostate Cancer

Request IRB comments
Submit Hopkins-specific Appendix M

5) [redacted] **protocol GT0401200202,** A phase II, multi-center, single arm evaluation of preoperative chemoradiation plus TNFerade biologic prior to esophagectomy for locally advanced respectable esophageal cancer, Amendment 2
This is an amendment that requests a 10-fold maximum dose increase from $4x10^{10}$ to $4x10^{11}$ particle units.
The IBC moved to approve protocol GT0401200202:

For Approval: 9
Disapproval: 0
Abstain: 0

Recombinant DNA/Pathogen Research Registrations
10 research registrations were presented for IBC consideration. All were approved unanimously (see attached list).

The meeting was adjourned at 5:15

Institutional Biosafety Committee Registrations
July 19, 2004 Meeting
Registrations from 6/9/04 -- 6/30/04

Title	IBC#	BSL	ABSL	Yes	No	Abstain
Mast Cells Signalling MMLV based retroviral vectors will be used to transduce cells with sphingosine kinase constructs. Transduced cells may be transferred to animals. DN--Uses recombinant DNA and viral vectors in mice *Supporting Document-Pathogen registration for MoMLV* *Supporting Document - Human Tissue Registration--Laboratory*	**DN0406100101** *P0406100201* *B0406100101*	**2**	**2**	**9**	**0**	**0**
[redacted]-induced model of advanced dry eye disease (keratoconjunctivitis sicca) [redacted] will be used in the eyes of mice *Toxin registration for* [redacted]	**T0406230101**	**2**	**1**	**9**	**0**	**0**
Lentivirus-mediated gene transfer in Parkinson's Disease research Lentiviral vectors will be used to transduce cell cultures and animals *Pathogen registration for Lentivirus*	**P0406170101**	**2**	**2**	**9**	**0**	**0**
Analysis of Anopheles responses to Plasmodium infection Plasmodium falciparum will be cultured and used in studies that include mosquito infection *Pathogen registration for Plasmodium falciparum*	**P0406100101**	**2**	**2**	**9**	**0**	**0**
Molecular pathogenesis of PKD Adenoviral vectors will be used to transduce cells in culture *Pathogen registration for Adenovirus*	**P0406280101**	**2**	**NA**	**9**	**0**	**0**
Metabolite regulation of the Insulin receptor Insulin growth factor receptors and ligands will be studied in Drosophila DN--Uses recombinant DNA in animals	**DN0406150101**	**1**	**1**	**9**	**0**	**0**
Microtubules in lung endothelial cell barrier regulation	**DN0406100201**	**2**	**NA**	**9**	**0**	**0**

Protein phosphatase 2A will be expressed in cells with adenoviral vectors DN--Uses recombinant DNA and viral vectors in cultured cells						
Establishment of a real time pcr for the detection of HHV6 HHV will be ordered from ATCC to extract DNA as a control *Pathogen registration for Human Herpes Virus 6*	**P0406300101**	**2**	**NA**	**9**	**0**	**0**
Microarray analysis of M. smegmatis genes in response to tuberculosis drug pyrazinamide M. smegmatis will be processed for microarray analysis *Pathogen registration for M. smegmatis*	**P0406110101**	**2**	**NA**	**9**	**0**	**0**
Response of H. pylori to weak acids H. pylori will be processed for microarray analysis following laboratory manipulation *Pathogen registration for H. pylori*	**P0406110201**	**2**	**NA**	**9**	**0**	**0**

Johns Hopkins Institutional Biosafety Committee

JHU IBC Minutes for August 16, 2004
Room B-600, 2024 E. Monument Street Building

Members Present: Dr. Hayward, Chair; Dr. Adams, Ms. Biedrzycki, Dr. Borrello, Dr. Dahl, Ms. MacAuley, Dr. Maouyo, Dr. Norris, Dr. Pan, Dr. Scott

Members Absent: Dr. McDevitt, Dr. Margolick, Dr. Rade,

Guests: None

The meeting was called to order at 3:17.

Human Subjects Gene Transfer/Pathogen Protocols
Three protocols were presented to the IBC, two ([redacted] GT0401200401 and GT0402160101) were follow-ups and one ([redacted] GT0408160101) is new.

1) [redacted] **Protocols GT0401200401** (rDEN2/4 Δ 30) **and GT0402160101** (Langat/Dengue 4)**:**

The IBC reviewed the history of the protocols, outside reviewer comments and considered the final decision:

a) The protocols involve the use of a live, recombinant virus to elicit an immune response.
b) The investigator expects no transmissibility issues due to attenuation of the recombinant virus stocks. Mosquito studies submitted by the investigator also suggest a low chance of transmission.
c) Mosquito populations of concern are present in the Baltimore area until the first freeze.
d) The viral agents in question have not been tested in humans.
e) The RAC accepted the vaccine exemption for the viral agents and declined to review.
f) The IBC questioned this decision to no avail, though the RAC did provide a list of experts that could be consulted for additional opinions.
g) The opinions of outside reviewers were solicited and their responses provided to the IBC. In general, the outside reviewers expected no problems, but recommended erring on the side of caution.

The IBC discussed additional points:

-- Dr. Hayward noted that the investigator previously discussed conducting trials of a previous construct between October and April. Also, in a paper discussing Langat constructs, the investigator has previously stated concern about its effects on the environment.

-- The fact that the mosquito studies were not performed in a blood-feeder mosquito was also noted by the IBC. It was also mentioned that the viremia plaque assays proposed require 3-4 days for interpretation.

-- The IBC noted that Fall is almost upon us. It was suggested that the first four patients should be done in house. The [redacted] protocol on the docket for today's meeting notes the existence of an inpatient facility available to the BSPH at Bayview.

-- The FDA has expressed concerns about the Vero cells used to generate the viral stocks and the use of bovine serum due to BSE concerns, but has not made any comments about the viral agents.

-- Hospitalization of the first few patients for titer assays followed by outpatient studies if all is ok seems reasonable.

-- The IBC should request that tick studies and studies with the correct species of mosquitos should be performed.

The IBC moved to vote to consider the final disposition of protocols GT0401200401 (rDEN2/4 Δ 30) and GT0402160101 (Langat/Dengue 4):

For Considering Approval: 10
Against Considering Approval: 0
Abstain: 0

Following this vote the IBC moved to vote on approval of the protocols as submitted:

For Approval: 0
Disapproval: 10
Abstain: 0

The IBC further discussed the protocols:

-- The mosquito we are most concerned about is the most frequent in the area

-- If patients were shown to have no viremia or if there is no mosquito transmission demonstrated in Aedis...then we'd probably be ok without seasonal or in-patient restrictions.

-- Nowhere does it say in the protocol that patient viremia is a reason for stopping the study.

-- If the protocol was restricted between October and April, could it go without the in-patient work?

OPTIONS DISCUSSED:

A) **First 4 in-house then no restrictions if no viremia observed**: First 4 patients in-house. Test viremia and report results to IBC. If no viremia, then study is ok to proceed. If viremia is seen, then the study may not commence until after first frost and must end at first mosquito or the study may be done entirely in-house. This would restrict to the months of November, December, January, February, and March. Viremia would be defined as 10^3/ml in serum in any one patient--not average. Evidence of viremia would trigger mandatory in-house study.

B) **First 4 in-house then seasonal restrictions if no viremia observed:** First 4 patients in-house. Test viremia and report results to IBC. If no viremia, then study is ok to proceed, but may not commence until

after first frost and must end at first mosquito. This would restrict to the months of November, December, January, February, and March or the study may be done entirely in-house. Viremia would be defined as 10^3/ml in serum in any one patient--not average. Evidence of viremia would trigger mandatory in-house study.

The IBC moved to vote on option "B" above

For Approval: 10
Disapproval: 0
Abstain: 0

It was decided the letter to the investigator would include the following:

1) Acknowledgement that this changes the study and will require additional communication with the IRB.
2) Study may be performed in-house at any time. Otherwise, first 4 patients in-house and all others seasonal.
3) Any patient that shows viremia equal or greater than 10^3 must be immediately reported to the IBC and this will trigger additional consideration of further outpatient studies.
4) A history of low viremia titers may result in relaxation of study terms.

---------End of Discussion regarding **Protocols GT0401200401** (rDEN2/4 Δ 30) **and GT0402160101**------

2) [redacted] **protocol GT0408160101,** Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety, Immunogenicity, and Protective Efficacy of Transcutaneous Immunization with Heat-Labile Enterotoxin of Escherichia coli to Reduce the Severity of Symptoms During Oral Challenge with E. coli E24377A

Transcutaneous exposure to E. coli toxin protein via a patch. The patients will then be challenged in-patient with virulent E. coli to assess efficacy of patch-based immunization. Investigator indicated that the patients must have 2 clear stool samples before being released from in-patient care.

The IBC stressed that it is important for the patients to complete their full regimen of antibiotics.

The IBC then moved to approve protocol GT0408160101:

For Approval: 9
Disapproval: 0
Abstain: 1

Recombinant DNA/Pathogen Research Registrations
9 research registrations were presented for IBC consideration. 8 were approved and one was held for additional information (see attached list).

The protocol held was the [redacted] protocol, **P0407230201,** which details the use of methicillin-resistant Staph. aureus. Concerns were raised about the proximity of the research area to hospital areas. The decision

was made to request additional information about the experiments proposed and inquire as to whether the animal component could be relocated to the Ross Building.

The meeting was adjourned at 5:30

Institutional Biosafety Committee Registrations
August 16, 2004 Meeting
Registrations from 7/9/04 – 8/2/04

Title	IBC#	BSL	ABSL	Yes	No	Abstain
Therapy of Breast Cancer; Hormone Resistance of Breast Cancer	**DN0408100101**	**2**	**2**	**10**	**0**	**0**
DNA methyltransferase (DNMT) will be transfected into MCF-7 breast cancer cells and transplanted into nude mice.						
DN--Uses recombinant DNA transfected into cells that are transplanted into mice						
Supporting Document - Human Tissue Registration--Laboratory	B0407300201					
Methods of gene expression in Hematopoietic Cells	**P0407130101**	**2**	**2**	**10**	**0**	**0**
MMLV based retroviral vectors will be used to transduce genes in cells and animals						
Pathogen registration for retrovirus (MMLV)						
Methods of gene expression in Hematopoietic Cells	**P0407130201**	**2**	**2**	**10**	**0**	**0**
Lentiviral vectors will be used to transduce genes in cells and animals						
Pathogen registration for lentivirus						
Methods of gene expression in Hematopoietic Cells	**P0407130301**	**2**	**2**	**10**	**0**	**0**
MSCV based retroviral vectors will be used to transduce genes in cells and animals						
Pathogen registration for retrovirus (MSCV)						
NF-kB function in the central nervous system	**DN0408020101**	**2**	**NA**	**10**	**0**	**0**
HIV-based lentiviral vectors will be used to transduce genes that encode signaling proteins in tissue cultured cells						
DN--Uses recombinant DNA and viral vectors in cultured cells						

Supporting Document-Pathogen registration for HIV-based lentiviruses	P0408020101					
Supporting Document-Pathogen registration for retroviruses	P0408020102					
Supporting Document - Human Tissue Registration--Laboratory	B0408020101					
Molecular genetics of Borrelia burgdorferi sensu stricto in rodent and tick populations in Maryland	**P0407210101**	**2**	**NA**	**9**	**0**	**1**
Borrelia afzelii will be obtained from CDC to extract DNA as a positive control						
Pathogen registration for Borrelia afzelii						
Cell Based Therapies in Mouse models of Parkinson's Disease	**DN0407270101**	**2**	**2**	**10**	**0**	**0**
Adenoviral and retroviral vectors will be used to transduce cell cultures and animals						
DN--Uses recombinant DNA and viral vectors in cultured cells and animals						
Supporting Document-Pathogen registration for retrovirus	P0407270101					
Supporting Document-Pathogen registration for adenovirus	P0407270201					
Supporting Document - Human Tissue Registration--Laboratory	B0407090101					
Comparative Activity of Mupifocin,moxifloxacin, and ciprofloxacin against genetically defined high level fluoroquinolone-resistant methicillin-resistant Staphylococcus aureus in rabbits model	**P0407230201**	**2**	**2**	**Hold for more information regarding animal housing and agent culture techniques and protocols**		
Staphylococcus aureus will be injected into the right eye of rabbit						
Pathogen registration for fluoroquinolone-resistant methicillin-resistant Staphylococcus aureus						
Use of primary cells to evaluate genetically encoded indicators	**P0407230101**	**2**	**NA**	**10**	**0**	**0**
Lentiviral vectors will be obtained from Invitrogen to transduce genes in cells						
Pathogen registration for lentivirus						

Johns Hopkins Institutional Biosafety Committee

JHU IBC Minutes for September 20, 2004
Room B-600, 2024 E. Monument Street Building

Members Present: Dr. Hayward, Chair; Dr. Adams, Dr. Dahl, Ms. MacAuley, Dr. Maouyo, Dr. McDevitt, Dr. Margolick, Dr. Norris, Dr. Pan, Dr. Scott

Members Absent: Ms. Biedrzycki, Dr. Borrello, Dr. Rade,

Guests: Drs. [redacted]

The meeting was called to order at 3:10

The minutes were approved 9-0-1 (with one abstention). A typo regarding Herpes B was noted and Dr. Dahl said it would be corrected.

Human Subjects Gene Transfer/Pathogen Protocols
An appeal was heard of Dr. [redacted] protocols that were voted on by the IBC at the August 2004 meeting ([redacted] GT0401200401 and GT0402160101).

The members of the IBC and the guests of Dr. [redacted] were introduced. Then Dr. [redacted] presented a slide show on the flavivirus vaccine trials

After the presentation the IBC discussed a number of issues with Dr. [redacted] and the guests. The discussion was heated at times.

Points covered included:

- The IBC noted that the first 20 subjects for Δ30/4 were done as inpatient. Why not these studies? Dr. [redacted] responded that these represented the first human trials. The trials indicated that the animal models did, indeed, predict the human transmissibility concerns. Thus, no additional inpatient studies were felt to be necessary. Further, Dr. [redacted] restressed the low level of activity in the T. splendens mid-gut injection study that was noted in Dr. [redacted] presentation above.

- Dr. [redacted] questioned the IBC whether all recombinants were to be mistrusted. She also asked about biologically derived molecules such as temperature-sensitive mutants. Members of the IBC indicated the responsibility of the IBC to review all recombinant molecules derived by combining DNA fragments outside of the organism as defined in the NIH guidelines. Temperature sensitive mutants would be assessed for safety due to oversight required of pathogens in human subjects as stated in JHU policies.

- The IBC asked where the investigators would draw the line. The investigators noted that Dengue 3 did not show proper attenuation so it was not pursued. Dr. [redacted] stated she would expect to retest if ever they saw viral loads higher than expected.

- It was noted that an IND meeting with the FDA just occurred and the FDA wants additional GLP studies in monkeys of 2/4. Langat has not been submitted yet.

- Dr. [redacted] noted that the transmission of the agent(s) through the study was a low probability event:
1) Viremic volunteers would have to high enough titers for transmission.
2) Viremic volunteers would have to be bitten by a vector capable of transmission
3) The virus would have to grow in the mosquito
4) The mosquito would have to be able to transmit the virus.

- Dr. Hayward noted the mutations that were required for Vero cell assays used to titer the virus from human subjects and inquired if there was a concern regarding the sensitivity of the assay and whether mutations could occur in the patients that render the virus incapable of Vero cell growth leading to underestimation of viral titers. A suggestion of Q-PCR for additional evaluation of titers followed and was strongly dismissed by Drs. [redacted] and [redacted] for inability to distinguish live virus from DNA fragment remnants. There was also a misunderstanding/discussion /clarification of RT-PCR vs. Q-PCR

- It was noted that new information was presented in the discussion and presentation that the IBC had not seen before.

The guests were thanked for their time and the IBC deliberated the information and request for appeal.

Dr. Adams suggested to approve the appeal with documentation signed off by both Dr. [redacted] and Dr. [redacted] regarding the unlikelihood of transmissibility.

The IBC moved to vote to consider the appeal of protocols GT0401200401 (rDEN2/4 Δ 30) and GT0402160101 (Langat/Dengue 4):

The following votes were taken:

1) [redacted] **Protocol GT0401200401** (rDEN2/4 Δ 30)
Vote to require seasonal restrictions with viremia data reported to the IBC with the understanding that the seasonal restriction may be lifted if viremia is low.

For Approval:	8
Against Approval:	2
Abstain:	0

Vote to approve the protocol with the restrictions above.

For Approval:	9
Against Approval:	0
Abstain:	1

2) [redacted] **Protocol GT0402160101** (Langat/Dengue 4)

Vote to approve the protocol with the restrictions above.

For Approval: 8
Against Approval: 1
Abstain: 1

It was decided that Dr. Dahl, Dr. Hayward, and Dr. Norris would draft the letter and submit to the investigator on behalf of the IBC.

---------End of Discussion regarding **Protocols GT0401200401** (rDEN2/4 Δ 30) **and GT0402160101**------

Old Business:
A response regarding the re-siting of the Staph. aureus project to Ross animal rooms (protocol submitted by **Dr.** [redacted] (protocol **P0407230201**)) was received and it was noted by the investigators that this would be difficult for the study. It was noted by the IBC that the use of meth-resistant Staph aureus in buildings adjoining hospital areas was potentially problematic. The IBC moved to have the protocol reviewed by Johns Hopkins Hospital Infection and Control. If Infection Control allows the study then the IBC would approve the study.

For Approval with Infection Control OK: 10
Against Approval with Infection Control OK: 0
Abstain: 0

DUE TO TIME CONSTRAINTS, 3 IBC MEMBERS HAD TO LEAVE THE MEETING

New Business:

[redacted] **amendment for protocol GT0308180101.**
The amendment did not involve biosafety issues.

The IBC then moved to approve the amendment to protocol GT0308180101:

For Approval: 7
Disapproval: 0
Abstain: 0

[redacted] **amendment for protocol GT0311170101.**
The amendment did not involve biosafety issues.

The IBC then moved to approve the amendment to protocol GT0311170101:

For Approval: 7
Disapproval: 0
Abstain: 0

Recombinant DNA/Pathogen Research Registrations
12 research registrations were presented for IBC consideration. All were approved (see attached list).

The meeting was adjourned at 5:45

Institutional Biosafety Committee Registrations
September 20, 2004 Meeting
Registrations from 7/30/04 – 9/08/04

Title	IBC#	BSL	ABSL	Yes	No	Abstain
Prevalence, Disease Association and Molecular Characterization of [redacted] Infections	**T0409130101**	**2**	**NA**	**7**	**0**	**0**
The genes coding for the [redacted] toxins ([redacted]) will be analyzed to evaluate for an association between these toxins and various presentations of [redacted]						
Toxin registration for [redacted] toxin						
Supporting Document-Pathogen registration for [redacted]	P0409130101					
Prevalence, Disease Association and Molecular Characterization of [redacted] Infections	**P0409130101**	**2**	**NA**	**7**	**0**	**0**
[redacted] will be identified and isolated from patients and further characterized by PCR						
Pathogen registration for [redacted]						
Gene Transfer for Treatment of ALS and Myasthenia	**DN0409070101**	**2**	**2**	**7**	**0**	**0**
The moiety of [redacted] fused to core streptavidin will be transduce into cell cultures and mouse using adenoviral and adenoviral associated viral vectors.						
DN–Uses recombinant DNA containing heavy chain of and viral vectors in mouse						
Supporting Document-Toxin registration for [redacted] toxin	T0409070101					
Supporting Document-Pathogen registration for AV & AAV	P0304110102					
Gene Transfer for Treatment of ALS and Myasthenia	**T0409070101**	**2**	**2**	**7**	**0**	**0**

[redacted] (200 nM) will be incubated with the N2A cultures containing the [redacted] recombinant fusion protein to test the specificity of binding of the recombinant fusion protein to cholinergic nerve terminals.

Toxin registration for [redacted]

DNA Methylation In Uterine Cervical Carcinogenesis Human tissue containing human papillomavirus (HPV) will be manipulated for research purposes. *Pathogen registration for HPV*	**P0408260101**	**2**	**2**	**7**	**0**	**0**
Genetic manipulation of EPEC type III Secretion System Lambda phage genes *exo, beta,* and *gem* will be transformed into island of enteropathogenic *E. coli* (EPEC) cells. DN--uses plasmid-based recombinant DNA transformed in EPEC cells *Supporting Document-Pathogen registration for EPEC*	**DN0409030101** P0409030101	**2**	**NA**	**7**	**0**	**0**
Characterization of Type III Secretion System of E. coli A wild type strain E2348/69 and a knock out strain CVD 452 of Enteropathogenic E. coli (EPEC) will be cultured for research purposes. *Pathogen registration for enteropathogenic E. coli (EPEC)*	**P0409030101**	**2**	**NA**	**7**	**0**	**0**
Comparison of Different Yersinia Strains The experiments will be carried out to compare the influence of different environmental factors on protein secretion by different Yersinia species (Y. enterocolitica versus Y. pseudotuberculosis) *Pathogen registration for Yersinia pseudotuberculosis*	**P0409030201**	**2**	**NA**	**7**	**0**	**0**
Screening for Bioactive Molecules in retinal Cell Culture	**DN0409080101**	**2**	**NA**	**7**	**0**	**0**

Adenoviral particles that were chemically conjugated to poly(L-lysine) and bound ionically to DNA molecules from Baylor College of Medicine or other viral vectors from commercial sources will be used to develop the technique to transduce genes into primary neuronal cell cultures. A standard reporter constructs containing GFP will be used to evaluate the technique.						
DN--Uses recombinant DNA and viral vectors in cultured cells						
Supporting Document-Pathogen registration for AV	P0408300101					
Supporting Document-Pathogen registration for Sticky AV	P0408300201					
Supporting Document-Pathogen registration for AAV	P0408300301					
Supporting Document-Pathogen registration for Lentivirus	P0408300401					
Screening for Bioactive Molecules in retinal Cell Culture	**P0408300101**	**2**	**NA**	**7**	**0**	**0**
Adenoviral vector AdEasy from Stratagene will be used to develop the technique to transduce genes into primary neuronal cell cultures. A standard reporter constructs containing GFP will be used to evaluate the technique.						
Pathogen registration for Adenovirus						
Screening for Bioactive Molecules in retinal Cell Culture	**P0408300201**	**2**	**NA**	**7**	**0**	**0**
Adenoviral particles that were chemically conjugated to poly(L-lysine) and bound ionically to DNA molecules from Baylor College of Medicine will be used to develop the technique to transduce genes into primary neuronal cell cultures. A standard reporter constructs containing GFP will be used to evaluate the technique.						
Pathogen registration for sticky Adenovirus						
Screening for Bioactive Molecules in retinal Cell Culture	**P0408300301**	**2**	**NA**	**7**	**0**	**0**
AAV Helper-Free system from Stratagene will be used to develop the technique to transduce genes into primary neuronal cell cultures. A standard reporter constructs containing GFP will be used to evaluate the technique.						
Pathogen registration for AAV						

Screening for Bioactive Molecules in retinal Cell Culture ViraPower Lentiviral expression system from Invitrogen will be used to develop the technique to transduce genes into primary neuronal cell cultures. A standard reporter constructs containing GFP will be used to evaluate the technique. *Pathogen registration for Lentivirus*	**P0408300401**	**2**	**NA**	**7**	**0**	**0**
Topical Voriconazole for Treatment of Fungal Keratitis In vivo Candida Albicans from ATCC will be injected into the right cornea of rabbits *Pathogen registration for Candida albicans*	**P0409070101**	**2**	**2**	**7**	**0**	**0**
Role of HOXA5 and Twist in Breast Cancer Genes will be transfected into human cell lines and transplanted into nude mice. DN--Uses plasmid-based recombinant DNA transfected in human cell lines and mice *Supporting Document - Human Tissue Registration--Laboratory*	**DN0409030201** B0409030101	**2**	**2**	**7**	**0**	**0**
HCV E1E2 Lentiviral Pseudoviruses Hepatitis C virus (HCV) envelope genes will be transduced into cell cultures using viral vectors. DN--Uses recombinant DNA and viral vectors in cultured cells *Supporting Document-Pathogen registration for HIV provirus* *Supporting Document-Pathogen registration for Lentivirus* *Supporting Document-Pathogen registration for Pantropic retrovirus* *Supporting Document - Human Tissue Registration--Laboratory*	**DN0409100101** P0407300101 P0407300201 P0407300301 B9612230107	**2**	**NA**	**7**	**0**	**0**
HCV E1E2 Lentiviral Pseudoviruses The pNL4-3. Luc.R-E- HIV provirus expression construct from the NIH AIDS Research and Reference Reagent Program will be used to transduce hepatitis C virus (HCV) envelope genes into cultured cells. *Pathogen registration for HIV provirus*	**P0407300101**	**2**	**NA**	**7**	**0**	**0**

HCV E1E2 Lentiviral Pseudoviruses ViraPower lentiviral expression system from Invitrogen will be used to transduce hepatitis C virus (HCV) envelope genes into cultured cells. *Pathogen registration for Lentivirus*	**P0407300201**	**2**	**NA**	**7**	**0**	**0**
HCV E1E2 Lentiviral Pseudoviruses Pantropic retroviral expression system from BD Bioscience will be used to transduce hepatitis C virus (HCV) envelope genes into cultured cells. *Pathogen registration for Pantropic retrovirus*	**P0407300301**	**2**	**NA**	**7**	**0**	**0**

Johns Hopkins Institutional Biosafety Committee

JHU IBC Minutes for October 12, 2004
Blalock Building, Room 1024B

Members Present:	Dr. Hayward, Chair; Dr. Adams, Dr. Dahl, Ms. MacAuley, Dr. McDevitt, Dr. Pan, Dr. Norris
Members Absent:	Ms. Biedrzycki (Leave of Absence), Dr. Borrello, Dr. Maouyo, Dr. Margolick, Dr. Rade, Dr. Scott
Guests:	None

The meeting was called to order at 3:15.

OLD BUSINESS:

Minutes were approved

1) [redacted] **Protocols GT0401200401** (rDEN2/4 Δ 30) **and GT0402160101** (Langat/Dengue 4):
Drs. [redacted] and [redacted] had agreed to serve as ad hoc reviewers in support of Dr. [redacted] appeal. To date the IBC has received nothing from Dr. [redacted] and about 10 lines from Dr. [redacted] as reported by Dr. Hayward.

The IBC discussed the parameters that would be used to remove seasonal restriction if so moved. The sensitivity of the viral titer assay was discussed and the following points made:

- Data show they find virus levels jumping up and down
- $2x10^{-2}$ LD50 for vero cells so assay is probably measuring virus 2 logs too low
- Virus was adapted to Vero cells, they may not measure the virus if its no longer adapted to Vero after "passage" through the human subject.
- Prefer assay done in Human cells at some point or QPCR for quantitative assay. Push [redacted] to come up with a better assay.

2) [redacted] **Protocol P0407230201** (methicillin-resistant Staphylococcus aureus):
This protocol is still awaiting a response from Johns Hopkins Hospital Infection Control. Dr. Dahl will contact the group to determine the status of their review.

NEW BUSINESS:

Sunshine Group
The Sunshine Group review of IBCs was handed out to each IBC member. Dr. Dahl explained the delays in sending the requested info to Mr. Edward Hammond of the Sunshine Group. Dr. Dahl also noted that the first set of minutes was redacted by Microsoft Word deletion of investigator's names which raised suspicions in Mr. Hammond. Thus, a second set, blacked out with sharpie, was sent to Mr. Hammond.

Website and email updates:
Dr. Dahl reported the website was up and running and could be found at www.hopkinsibc.org. It was also noted that a group email account for the IBC had been obtained from JHEM that routes to hopkinsibc@jhu.edu and hopkinsibc@jhmi.edu. Both emails feed to the single server and at present are forwarded directly to Dr. Dahl's email. In the future, a staff member will be assigned to handle IBC email as noted below.

New Staff Request
Dr. Dahl reported progress in obtaining an IBC liason to work in the Biosafety Office and handle calls, scheduling, registration management, emails, etc. The request for this staff person awaits approval from Richard Grossi.

Brain Tissue Lab
Dr Dahl reported that he had been contacted by Dr. [redacted] for recommendations regarding the dedication of a laboratory in which human tissue will be handled including the homogenization of human brain tissue.

The IBC discussed the potential risk of prion exposure in addition to the usual blood-borne pathogens and made the following recommendations:

1) Restrict all handling to the Biosafety Cabinet.
2) Restrict homogenization to one room.

Miscellaneous:
Dr. Dahl reported an investigator coming from NIH inquired about restrictions concerning Borna virus. Dr. Adams pointed out that Borna is currently used on campus. Borna is transmissible via injection but not between cages. Animals are kept in microisolators. USDA restrictions exist for transport and must approve license

Dr. Dahl also noted he had been contacted by Dr. [redacted] with regard to the packaging of a product intended for human trials. The IBC noted that FDA regs must exist for this and it is really not an IBC issue. It was recommended that Dr. [redacted] contact the GMP lab for advice.

Recombinant DNA/Pathogen Research Registrations

Institutional Biosafety Committee Registrations
October 12, 2004 Meeting
Registrations from 9/9/04 – 10/12/04

Title	IBC#	BSL	ABSL	Yes	No	Abstain
Construction of Expression Vectors for Dengue Proteins and DNA Immunizations of HLA Transgenic Mice	**DN0410050101**	**2**	**2**	**7**	**0**	**0**
All 10 dengue genes or LAMP-DEN chimera genes will be cloned into pcDNA/pITR plasmid expression vectors and injected into HLA transgenic mice.						
DN–Uses plasmid-based recombinant DNA in animals						
Supporting Document-Pathogen registration for Dengue viruses	**P0410050101**					
Dorsomedial Hypothalamic Pathways and Energy Balance	**DN0410060101**	**2**	**2**	**7**	**0**	**0**
Adeno-associated viral vector from Strategene will be used to transduce GFP and cholecyctokinin receptor into cultured cells and rat.						
DN–Uses recombinant DNA and viral vectors in cultured cells and animals						
Supporting Document-Pathogen registration for AAV	**P0410060101**					

Supporting Document-Human Tissue Registration--Laboratory	**B0410060101**					
Axon Pathology in MOG EAE Pertussis toxin will be injected into mice to establish the animal model for multiple sclerosis *Toxin registration for Pertussis toxin*	**T0409290101**	**2**	**2**	**7**	**0**	**0**
Role of HDGF in Growth and Disease Adenoviral and retroviral vectors will be used to manipulate the gene expression of hepatoma derived growth factor (HDGF) in cultured cells. DN--Uses recombinant DNA and viral vectors in cultured cells	**DN0409150101**	**2**	**NA**	**7**	**0**	**0**
Supporting Document-Pathogen registration for AV	P0409150101					
Supporting Document-Pathogen registration for Retrovirus	P0409150201					
Supporting Document-Human Tissue Registration--Laboratory	B0409150101					
Transcriptional Control of Hematopoiesis Viral vectors will be utilized to express candidate regulatory transcription factors, dominant negative forms of the same, RNAi to block expression of the same in cultured cells and mouse. DN--Uses recombinant DNA and viral vectors in cultured cells and animals	**DN0410110101**	**2**	**2**	**6**	**0**	**1**
Supporting Document-Pathogen registration for Lentivirus	P0410110101					
Supporting Document-Pathogen registration for Retrovirus	P0410110201					
Transcriptional Control of Hematopoiesis Lentiviral vector will be utilized to express candidate regulatory transcription factors, dominant negative forms of the same, RNAi to block expression of the same in cultured cells and mouse. *Pathogen registration for Lentivirus*	**P0410110101**	**2**	**2**	**6**	**0**	**1**
Transcriptional Control of Hematopoiesis Retroviral vector will be utilized to express candidate regulatory transcription factors, dominant negative forms of the same, RNAi to block expression of the same in cultured cells and mouse. *Pathogen registration for Retrovirus*	**P0410110201**	**2**	**2**	**6**	**0**	**1**
Epidemiology and Impact of C. difficile Colonization *Clostridium difficile will be identified and isolated from stool samples from patients, and further cultured for testing for toxin production.* *Pathogen registration for Clostridium difficile*	**P0409200101**	**2**	**NA**	**7**	**0**	**0**
Studying Methicillin-Resistant Staphylococcocus aureus Acquisition and Colonization in Healthcare Workers Specimens of anterior nares and hands will be collected from healthcare workers and cultured for screen for MRSA carriage. The positive isolates will be further analyzed by molecular techniques. *Pathogen registration for Methicillin-resistant Staphylococcus aureus (MRSA)*	**P0410110301**	**2**	**NA**	**7**	**0**	**0**
Role of Lipoate Metabolic Pathways in Plasmodium Virulence Plasmodium falciparum will be passaged in culture flasks using human red blood cells as substrate for studying the metabolic pathway for synthesizing lipoate. *Pathogen registration for Plasmodium falciparum*	**P0410070101**	**2**	**NA**	**7**	**0**	**0**
Supporting Document-Human Tissue Registration--Laboratory	**B0410070101**					
Genetic Alterations in Lung Tumor Progression Adenoviral vectors will be used to transduce cancer genes into cultured cells *Pathogen registration for Adenovirus*	**P0409300101**	**2**	**NA**	**7**	**0**	**0**

Johns Hopkins Institutional Biosafety Committee

JHU IBC Minutes for November 15, 2004
Room B-600, 2024 E. Monument Street Building

Members Present: Dr. Hayward, Chair; Dr. Adams, Dr. Borrello, Dr. Dahl, Ms. MacAuley, Dr. Maouyo, Dr. Margolick, Dr. McDevitt, Dr. Pan, Dr. Rade, Dr. Scott

Members Absent: Ms. Biedrzycki (Leave of Absence), Dr. Norris

Guests: None

The meeting was called to order at 3:15.

OLD BUSINESS:

1) [redacted] **Protocols GT0401200401** (rDEN2/4 Δ 30) **and GT0402160101** (Langat/Dengue 4):
The appeal decision taken at the October IBC meeting regarding the above protocols is also being appealed. The investigator believes the seasonal restrictions are uncalled for. The chair requested that the investigator's response be forwarded to all the IBC members.

2) [redacted] **Protocol P0407230201** (methicillin-resistant Staphylococcus aureus):
This protocol had been sent to Johns Hopkins Hospital Infection Control for comment given the nature of the agent and the use of the agent in a building adjacent to patient care areas. The infection control response has now been received and requests the following from the investigator:

1) All staff needs to be instructed in proper precautions (gowns and glove use)
2) If during any injections there is the possibility of aerosolization the staff person must have on a face shield.
3) No travel through patient care areas at any time.
4) Good hand hygiene at all times.
5) Housekeeping - Through cleaning and disinfection daily

Since Infection Control had no major objections to the research protocol, the IBC moved to vote:

For Approval: 11
Disapproval: 0
Abstain: 0

NEW BUSINESS:

Human Subjects Gene Transfer/Pathogen Protocols
Three new protocols were presented to the IBC for consideration.

1) [redacted] **Protocol GT0411150101,** Phase I study of the safety and immunogenicity of west nile/dengue-4 3' Δ30 chimeric virus vaccine (WN/DEN4-3' Δ30), a live attenuated vaccine for west nile encephalitis.

This protocol uses the same Dengue background as the investigator's other most recent protocols. The inserts for this project are the prM and E protein genes of West Nile virus. The virus has not been used in humans to date.

The IBC discussed the protocol in relation to the others recently submitted (Dengue 2/4, Langat):

-- Different hosts respond differently (immune response in horse, none in geese)
-- Different species of mosquitos show differences in infectivity. Dengue background is ok, but when one adds different inserts the properties change. This further emphasizes the need for each construct of the series to be reviewed carefully.
-- Albopictus mosquito is able to get virus in the head. Investigator notes that West Nile is already in the Baltimore area. Presumably this minimizes concern for escape of the recombinant viral construct.
-- This agent can get into the environment it appears.
-- Titers an issue again. Recombinant virus are always adapted to grow in Vero cells. Is the wild-type virus Vero adapted too?
-- Species differences do happen. For example, human serum contains factors that inactivate mouse retroviruses.

The IBC moved to approve protocol GT0411150101 with seasonal restrictions. The project may commence immediately, but no injections may occur past April 1, 2005 without IBC approval based on data regarding patient titers. The investigator will be encouraged to identify alternate titering protocols, perhaps including Q-pcr:

For Approval: 11
Disapproval: 0
Abstain: 0

2) [redacted] **Protocol GT0411150201,** A phase I clinical trial to evaluate the safety of a multiclade recombinant adenoviral vector HIV-1 vaccine administered to healthy, HIV-1 uninfected, adult participants who received DNA plasmid vaccine or placebo in the HVTN 052 clinical trial (HVTN 057, Version 1):

The protocol builds on a previous study, GT0401200101, which tested the safety and immunogenicity of a multiclade HIVB-1 DNA plasmid vaccine. This study, and the one under review constitute a "prime-boost" study for the immunogens being tested. In this study, participants who received the plasmid-based vaccine will now receive a replication-defective adenoviral vector expressing HIV-1 based immunogenic protein fragments.

The IBC found the study to be similar to others the investigator has submitted to the IBC and found no exceptional biosafety issues requiring further discussion.

The IBC then moved to approve protocol GT0411150201:

For Approval: 11
Disapproval: 0
Abstain: 0

3) [redacted] **Protocol GT0411150301,** A phase I safety and immunogenicity trial of an alphavirus replicon HIV-1 subtype C gag vaccine (AVX101) in healthy HIV-1 uninfected adult participants (HVTN 059, Version 1):
This protocol is actually based on a previous protocol, GT0306030101, (HVTN40), with the same title as above. The prior protocol ran into difficulty when it was noted that the alphaviral preparation had stability

issues when stored at -20° C. at the two upper doses approved for the study, 10^6 and 10^7. The storage buffer has now been reformulated and the agent is now stable at these concentrations. The new protocol requests approval for an additional dosing at 10^8 particles.

The IBC noted the alphavirus replicon is designed to be replication deficient. Adverse events for protocol GT0306030101 have been reported by the investigator as mild or absent.

The IBC then moved to approve protocol GT0411150301:

For Approval: 11
Disapproval: 0
Abstain: 0

Recombinant DNA/Pathogen Research Registrations
7 research registrations were presented for IBC consideration. All were approved (Registration P0407230201 listed previously in these minutes were included below for consistency).

The meeting was adjourned at 5:30

Institutional Biosafety Committee Registrations
November 15, 2004 Meeting
Registrations from 7/9/04 -- 8/2/04

Title	IBC#	BSL	ABSL	Yes	No	Abstain
Role of Estrogen and Angiogenesis in Stroke Prevention	**DN0410280101**	**2**	**2**	**11**	**0**	**0**
Adenoviral vectors will be used to transduce angiopoietin-1 full length DNA and truncated DNA into rat.						
DN--Uses recombinant DNA and viral vectors in cultured cells and animals						
Supporting Document-Pathogen registration for AV	**P0410280101**					
HIMF Family of Proteins and Pulmonary Diseases	**DN0410220101**	**2**	**2**	**11**	**0**	**0**
Adenoviral and adeno-associated viral vector from Stratagene will be used to transduce mouse HIMF, mouse RELM-gamma or human HIMF into cultured cells, mouse and rat.						
DN--Uses recombinant DNA and viral vectors in cultured cells and animals						
Supporting Document-Pathogen registration for AV	**P0302260102**					
Supporting Document-Pathogen registration for AAV	**P0410220101**					
Supporting Document-Human Tissue Registration--Laboratory	**B0302260102**					
Epidemiology of Healthcare-associated Drug-Resistant Gram Negative Bacilli	**P0411080101**	**2**	**NA**	**11**	**0**	**0**

Specimens will be collected from patients and cultured for screen for infection with Acinetobacter. The positive isolates will be further analyzed by molecular techniques. *Pathogen registration for Acinetobacter*						
Epidemiology of Healthcare-associated Drug-Resistant Gram Negative BacIII Specimens will be collected from patients and cultured for screen for infection with Pseudomonas. The positive isolates will be further analyzed by molecular techniques. *Pathogen registration for Pseudomonas*	**P0411080201**	**2**	**NA**	**11**	**0**	**0**
Epidemiology of Healthcare-associated Drug-Resistant Gram Negative BacIII Staphylococcus aureus subspecies NCTC 8325 will be used as the molecular weight standard for molecular strain typing for Acinetobacter and Pseudomonas. *Pathogen registration for Staphylococcus aureus*	**P0411080301**	**2**	**NA**	**11**	**0**	**0**
Transgenic Modeling of Asthma, COPD, Acute Lung Injury and Pulmonary Inflammation Adenoviral vectors will be used to transduce Th1/Th2 cytokine genes and phosphatase genes into cultured cells and mouse. DN–Uses recombinant DNA and viral vectors in cultured cells and animals *Supporting Document-Pathogen registration for AV* *Supporting Document-Human Tissue Registration--Laboratory* *Pathogen registration for Borrelia afzelii*	**DN0411090101** **P0411090101** **B0411090101**	**2**	**2**	**11**	**0**	**0**
Comparative Activity of Mupifocin,moxifloxacin, and ciprofloxacin against genetically defined high level fluoroquinolone-resistant methicillin-resistant Staphylococcus aureus in rabbits model *Staphylococcus aureus will be injected into the right eye of rabbit* *Pathogen registration for fluoroquinolone-resistant methicillin-resistant Staphylococcus aureus*	**P0407230201**	**2**	**2**	**11**	**0**	**0**

Johns Hopkins Institutional Biosafety Committee

JHU IBC Minutes for December 20, 2004
Room 126, Billings Administration Building

Members Present: Dr. Hayward, Chair; Dr. Adams, Dr. Dahl, Ms. MacAuley, Dr. Maouyo, Dr. McDevitt, Dr. Norris

Members Absent: Ms. Biedrzycki (Leave of Absence), Dr. Borrello, Dr. Margolick, Dr. Pan, Dr. Rade, Dr. Scott

Guests: None

The meeting was called to order at 3:10.

APPROVAL OF MINUTES:

The minutes for October were unanimously approved pending correction of the itemized list by Dr. Dahl
The minutes for November were unanimously approved.

OLD BUSINESS:

1) [redacted] **Protocol GT0411150101** (West Nile/Dengue 4-3' Δ30):

The committee was informed that the investigator believes the seasonal restrictions are uncalled for and has indicated she will appeal this decision. The chair requested that the investigator's response be forwarded to all the IBC members.

The committee was given a copy of a letter dated November 22 that was addressed to Dr. [redacted] from Dr. [redacted] of NIH. Dr. [redacted] is one of the investigators who has supplied viral constructs and financial backing to Dr. [redacted] recent protocols. Dr. [redacted] letter is divided into two concerns: 1) timeliness of review including the procedures followed by the JHU IBC for review and 2) the quality of the decision process of the JHU IBC. Dr. [redacted] letter suggests funding will not be given to JHU investigators unless changes are made in the IBC. The IBC members discussed the letter and noted many factual inaccuracies including lack of knowledge of Dr. [redacted] presentations to the IBC, overstatement of the time for review (Dr. [redacted] states "more than 12 months, in actuality the review process took 9 ½ months from submission to first conditional approval.), denigration of the outside reviewer comments.

Dr. Hayward handed out a manuscript from the Journal of Clinical Microbiology by Papin et al, "Syber Green-based Real-Time Quantitative PCR Assay for Detection of West Nile Virus Circumvents False-negative Results Due to Strain Variability" Dr. Hayward indicated this was forwarded to Dr. [redacted].

NEW BUSINESS:

1) **Biographical Sketches**
Dr. Dahl reminded the IBC membership that updated biographical sketches were due at the end of December for submission to OBA for their annual membership update requirement.

2) **Adverse Event Reports**

The IBC received adverse event reports from Dr, [redacted] Protocol GT0006230101 and from Dr. [redacted], Protocol GT0302250101. The studies are not related. Both Investigator's reports concerned patients at sites other than JHMI and both were suggested to be "possibly related" to their respective studies. The IBC noted that the FDA and IRBs had been notified of the events as required.

3) **Protocol Amendment, [redacted]GT0402160301**
The IBC received notification that the above protocol was before the IRB for approval of an amendment. The IBC noted the amendment involved consent forms and no action was necessary on the IBC's part.

4) **Suspected non-compliance**
Dr. Dahl reported that he had received a 50 page print-out from [redacted] detailing all active and inactive protocols that had gone before the [redacted]. Dr Dahl said he had gone through the titles of all the protocols and had identified over twenty that looked like they may involve either recombinant DNA and/or pathogens and were never submitted to the IBC for review. Dr. Dahl indicated he would have to review each protocol individually before actual numbers would be available.

5) **Hanta Virus**
Dr. Dahl reported that Dr. [redacted] had expressed interest in using the BSL3 facility on the 9th floor of BSPH to work with Hanta. Dr. Dahl said that the facility would be inspected for suitability and would report back to the IBC concerning findings.

Recombinant DNA/Pathogen Research Registrations
12 research registrations were presented for IBC consideration. All were approved.

The meeting was adjourned at 5:30

Institutional Biosafety Committee Registrations
December 20, 2004 Meeting
Registrations from 11/05/04 – 12/10/04

Title	IBC#	BSL	ABSL	Yes	No	Abstain
Candidate Genes for Dengue Hemorrhagic Fever Dengue viruses will be used to infect human peripheral mononuclear cells to study the candidate genes for Dengue Hemorrhagic fever *Pathogen registration for Dengue viruses serotype 1, 2,3 and 4*	P0412060201	2	NA	7	0	0
Characterization of Cryptococcus Neoformans SREBP Cryptococcus Neoformans will be cultured to determine if CnSre 1 is required for hypoxic growth. *Pathogen registration for Cryptococcus neoformans*	P0411180101	2	NA	7	0	0
Molecular Physiology of Cochlear Hair Cells	T0411220101	2	NA	7	0	0

Tetrodotoxin will be applied to excised organ of Corti to block voltage-gated sodium channels in hair cells or neurons *Toxin registration for Tetrodotoxin*						
Afferent Synaptic Transmission in the Mammalian Cochlea [redacted] will be applied to excised organ of Corti to block voltage-gated sodium channels in hair cells or neurons *Toxin registration for* [redacted]	**T0411220201**	**2**	**NA**	**7**	**0**	**0**
Role of PA Protein ExoS ExoS toxin will be isolated and the biochemical properties studied *Toxin registration for ExoS*	**T0412090101**	**2**	**NA**	**7**	**0**	**0**
Molecular Mechanism of Double-Strand Break Repair Inactivation by Adenovirus Adenovirus will be used to infect mammalian cells to elucidate the effect of adenoviral infection on non-homologous end joining DNA repair. *Pathogen registration for Adenovirus*	**P0412060101**	**2**	**NA**	**7**	**0**	**0**
Markers of Drug Resistance Using Genome-Wide RNAi Screening GeneNet Lentiviral siRNA library from System Biosciences will be used to transfect mammalian cancer cells for identifying the markers for drug resistance. DN–Uses recombinant DNA and viral vectors in cultured cells *Supporting Document-Pathogen registration for Lentivirus*	**DN0411290101** **P0411290101**	**2**	**NA**	**7**	**0**	**0**
Contribution of Microtubules to Salmonella SCV Formation Salmonella C5 will be grown in culture to yield infectious stocks and these infectious stocks will be used to infect cultured epithelial cells. *Pathogen registration for Salmonella C5*	**P0411230101**	**2**	**NA**	**7**	**0**	**0**
Contribution of Microtubules to Salmonella SCV Formation Salmonella 14028 will be grown in culture to yield infectious stocks, and these infectious stocks will be used to infect cultured epithelial cells. *Pathogen registration for Salmonella 14028*	**P0411230201**	**2**	**NA**	**7**	**0**	**0**
Contribution of Microtubules to Salmonella SCV Formation	**P0411230301**	**2**	**NA**	**7**	**0**	**0**

Salmonella LT2 will be grown in culture to yield infectious stocks, and these infectious stocks will be used to infect cultured epithelial cells. *Pathogen registration for Salmonella LT2*						
Chemotaxis in Shewanella Oneidensis Shewanella Oneidensis will be isolated from lake and cultured to study its ability to respond to various attractant and repellent stimuli *Pathogen registration for Shewanella Oneidensis*	**P0411160101**	**1**	**NA**	**7**	**0**	**0**
Modeling Neurodegenerative Disease Retroviral vectors will be used to transduce Rheb gene into cultured cells and mouse. DN--Uses recombinant DNA and viral vectors in cultured cells	**DN0412010101**	**2**	**2**	**7**	**0**	**0**
Supporting Document-Pathogen registration for Retrovirus	**P0412010101**					
Human Tissue Registration--Laboratory	**B0412020101**					

Johns Hopkins Institutional Biosafety Committee

JHU IBC Minutes for January 18, 2005
Room 1024B, Blalock Building

Members Present: Dr. Hayward, Chair; Dr. Adams, Dr. Dahl, Ms. MacAuley (by phone), Dr. McDevitt, Dr. Pan, Dr. Rade

Members Absent: Ms. Biedrzycki (Leave of Absence), Dr. Borrello, Dr. Margolick, Dr. Maouyo, Dr. McDevitt, Dr. Norris, Dr. Scott

Guests: Dr. [redacted]

The meeting was called to order at 11:00am.

[redacted] COMPLIANCE INQUIRY:

Dr. [redacted] had asked to meet with the IBC regarding three studies she had initiated without IBC review and approval. Dr. [redacted] noted, and it was agreed, that the rules were confusing regarding the exemption of certain vaccine trials from RAC review and whether this also exempted from IBC review.
Dr. Dahl noted that there were a number of studies from [redacted] that appeared to be in violation of the NIH Guidelines and/or Johns Hopkins policies as determined by initial screen of titles provided by the [redacted]. Dr. Dahl indicated he would have to read each protocol to determine whether the project was actually in violation. This review would take place in the coming few weeks.

Dr. [redacted] provided copies of all the studies she had initiated and also provided an overview sheet that outlined the three studies:

00-03-03-03 – Study was initially approved by the IRB 4/11/00, status is terminated. This study involved a recombinant virus vaccine

H22.02.04.04.A1 – Study was initially approved by the IRB 6/10/02, status is terminated. This study involved a similar viral-based vaccine as that above.

01-06-11-01 ([redacted]) – Study was initially approved by the IRB 12/4/01. Subject enrollment has been terminated. The study is open for data analysis only. This study involved a recombinant chimera human/bovine parainfluenza virus vaccine. This study was terminated by the investigators because the agent was "less attenuated than hoped."

It was noted that Dr. [redacted] had registered the RSV vaccine as a pathogen with the Biosafety Office, but the study was not submitted to the IBC and the Biosafety Office at the time failed to note the necessary additional scrutiny.

A discussion of adverse event reporting followed the presentation with concern being expressed for the Investigator's and their already heavy compliance reporting burden juxtaposed to the requirement detailed in the NIH Guidelines for the IBC to ensure SAEs are reported.

OLD BUSINESS:

No Old Business was presented at this IBC meeting

NEW BUSINESS:

[redacted]

2) **Upcoming Inspection of the BRB BSL3 Vivarium**
Dr. Dahl reported that inspectors from World BioHazTec had been contracted to inspect the new BRB BSL3 Vivarium prior to it going "hot". Inspectors will arrive on February 1. The Vivarium is expected to house TB and Hanta-infected animals.

Recombinant DNA/Pathogen Research Registrations
7 research registrations were presented for IBC consideration. All were approved.

The meeting was adjourned at 12:50pm

Institutional Biosafety Committee Registrations
January 18, 2005 Meeting
Registrations from 12/11/04 – 1/13/05

Title	IBC#	BSL	ABSL	Yes	No	Abstain
Molecular Mechanisms of Myoblast Fusion Molecular mechanisms of myoblast fusion will be studied in Drosophila DN--Recombinant DNA will be used in animals	DN0412270101	2	1	7	0	0
Gene Transfer Based Prostate Cancer Imaging Adenoviral vectors will be used to transduce Herpes Simplex virus thymidine kinase and green fluorescent protein fusion gene into cultured cells and mouse. DN--Uses recombinant DNA and viral vectors in cultured cells and animals *Supporting Document-Pathogen registration for AV*	DN0501130101 Pending	2	2	7	0	0

Supporting Document-Human Tissue Registration--Laboratory	Pending					
Rickettsial-endothelial Cell Interaction *Rickettsia montanensis* will be propagated in Vero cells, purified and introduced into endothelial cell cultures to study how *rickettsiae* alters endothelial cells and endothelial barrier function. *Pathogen registration for Rockettsia montanensis*	**P0412300101**	**2**	**NA**	**7**	**0**	**0**
Analysis of Mesothelin-specific T-cell Response and Augmentation of GM-CSF + Listeria Based Vaccines *Listeria monocytogenes* will be injected into experimental mice to enhance the anti-pancreatic tumor response *Pathogen registration for Listeria monocytogenes*	**P0501060101**	**2**	**2**	**7**	**0**	**0**
Computational Model of cellular Adhesion in Bulk Flows *Staphylococcal Aureus* will be cultured and harvested for studying its interaction with polymorphonuclear leukocyte in vitro. *Pathogen registration for Staphylococcus Aureus*	**P0501130101**	**2**	**NA**	**7**	**0**	**0**
Prevention of Candidiasis in Critically Ill Patients Candida will be isolated from patient specimens and sub-cultured for antifungal susceptibility testing and other routine microbiology procedures. *Pathogen registration for Candida*	**P0501100101**	**2**	**NA**	**7**	**0**	**0**
Tumor Suppressors and Growth Control Tumor suppressor genes will be expressed in *E. coli* and Drosophila DN--Recombinant DNA will be used in bacteria, tissue culture cells and animals	**DN0412280101**	**2**	**1**	**7**	**0**	**0**

Johns Hopkins Institutional Biosafety Committee

JHU IBC Minutes for February 21, 2005
Room B-600, 2024 E. Monument Street Building

Members Present: Dr. Hayward, Chair; Dr. Adams, Dr. Dahl, Dr. McDevitt, Dr. Maouyo, Dr. Pan, Dr. Rade, Dr. Scott

Members Absent: Ms. Biedrzycki (Leave of Absence), Dr. Borrello, Ms. MacAuley, Dr. Margolick, Dr. Norris,

Guests: None

The meeting was called to order at 3:27pm.

APPROVAL OF MINUTES

The Minutes for January 2005 were unanimously approved.

OLD BUSINESS:

1) [redacted] **NIH Compliance Issue**
The IBC membership discussed the Compliance issues discovered at [redacted].
Dr. Dahl reported that he was in the process of sorting through the [redacted] data on projects that might involve recombinant DNA and Gene Transfer. He also stated he had consulted with JHU Legal as well as Dr. Bernacki regarding the letter to be sent to OBA. A review of Biosafety Registration records is still underway as is a review of SOM IRB records.

Dr. Hayward noted that he had drafted a questionnaire to be sent to the PI's to determine the status of their studies. He stressed that it was important to determine how many were still active and how many had been terminated and/or were no longer active with regard to the subjects. [redacted] considers data analysis still an active project.

NEW BUSINESS:

1) **GMP Facility Presentation needs to be scheduled.**
New [redacted] protocol will involve product manufactured in the facility. An investigator's brochure should be provided/requested.

2) [redacted] **Protocol GT0502210101** "A long-term follow-up study to evaluate the safety of ex-vivo cultured adult human mesenchymal stem cells Provacel in subjects following acute myocardial infarction."

Note: This is a follow-up study. The original did not come before the IBC and may be in violation of JHU, but not NIH, policy. The introduction of human cells into human subjects may fall under the "pathogen" category of JHU Policy.

This study utilizes bone marrow-derived mesenchymal stem cells "Provacel" as a treatment to acute myocardial infarction. Provacel is reported to improve myocardial self-repair following infarction and thus

reduce myocardial "negative" remodeling – myocyte slippage and fibroblast proliferation in the infracted muscle scar tissue.

The protocol notes that the human mesenchymal stem cells are isolated from unrelated, unmatched donor-derived bone marrow aspirates after donor testing according to the FDA Donor Suitability Guidance.

Dr. McDevitt noted the study focuses on the cardiac function as titled, but does not take into account the possibility of blood toxicity. The stem cells will most likely set up in tissues other than the heart, certainly the marrow. There is no indication of studies to ensure that these potential issues are considered. For example, is a Graft vs. Host response possible? Has it been assessed? None of this is covered in the proposed study.

The IBC moved to approve protocol **GT0502210101** pending investigator response to the questions raised in the discussion. Dr. Hayward and Dr. Dahl would monitor the response and note final approval:

For Approval: 8
Disapproval: 0
Abstain: 0

3) [redacted] **Protocol GT0502210201** Safety and immunogenicity of one and two doses of the live, attenuated oral ETEC candidate vaccine BB01 in healthy adults (Stage I) followed by a conditional challenge stage with a virulent ETEC strain (Stage II) – a phase I, randomized, double-blind, placebo-controlled study.

Human subjects will be vaccinated with a live, recombinant Vibrio cholerae vaccine, BB01, that expresses ETEC (Enterotoxigenic E. coli) pili components. In the second stage of the project, vaccinated subjects will be given a challenge strain of bacteria (H10407) in the inpatient isolation unit of Mason Lord Building on the Bayview campus.

The investigator has done similar projects that have been approved by the IBC. This project differs in that the challenge is a recombinant agent.

Data provided by the sponsor's brochure suggests that the vaccine strain does not survive in the environment.

Questions raised by IBC members included:

-- 3% transmission was noted in non-hygenic environments. Fecal-oral training or education could perhaps lower this rate.

-- Questions were raised regarding the transport of the agent from Hampton House to Bayview

-- Evidence that adding pili genes does not increase pathogenicity was requested.

--SOP for how the investigators would handle the material, including disposal, was requested including procedures in place to keep the agent from going into the environment.

The IBC moved to approve protocol **GT0502210201** pending investigator response to the questions raised in the discussion. Dr. Hayward and Dr. Dahl would monitor the response and note final approval:

For Approval: 8
Disapproval: 0
Abstain: 0

Recombinant DNA/Pathogen Research Registrations
7 research registrations were presented for IBC consideration. All were approved.

The meeting was adjourned at 5:15pm

Institutional Biosafety Committee Registrations
February 21, 2005 Meeting
Registrations from 1/14/05 – 2/4/05

Title	IBC#	BSL	ABSL	Yes	No	Abstain
Gene Expression Changes in Dengue Infected Mononuclear Cells	**P0501260101**	**2**	**NA**	**8**	**0**	**0**
Yellow fever virus will be used to infect human peripheral blood mononuclear cells.						
Pathogen registration for Yellow fever 17D(9-97) vaccine virus						
DNA Damage Signaling in Human Cells	**DN0502020201**	**2**	**NA**	**8**	**0**	**0**
Adeno-associated viral vector will be used to transduce various human genomic fragments that involving in DNA damage responses into cultured cells.						
DN--Uses recombinant DNA and viral vectors in cultured cells						
Supporting Document-Pathogen registration for Adeno-associated virus	P0502020301					
Human Tissue Registration--Laboratory	B0502020201					
Interactions between Dietary Factors and Inflammation in Prostate Carcinogenesis	**P0501310201**	**2**	**2**	**8**	**0**	**0**
Vaccinia virus will be injected to rats to induce prostate inflammation.						
Pathogen registration for Vaccinia virus						
Wilmer Gene Vector Production Unit	**DN0502180101**	**2**	**NA**	**8**	**0**	**0**
Adenoviral, adeno-associated viral, lentiviral vectors, as well as custom vectors using these viral vectors to transduce genes into cells will be produced for the Johns Hopkins research community.						
DN--Uses recombinant DNA and viral vectors in cultured cells						
Supporting Document-Pathogen registration for Adenovirus	P0502180101					
Supporting Document-Pathogen registration for Adeno-associated Virus	P0502180201					
Supporting Document-Pathogen registration for Lentivirus	P0502180301					

Human Tissue Registration--Laboratory	B0502180101					
Molecular Regulation of Pulmonary Aquaporins	**P0502040101**	**2**	**NA**	**8**	**0**	**0**
Adenoviral vectors from BD will used to transduce aquaporin-5 into cultured cells.						
Pathogen registration for Adenovirus						
Supporting Document-Recombinant DNA registration	D0109250103					
Supporting Document - Human Tissue Registration--Laboratory	B0502040201					
Proteomic Study of IBD	**P0502xxxxx**	**2**	**2**	**Hold for more info**		
E. coli strain LF82, isolated from a patient with Crohn's Disease, will be studied to determine its contribution to inflammatory bowel disease						
Mechanisms of Protection against Plasmodium yoelii in mice infected with M. tuberculosis	**P0501310101**	**2**	**2**	**8**	**0**	**0**
Plasmodium yoelii will be used to infect mice.						
Pathogen registration for Plasmodium yoelii						
Regulation and Biogenesis of Mammalian MicroRNAs	**DN0502020301**	**2**	**NA**	**8**	**0**	**0**
Retroviral vector from Clontech will be used to transduce C13orf25 and microRNAs into cultured cells.						
DN--Uses recombinant DNA and viral vectors in cultured cells						
Supporting Document-Pathogen registration for Retrovirus	P0502020401					
Human Tissue Registration--Laboratory	B0411120201					
Arrhythmias in Cultured Cardiac Cell Monolayer	**DN0502020101**	**2**	**NA**	**8**	**0**	**0**
Adenoviral and lentiviral vectors will be used to transduce Ca2+ and K+ ion channels, GFP, murine ET-1, CT-1 and FGF-2 into cultured cells.						
DN--Uses recombinant DNA and viral vectors in cultured cells						
Supporting Document-Pathogen registration for Adenovirus	P0502020101					
Supporting Document-Pathogen registration for Lentivirus	P0502020201					
Human Tissue Registration--Laboratory	B0502020101					
Construction of Virus Like Particles of Avian Influenza A Virus	**DN0502010101**	**2**	**NA**	**8**	**0**	**0**

The genes from influenza A will be subcloned and expressed using baculovirus express vectors. DN– Recombinant DNA will be used in cultured cells. *Supporting Document-Pathogen registration for Baculovirus*	P0502020501					
Etiology of Giant Cell Arteritis Human coronaviruses from ATCC will be used as a positive control to screen Giant Cell Arteritis (GCA) tissue banks for various viruses. *Pathogen registration for human coronavirus*	**P0502010101**	**2**	**2**	**8**	**0**	**0**

Johns Hopkins Institutional Biosafety Committee

JHU IBC Minutes for March 29, 2005
Room B-600, 2024 E. Monument Street Building

Members Present: Dr. Hayward, Chair; Dr. Adams, Dr. Dahl, Ms. MacAuley, Dr. Maouyo, Dr. Pan, Dr. Scott

Members Absent: Ms. Biedrzycki (Leave of Absence), Dr. Borrello, Dr. Margolick, Dr. Norris, Dr. Rade

Guests: Dr. [redacted], Dr. [redacted]

The meeting was called to order at 1:10 pm.

INVESTIGATOR PRESENTATION, GT0503290201, Phase I inpatient study of the safety and immunogenicity of H9N2 (6-2) AA ca reassortant (A/chicken/Hong Kong/G9/97x A/Ann Arbor/6/60 ca), a live attenuated virusvaccine candidate for prevention of avian influenza H9N2 infection in the event of a pandemic.

The principal investigator gave a brief overview of the study. The backbone of the virus is the same as Flumist. The surface glycoproteins encoded by the virus are H9 and N2 which represent an avian strain with low pathogenicity. H9N2 was chosen as a "proof of concept" strain for the initial studies. If successful, additional strains will be tested. Live vaccine was chosen because it more rapidly induces an immune response and is more durable. Also, live vaccines are better with drifted or shifted virus strains. (Drifted = amino acid change, Shifted = new genes added).

Study is a dose de-escalation study. Will start with 10^7 dose and work down from there. This allows for determination of the lower threshold for immunity.

Protections built into the study include:
1) Only do study from April 1 till September 30 to avoid flu season
2) Restrictions placed on subjects chosen including recent south Asia or curise ship travel, recent investigational vaccine or drug use (30 days), involvement with poultry industry.
3) Study performed in isolation facility
4) Associated staff stay home if they show signs of upper respiratory illness and have viral testing to identify the virus involved in their symptoms.

Members of the IBC asked a number of questions including:

Q: Is it OK to send staff members home when sick if the illness could be the vaccine strain?
A: Transmission of virus was 0.58% for a study in a daycare center with no PPE used. Investigators' concerns regarding release of the vaccine strain into the community are centered on potential reassorment with other strains of flu. Not the vaccine strain. By limiting the season, the chance of infection with flu and the vaccine is minimized.

Q: Do any staff have small children?
A: Small children have not been made an exclusion in the study.

Q: Is the vaccine sensitive to Tamiflu?
A: Both this strain and Flumist are sensitive to Tamiflu.
Q: How long post Tamiflu is the anti-viral response?
A: Viral titers decrease 24-36 hours post-initiation of Tamiflu treatment

Additional PI comments:

- FDA says to start Tamiflu at appearance of symptoms.
- The investigators asked the City Health Commissioner of Baltimore (Peter Beilenson) if they wanted the subjects quarantined and the answer was "not necessary".
- H3N2 is the strain that circulates around Baltimore most
- PCR will be used to identify the virus strain if staff get ill because of the speed of the assay. Viral culture will be used for the subjects in order to get quantitive data for the study.

GMP FACILITY PRESENTATION

Dr. [redacted] presented a brief overview of the GMP facility. Dr. [redacted] included a description of the processing of the Panc.10.05 and Panc 6.03 cell lines including a description of how the GMP facility replicates the procedures used by BioReliance.

Dr. [redacted] covered changes instituted to increase yield as well as the procedures used for turn-over when the facility changes from one project to the next. Typical turnover time is 10-12 days and includes disposal of all open packages of materials, sporklenz of surfaces including walls, ceilings, equipment (all done by outside contractor). Then GMP staff clean every piece of equipment and ethanol wash. Swabs are then done and incubated at 32° C for 2 days.

Dr. [redacted] offered to give an "external" tour to any interested members of the IBC.

Dr. [redacted] left toward the end of Dr. [redacted] presentation and was thanked for her efforts. Dr. [redacted] received a similar thank you after his presentation and departure.

APPROVAL OF MINUTES

The Minutes for February 2005 were unanimously approved with a change regarding the absence of Ms. MacAuley who was inadvertently left off the attendance header. Ms. MacAuley was not present at the February 2005 meeting and the minutes will be adjusted to reflect this fact.

NEW BUSINESS:

[redacted] **Protocol GT0503290201** "Phase I inpatient study of the safety and immunogenicity of H9N2 (6-2) AA ca reassortant (A/chicken/Hong Kong/G9/97x A/Ann Arbor/6/60 ca), a live attenuated virus vaccine candidate for prevention of avian influenza H9N2 infection in the event of a pandemic."

The IBC expressed some concern about allowing potentially infected staff members to leave the facility and be treated at home, but felt the study had covered the major concerns well.

The IBC moved to approve protocol **GT0503290201** pending FDA approval:

For Approval:	7
Disapproval:	0
Abstain:	0

[redacted] **Protocol GT0503290301,** "A safety and efficacy trial of lethally irradiated allogeneic pancreatic tumor cells transfected with the GM-CSF gene in combination with Erbitux (Cetuximab) for the treatment of advanced pancreatic adenocarcinoma"

The IBC noted that the protocol is similar to the investigator's previously approved study, save for the switch from BioReliance as the supplier of the material to the JHU GMP facility. The IBC felt Dr. [redacted] presentation covered any issues regarding quality control of the material and moved to approve the protocol **GT0503290301** pending FDA approval:

For Approval: 7
Disapproval: 0
Abstain: 0

[redacted] **Protocol GT0503290101,** "A phase I dose ranging study of the safety, tolerability, and immunogenicity of a 3 dose regimen of the MRKAd5 HIV-1 trigene and the MRKAd6 HIV-1 trigene vaccines alone and in combination in healthy adults."

The IBC noted that the protocol involves agents that have been previously approved by the IBC. One addition is the inclusion of both Ad5 and Ad6 due to the chance that someone may be refractory to the treatment due to prior exposure to one or the other of the adenovirus strains. The inclusion of two different strains is hoped to avoid this problem.

The IBC moved to approve protocol **GT0503290101** pending FDA approval:

For Approval: 7
Disapproval: 0
Abstain: 0

OLD BUSINESS:

1) [redacted] **Protocol GT0502210201** Safety and immunogenicity of one and two doses of the live, attenuated oral ETEC candidate vaccine BB01 in healthy adults (Stage I) followed by a conditional challenge stage with a virulent ETEC strain (Stage II) – a phase I, randomized, double-blind, placebo-controlled study.

The IBC received and discussed the response to the letter generated by the IBC to the PI sent last month. It was noted that the FDA is satisfied with the study at this point. Additional concern was regarding what happened to the suggestion that chlorox be used to treat waste in the subject's home toilets during the vaccination stage. Also, a question was raised regarding what it was that convinced the FDA that outpatient was ok given some of the discussion provided in transcripts the PI submitted in the response letter. Dr. Hayward said he would pursue these issues with the PI.

2) [redacted] **Protocol GT0502210101** "A long-term follow-up study to evaluate the safety of ex-vivo cultured adult human mesenchymal stem cells Provacel in subjects following acute myocardial infarction."

It was noted that the investigator did not respond to the IBC's letter. During discussions it was pointed out that we do not regulate tissue transplants on campus and that this study would fall under that "umbrella". Thus, the IBC decided to not pursue a response from Dr. [redacted].

3[redacted] **NIH Compliance Issue**
The IBC membership discussed the Compliance issues discovered at [redacted].
Dr. Dahl and Dr. Hayward noted that responses have been received from Drs. [redacted], [redacted], and [redacted]. No responses have been received from Drs. [redacted] or [redacted]. Dr. Hayward said he would pursue these responses.

NEW BUSINESS:

1) JHU Singapore

Dr. Dahl reported that Kam Wai-Kuen, the Biosafety Officer for JHU Singapore had contacted his office regarding IACUC review, IRB review and IBC review assistance. Dr. Dahl reported he contacted Dr. Nancy Ator of the IACUC and Dr. Michael Klag of the SOM IRB for guidance. Dr. Ator reported that Mike Amey had told her that the IACUC did not do JHU Singapore work. Dr. Klag expressed interest in JHU Singapore's IRB issues and agreed to correspond with Kam Wai-Kuen directly. Dr. Dahl asked the IBC for guidance regarding IBC assistance and the issues were discussed including:

1) lab inspections
2) external members from the community
3) compliance issues and enforcement

[redacted]

Recombinant DNA/Pathogen Research Registrations

7 research registrations were presented for IBC consideration. All were approved.

The meeting was adjourned at 4:20 pm

See attached sheets for Research Registration information

Institutional Biosafety Committee Registrations
March 29, 2005 Meeting
Registrations from 2/4/05 -- 3/29/05

Title	IBC#	BSL	ABSL	Yes	No	Abstain
Development of An Alzheimer's Disease Rat Model Using Lentiviral Vectors Lentiviral vector will be used to transduce amyloid precursor protein, siRNA and other AD genes into rat. DN--Uses recombinant DNA and viral vectors in rat. *Supporting Document-Pathogen registration for Lentivirus*	DN0503080101	2	2	7	0	0

Ocular Evaluation of Viral Vectors Containing Anti-angiogenic Factors, Anti-proliferative Factors and reporter genes. Adeno-associated viral, adenoviral, and lentiviral vectors will be used to transduce anti-angiogenic and anti-proliferative genes into animals. DN--Uses recombinant DNA and viral vectors in animals *Supporting Document-Pathogen registration for Adenovirus* *Supporting Document-Pathogen registration for Adeno-associated Virus* *Supporting Document-Pathogen registration for Lentivirus*	**DN0503090101** P0502180101 P0502180201 P0502180301	**2**	**2**	**7**	**0**	**0**
A method of drug delivery for control of Schistosomiasis and other cercarid-derived trematode infections Snails will be maintained infected with Schistosoma mansoni for studies of infection in mice. *Pathogen registration for Schistosoma mansoni*	**P0503290101**	**2**	**2**	**Hold for more info**		
Role of Rho-GTPase in the Trafficking of CFTR Clostridium difficile toxin B (TxB) will be used to treat cultured cells to elucidate the mechanism of up-regulation of CFTR by TxB. *Toxin registration for Clostridium difficile toxin B*	**T0503030101**	**2**	**NA**	**8**	**0**	**0**
Transduction of Mouse Retina with Defective Lentivirus Lentiviral vector (ViraPower) from Invitrogen will be used to transduce endothlin-2 promoter-GFP into cultured cells and mouse. DN--Uses recombinant DNA and viral vectors in cultured cells and mouse. *Supporting Document-Pathogen registration for Lentivirus* *Human Tissue Registration--Laboratory*	**DN0502250101** B0502250101 B0502250101	**2**	**2**	**7**	**0**	**0**
The Role of Narp in Drug Abuse	**DN0503100101**	**2**	**2**	**7**	**0**	**0**

Adeno-associated viral vector will be used to transduce Narp wild type and mutant genes into cultured cells and animals DN--Uses recombinant DNA and viral vectors in cultured cells and animals. *Supporting Document-Pathogen registration for AAV*	P0503100101					
Radiosensitivity of Fungal Organisms Cryptococcus neoformans will be cultured, irradiated and re-plated for colony formation. *Pathogen registration for Cryptococcus neoformans*	**P0503180101**	**2**	**NA**	**7**	**0**	**0**
RTP801 cDNA Delivery for Gain of Function Studies in Emphysema RTP801 cDNA will be transfected into E. coli, then isolated, purified and deliver into mouse lung via intratracheal instillation. DN-- Recombinant DNA will be used in cultured cells and mice	**DN0503010101**	**2**	**1**	**7**	**0**	**0**
A Mouse Model of Oncogenic Hedgehog Signaling in the Lung Adenoviral vector will be used to transduce Cre recombinase into mouse. DN--Uses recombinant DNA and viral vectors in cultured cells and animals. *Supporting Document-Pathogen registration for AV* *Human Tissue Registration--Laboratory*	**DN0503110101** P0503110101 B0411120201	**2**	**2**	**7**	**0**	**0**
Arrhythmias in Cultured Cardiac Cell Monolayer Adenoviral and lentiviral vectors will be used to transduce Ca2+ and K+ ion channels, GFP, murine ET-1, CT-1 and FGF-2 into cultured cells. DN--Uses recombinant DNA and viral vectors in cultured cells *Supporting Document-Pathogen registration for Adenovirus* *Supporting Document-Pathogen registration for Lentivirus* *Human Tissue Registration--Laboratory*	**DN0502020101** P0502020101 P0502020201 B0502020101	**2**	**NA**	**7**	**0**	**0**

Construction of Virus Like Particles of Avian Influenza A Virus	**DN0502010101**	**2**	**NA**	**7**	**0**	**0**
The genes from influenza A will be subcloned and expressed using baculovirus express vectors.						
DN– Recombinant DNA will be used in cultured cells.						
Supporting Document-Pathogen registration for Baculovirus	P0502020501					
Etiology of Giant Cell Arteritis	**P0502010101**	**2**	**2**	**7**	**0**	**0**
Human coronaviruses from ATCC will be used as a positive control to screen Giant Cell Arteritis (GCA) tissue banks for various viruses.						
Pathogen registration for human coronavirus						

Johns Hopkins Institutional Biosafety Committee

JHU IBC Minutes for April 18, 2005
Room B-600, 2024 E. Monument Street Building

Members Present: Dr. Hayward, Chair; Dr. Adams, Dr. Dahl, Dr. Maouyo, Dr. Margolick, Dr. Pan, Dr. Scott

Members Absent: Ms. Biedrzycki (Leave of Absence), Dr. Borrello, Ms. MacAuley, Dr. Norris, Dr. Rade

Guests: Dr. [redacted]

The meeting was called to order at 3:17 pm.

INVESTIGATOR PRESENTATION, [redacted] Protocol, GT0504180101, A Phase 2, Randomized, Double-blind, Placebo-controlled, Parallel-group, Multicenter, Dose-selection study of Ad2/Hypoxia Inducible Factor (HIF)-1alpha/VP16 in Patients with Intermittent Claudication (IMPROVE) with Amendment 1, dated 6 December 2004.

The principal investigator gave a brief overview of the study. The previous VegF165 adeno trial was halted prior to initiation. FGF naked plasmid DNA studies have previously been done. Evaluation involved a walking assay to the point of pain and then until the patient couldn't continue. It was a company decision to favor adenovirus over naked plasmid DNA. Current evaluation is blood pressure at a given arm to leg ratio. This should be 1.0. The vector persistence should be about two weeks or so. Modified HIF a peaked at two days with small amounts persisting up to 60 days.

Members of the IBC asked a number of questions including:

Q: Is the PI aware of any reports of neovascularization of the eye?
A: No. There was a vascularization tumor reported, but it is hard to know if it was related to the study.

Q: Were there any IRB concerns?
A: No. Is waiting for conflict of interest approval.

Q: Who will administer the virus? Will eye protection be used?
A: Dr. [redacted], the PI. Yes, eye protection will be used.

Q: There was crude prep lethatlity observed in animal studies, but not purified prep. Is the origin of the lethality known?
A: The PI will query the company on this.

With no further questions, Dr. [redacted] was thanked for her presentation and left the IBC meeting.

Later in the meeting the IBC moved to approve protocol GT0504180101:

For Approval:	7
Disapproval:	0
Abstain:	0

APPROVAL OF MINUTES

The Minutes for March 2005 were approved with 6 members voting for approval and one abstention due to the member having not read the minutes.

OLD BUSINESS:

1) Status of IBC Update
Dr. Hayward and Dr. Dahl briefed the IBC membership on the meetings of Biosafety and the Deans regarding the IBC and revision of the IBC policy, HSE500.

2) [redacted] Human Gene Transfer Non-compliance Update
Dr. Hayward and Dr. Dahl discussed the various protocols from the [redacted] that were never submitted for IBC approval. Responses from PIs, specifically Dr. [redacted] and Dr. [redacted], indicate that they understood the vaccine exemption in the NIH Guidelines to refer to IBC approval as well. It was noted that the language could be clearer in the Guidelines.

Dr. [redacted] protocols from [redacted] records show adenoviral studies: [redacted] 008, 012, 016, 018, 019, and 022 involved recombinant DNA. Dr. Hayward noted that a protocol was reviewed for Dr[redacted] in late 2000/early 2001 which appears to be [redacted] 014. On this, [redacted] initially considered the protocol exempt from IBC review because of the vaccine exemption noted above. Eventually they did produce an Appendix M. When Dr. [redacted] took over [redacted] he stated there would be a lot to review, but we only did one, [redacted] 018 for Dr. [redacted]. We never saw the others. Dr. [redacted] thought we did them all.

The viral vectors and inserts under review include:
Ad5 with expression of gag
Ad5 with expression of gag, env, and nef
Ad6 as well – trivalent

Note, [redacted] 18 is the exact same protocol done by [redacted] in Malawi.

The IBC reviewed the information provided by Dr. [redacted] on the above protocols.

The IBC also reviewed Protocol **V520 022-01**
This protocol is the same as the others that have been looked at except it is used in hepatitis patients. 20 patients receive the higher dose, 20 receive the lower dose. It is not clear if there is any evidence of efficacy. Upper dose is 10^9 to 10^{10} particles/ml. This is an acceptable range.

The IBC moved to approve the protocols retroactively with the advisory that eye protection is appropriate when recombinant viral agents are used and splash or spray is possible.
Motion to approve is to be worded theat:

"The IBC would have approved these studies"

For Approval: 7
Disapproval: 0
Abstain: 0

[redacted]

4) JHU Singapore
No new information is available. The IBC membership suggested that the ability of the JHU IBC to provide proper review services to JHU Singapore would be difficult due to infamiliarity with the laboratory spaces and issues of oversight and jurisdiction.

5) Flow Cytometry issues
Dr. [redacted] briefly touched on biosafety issues regarding cell sorters.

With an open chamber you will spread droplets
Dilution factor is 106 so it is greatly diluted.
No infection has been shown from operation of a Flow cytometry center
PAPR is available, but not required in Dr. [redacted] facility.

Recombinant DNA/Pathogen Research Registrations
7 research registrations were presented for IBC consideration. All were approved.

The meeting was adjourned at 5:05 pm

Institutional Biosafety Committee Registrations
April 18, 2005 Meeting
Registrations from 3/18/05 -- 4/06/05

Title	IBC#	BSL	ABSL	Yes	No	Abstain
Yellow Fever Vaccine Epitope Discovery Yellow fever vaccine strain 17DD will be used to immunize mouse for identification of immune T-cell epitopes of the viral protein. *Pathogen registration for Yellow fever vaccine strain 17DD*	P0504060101	2	2	7	0	0
Structure-based Thermodynamic Studies of Molecular Recognition HMG-CoA reductase, malarial protease, plasmepsin, B-lactamase, HIV-1 protease, Nef, gp120 and SARS protease will be transfected into cultured cells	DN0504130101	2	NA	7	0	0

DN--Uses plasmid-based recombinant DNA including HMG-CoA reductase, malarial protease, plasmepsin, B-lactamase, HIV-1 protease, Nef, gp120 and SARS protease transfected in cells						
Rac I Function in Sympathetic Axon Growth	**DN0503180101**	**2**	**NA**	**7**	**0**	**0**
Adenoviral vector (Ad Easy system) will be used to transduce Racl N17 into cultured cells.						
DN--Uses recombinant DNA and viral vectors in cultured cells.						
Supporting Document-Pathogen registration for Adenovirus	**P0503180201**					
Human Tissue Registration--Laboratory	**B0503180201**					
The Effect of LPS, TG, non-methylated CpG, and Bacterial Injection in the Prostate of MSR1 Knockout Mice	**P0504040101**	**2**	**2**	**7**	**0**	**0**
Stenotrophomonas maltophilia from ATCC will be cultured, killed by paraformaldehyde and injected into MSR1 knockout mice						
Pathogen registration for Stenotrophomonas maltophilia						
The Effect of LPS, TG, non-methylated CpG, and Bacterial Injection in the Prostate of MSR1 Knockout Mice	**P0504040201**	**2**	**2**	**7**	**0**	**0**
Corynebacterium matruchotii from ATCC will be cultured, killed by paraformaldehyde and injected into MSR1 knockout mice						
Pathogen registration for Corynebacterium matruchotii						
The Effect of LPS, TG, non-methylated CpG, and Bacterial Injection in the Prostate of MSR1 Knockout Mice	**P0504040301**	**2**	**2**	**7**	**0**	**0**
Chlamydia trachomatis from ATCC will be killed by paraformaldehyde and injected into MSR1 knockout mice						
Pathogen registration for Chlamydia trachomatis						
The Effect of LPS, TG, non-methylated CpG, and Bacterial Injection in the Prostate of MSR1 Knockout Mice	**P0504040401**	**2**	**2**	**7**	**0**	**0**
Neisseria gonorrhoeae from ATCC will be killed by paraformaldehyde and injected into MSR1 knockout mice						

Pathogen registration for Neisseria gonorrhoeae						
The Effect of LPS, TG, non-methylated CpG, and Bacterial Injection in the Prostate of MSR1 Knockout Mice	**P0504040501**	**2**	**2**	**7**	**0**	**0**
Pseudomonas fluorescens from ATCC will be cultured, killed by paraformaldehyde and injected into MSR1 knockout mice						
Pathogen registration for Pseudomonas fluorescens						
Studies pf Pathogenesis of Hepatitis Viruses	**DN0503310101**	**2**	**NA**	**7**	**0**	**0**
The pNL4-3.Luc.R-E- HIV proviral, lentiviral and the pantropic retroviral vectors will be used to transduce HCV envelope E1E2 and hTERT into cultured cells.						
DN--Uses recombinant DNA and viral vectors in cultured cells						
Supporting Document-Pathogen registration for HIV provirus	**P0503310101**					
Supporting Document-Pathogen registration for Lentivirus	**P0503310201**					
Supporting Document-Pathogen registration for Retrovirus	**P0503310301**					
Human Tissue Registration--Laboratory	**B0503310101**					
Interaction of HIV with Brain Endothelium	**DN0503250101**	**3**	**NA**	**7**	**0**	**0**
HIV-1/GFP reporter vector will be generated by transfection of viral pseudo backbone and env into CD+ T cells. Pseudo viral particles will be incubated with human brain microvascular endothelial cells (HBMEC) to assess the mechanism of entry HIV-1 into the brain.						
DN--Uses recombinant DNA and viral vectors in cultured cells.						
Supporting Document-Pathogen registration for HIV	**P0403240102**					
Human Tissue Registration--Laboratory	**B0403240102**					

Johns Hopkins Institutional Biosafety Committee

JHU IBC Minutes for May 23, 2005
Room B-600, 2024 E. Monument Street Building

Members Present: Dr. Hayward, Chair; Dr. Adams, Dr. Borrello, Dr. Dahl, Dr. Kobrin, Ms. MacAuley, Dr. Margolick, Dr. Maouyo, Dr. Pan, Dr. Rade

Members Absent: Ms. Biedrzycki (Leave of Absence), Dr. Norris, Dr. Scott

Guests: None

The meeting was called to order at 1:15 pm.

WELCOME TO NEW IBC MEMBER
The Chair welcomed Dr. Barry Kobrin to the IBC and noted Dr. Kobrin's scientific expertise and experience with the GMP facility on campus are welcome additions.

NEW BUSINESS:

[redacted] **Protocol GT0505230101** "Pilot study of rituximab, high dose cyclophosphamide, and GM-CSF based immunotherapy for relapsed Hodgkin's lymphoma."

The protocol was described as "basically GVAX with EBV antigens". The protocol uses an allogeneic tumor vaccine (KGEL vaccine) derived from a human cell line (K562) engineered to express GM-CSF and the Epstein-Barr virus tumor antigen LMP-2. This vaccine will be used in conjunction with rituximab and cyclophosphamide. This is a pilot study and will involve 20 patients. There is no placebo arm of the study.

The following comments were made during discussion:

- 50% of Hodgkin's lymphomas are caused by EBV.

- Most Hodgkin's patients are EBV+. Perhaps 70% or 2/3. The other 30% or 1/3 are presumably antigenic candidates for any lymphoma not specifically Hodgkin's.

- The construct in the K562 cells retains the antibiotic resistance.

- The dose of GM-CSF received is about half that given if using the recombinant protein.

- Graft Engineering Lab (GEL) takes possession of frozen cells from the GMP facility.

The patients are relapsed, but have not had a bone marrow transplant (BMT). This is an issue. There are data that BMT can salvage a patient. The study may be precluding a patient from an effective treatment. This is an issue for the IRB to decide, not biosafety however.

The IBC moved to approve protocol **GT0505230101**:

For Approval: 9
Disapproval: 0
Abstain: 1

[redacted] appeal for BSL1 containment rather than BSL2

Dr. Dahl reported that Dr. [redacted] will be expressing specific proteases and other proteins from HIV and other agents to perform biophysical analyses. The proteins are expressed in E. coli. Only single genes expressing single proteins are used. The laboratory does not maintain full genomes of any of the agents studied. Dr. Dahl stated that he thought BSL1 was appropriate.

The IBC moved to approve BSL1 containment for the project:

For Approval: 10
Disapproval: 0
Abstain: 0

Report of "Important Event"
[redacted] Protocol GT0308180101, "A Phase I Vaccine Safety and Chemotherapy Dose-Finding Trial of an Allogeneic GM-CSF-secreting Breast Cancer Vaccine Given in a Specifically Timed Sequence with Immunomodulatory Doses of Cyclophosphamide and Doxorubicin."

The IBC noted that a new category of events termed the Important Event has been added by the SOM IRB. The IBC discussed the new category. It was decided that the IBC would acknowledge the receipt of important events, but not formally review these documents.

OLD BUSINESS:

1) Status of IBC charter. Dr. Dahl stated that JHU policy HSE500 which describes the functions of the IBC was reworked by Dr. Bernacki in April and scheduled to be voted on at the Joint Committee on Health Safety and Environment in May. This vote was delayed due to concerns expressed from Dean Krag's office at BSPH. Dr. Dahl will meet with staff from Dean Krag's office to modify the document.

2) OBA Update. Dr. Dahl reported that he had not received a response to the request from OBA for additional information regarding the vaccine trials in BSPH that had not received IBC review.

[redacted]

[redacted]

Recombinant DNA/Pathogen Research Registrations
8 research registrations were presented for IBC consideration. All were approved.

The meeting was adjourned at 3:30 pm
See attached sheets for Research Registration information

Institutional Biosafety Committee Registrations
May 23, 2005 Meeting
Registrations from 4/7/05 -- 5/5/05

Title	IBC#	BSL	ABSL	Yes	No	Abstain
Retroviral Regulatory Sequences Rous sarcoma viral genes will be transfected into cultured cells. DN--Uses recombinant DNA and viral vectors in cultured cells	**DN0505050201**	**2**	**NA**	**10**	**0**	**0**
Short-term and Long-term Gene Therapy of Dominant Negative RhoA/Rho-kinase for Erectile Dysfunction Adeno-associated viral vector from Stratagene will be used to transduce RhoA gene into cultured cells and rat. DN--Uses recombinant DNA and viral vectors in cultured cells and animals. *Supporting Document-Pathogen registration for Adeno-associated virus* *Human Tissue Registration--Laboratory*	**DN0505050101** P0505050101 B0505050101	**2**	**2**	**10**	**0**	**0**
Molecular Evolution of Enterotoxigenic B. Fragilis Bacteroides Fragilis toxin gene will be cloned and expressed in E. coli. DN--Uses plasmid-based recombinant DNA in cultured cells and animals. *Supporting Document-Pathogen registration for Bacteroides Fragilis*	**DN0505020101**	**2**	**2**	**10**	**0**	**0**
Molecular Evolution of Enterotoxigenic B. Fragilis Bacteroides Fragilis will be used to infect rabbits. *Pathogen registration for Bacteroides Fragilis*	**P0505020301**	**2**	**2**	**10**	**0**	**0**
The Promise of Hypoxia Inducible Factor 1 Alpha (HIF1a) for a Bioengineered System with Potential to Heal War Wounds	**P0505020201**	**2**	**2**	**10**	**0**	**0**

Pseudomonas aeruginosa will be cultured and applied onto cutaneous wounds in rat *Pathogen registration for Pseudomonas aeruginosa*						
Signal Transduction Lenti siRNA vector from GenScript will be used to silence the genes that involving cell signaling in cultured cells. *Pathogen registration for Lentivirus*	**P0505200101**	**2**	**NA**	**10**	**0**	**0**
Molecular Mechanisms of Oxidative Metabolism Lentiviral vector will be used to transduce the genes that control metabolic pathway into cultured cells. *Pathogen registration for Lentivirus*	**P0505050201**	**2**	**NA**	**10**	**0**	**0**
Plasmodium and the Blood Brain Barrier in cerebral Malaria Plasmodium falciparum will be cultured, purified and used to infect human brain endothelial cells. *Pathogen registration for Plasmodium falciparum*	**P0505030101**	**2**	**NA**	**10**	**0**	**0**

Johns Hopkins Institutional Biosafety Committee

JHU IBC Minutes for June 20, 2005
Room B-600, 2024 E. Monument Street Building

Members Present:	Dr. Hayward, Chair; Dr. Adams, Dr. Dahl, Dr. Kobrin, Dr. Maouyo, Dr. Norris, Dr. Pan, Dr. Scott
Members Absent:	Ms. Biedrzycki (Leave of Absence), Dr. Borrello, Ms. MacAuley, Dr. Margolick, Dr. Rade
Guests:	None

The meeting was called to order at 3:16 pm.

APPROVAL OF MINUTES

The Minutes for May 2005 were unanimously approved.

OLD BUSINESS:

1) BSPH Non-Compliance Update
Dr. Dahl noted that OBA had not responded to the additional information Dr. Dahl provided to clarify issues OBA had inquired about.

2) IBC Policy Update
Dr. Dahl reported that Ms. Leah Mendelsohn, JD, from the Bloomberg School of Public Health were in the process of updating HSE500, the policy that defines the working of the IBC. This work was initiated at the request of the Research Deans and Dr. Bernacki.

3) Risk of Pathogens/Infectious Agents on Campus Worksheet
Dr. Dahl noted that two previous attempts to get responses to the relative risk of the agents listed in the database had not received replies. Dr. Dahl handed out the form for the IBC members to consider.

NEW BUSINESS:

1) Potential for a New Meeting Time
Dr. Dahl reported on the survey that was sent to the IBC membership concerning a potential change in meeting time for the full IBC. A chart was handed out indicating that the 3rd Monday afternoon, the 3rd Tuesday noon, and the fourth Monday afternoon were the best so far. Dr. Dahl indicated that a number of IBC members had yet to respond to the survey.

2) Discussion of Recent RAC Meeting and the New CDC/NIH Influenza Guidelines
Dr. Dahl reported on the recent RAC meeting (6/16/05) that discussed changes in the handling of influenza research proposed by the CDC and NIH. Dr. Dahl reported that the new BMBL (5th edition) is expected to be released at the end of the year. Currently influenza is listed in the 4th edition as an agent requiring BSL2 containment. The new guidelines propose to differentiate "contemporary" from "non-contemporary" strains

of flu. Contemporary strains would be allowed to be manipulated at BSL2. Non-contemporary would require BSL3. In addition, high-risk avian strains would require BSL3 containment as well. Dr. Dahl reported that there was much discussion among the RAC members regarding the ability of IBCs to identify contemporary from non-contemporary. There was some discussion that all influenza should be at BSL3 with the IBC being allowed to downgrade to BSL2 based on a risk assessment

3) Appeal of BSL3 Assignment for M. bovis, BCG

Dr. [redacted] forwarded a letter for distribution to the IBC requesting that the IBC reconsider the BSL3 assignment received for his work with M. bovis in rabbits. The IBC membership noted Dr. [redacted] comments but deferred to the BMBL which expressly states that BSL3 is the appropriate containment except mice and guinea pigs which may be handled at BSL2.

Recombinant DNA/Pathogen Research Registrations

12 research registrations were presented for IBC consideration. 10 were approved and 2 were held for additional information.

The meeting was adjourned at 5:00 pm

Institutional Biosafety Committee Registrations
June 20, 2005 Meeting
Registrations from 5/6/05 – 6/10/05

Title	IBC#	BSL	ABSL	Yes	No	Abstain
Properties and Function of Keratins in Epithelia	**DN0505120101**	**2**	**NA**	**8**	**0**	**0**
Adenoviral vector will be used to transduce mouse keratin 14 gene into cultured cells.						
DN--Uses recombinant DNA and viral vectors in cultured cells						
Supporting Document-Pathogen registration for Adenovirus	*P0505120101*					
Human Tissue Registration--Laboratory	*B0505120101*					
Combinatorial Vaccination Strategies for Breast Cancer Treatment	**DN0506200101**	**2**	**2**	**8**	**0**	**0**
Lentiviral vectors will be used to transduce cells which will subsequently be transferred to animals.						
DN--Uses recombinant DNA and viral vectors in cultured cells						
Supporting Document-Pathogen registration for Lentivirus	*P0506200101*					
Analysis and Recapitulation of Diabetes-Resistance Caused by Gld Mutation	**DN0506090201**	**2**	**2**	**8**	**0**	**0**
pFIV-Hi-copGFP from System Bioscience will be used to silence the Fas ligand in mice.						
DN--Uses recombinant DNA and viral vectors in cultured cells and animals.						
Green Fluorescent Protein as A Reporter for neural Cells In Vitro and In Vivo	**DN0506090101**	**2**	**2**	**8**	**0**	**0**

The plasmid containing green fluorescent protein will be transfected into mammalian cells and rat. DN--Uses plasmid-based recombinant DNA transfected in cultured cells and animals.						
Local and Retrograde Signaling by Target-derived Neurotrophins Adenoviral and sindbis viral vectors will be used to transduce the family of Trk receptors into cultured neurons. DN--Uses recombinant DNA and viral vectors in cultured cells. *Supporting Document-Pathogen registration for Adenovirus* *Supporting Document-Pathogen registration for Sindbis virus*	**DN0506030101** *P0506030101* *P0506030201*	**2**	**NA**	**8**	**0**	**0**
Immunopathogenesis of Lung Allograft Rejection Recombinant murine CMV (MCMV) will be constructed by inserting b-gal expression cassette into the MCMV genome and used to infect mice. DN--Uses recombinant DNA technique to creat the recombinant virus and introduces the recombinant virus into animals. *Supporting Document-Pathogen registration for MCMV*	**DN0506080101** *P0506080101*	**2**	**2**	**8**	**0**	**0**
Andenoviral Transfection of Cultured Neurons and Glia Adenoviral vector will be used to transduce GFP into cultured cells. DN--Uses recombinant DNA and viral vectors in cultured cells. *Supporting Document-Pathogen registration for Adenovirus*	**DN0506010101** *P0506010101*	**2**	**NA**	**8**	**0**	**0**
Engraftment of Hepatocytes in Immunodeficient RAG2 and IL2-Rrc Ko Mice Human hepatocyte growth factor(HGF), matrix metalloproteinase 9 (MMP9) and stromal cell derived factor-1 (SDF-1) will be sub-cloned into plasmid vector. The purified plasmids will be transfected into mammalian cells as well as injected into mice. DN--Uses plasmid-based recombinant DNA transfected in cultured cells and animals.	**DN0506080201**	**2**	**1**	**8**	**0**	**0**
Immune Response to Pathogens in Mice Engrafted with Human CD34+ Peripheral Blood Stem Cells Attenuated adenovirus will be used to infect mice. *Pathogen registration for Adenovirus*	**P0506090101**	**2**	**2**	**8**	**0**	**0**

The Role of Narp in the Immune System	**T0505270101**	**2**	**NA**	**Hold for more information**		
Taipoxin will be conjugated to Sepharose beads, which will be used to concentrate Narp.						
Toxin registration for Taipoxin						
Axon Regeneration	**DN0506100201**	**2**	**NA**	**Hold for more information**		
Lentiviral vector will be used to transduce EGFP into cultured cells.						
DN--Uses recombinant DNA and viral vectors in cultured cells.						
Supporting Document-Pathogen registration for Lentivirus	*P0506100301*					
Pathogenesis of Enterotoxigenic Bacteroides fragilis Infections	**DN0506100101**	**2**	**NA**	**8**	**0**	**0**
Lentiviral and retroviral vectors will be used to transduce human E-cadherin gene and mutated T cell factor into cultured cells.						
DN--Uses recombinant DNA and viral vectors in cultured cells.						
Supporting Document-Pathogen registration for Lentivirus	*P0506100101*					
Supporting Document-Pathogen registration for Retrovirus	*P0506100201*					

Johns Hopkins Institutional Biosafety Committee

JHU IBC Minutes for July 18, 2005
Room B-600, 2024 E. Monument Street Building

Members Present: Dr. Hayward, Chair; Dr. Dahl, Dr. Kobrin, Dr. Maouyo, Dr. Margolick, Dr. Pan, Dr. Rade, Dr. Scott

Members Absent: Dr. Adams, Ms. Biedrzycki (Leave of Absence), Dr. Borrello, Ms. MacAuley, Dr. Norris

Guests: None

The meeting was called to order at 3:15 pm.

APPROVAL OF MINUTES

The Minutes for June 2005 were unanimously approved.

NEW BUSINESS:

1) [redacted] **Protocol, GT0507180101** "A phase I, open-label study to evaluate the safety and tolerability of recombinant HIV-1 vaccines in HIV-1 infected young adults with control of HIV-1 replication and on stable highly active antiretroviral therapy (HAART)."

Dr. Dahl reported that an invitation had been extended to Dr. [redacted] to attend the meeting or to provide answers to questions via e-mail. No responses were received however the Investigators Brochure was provided. Dr. Dahl distributed copies of the brochure from [redacted] for review.

a) The study uses the same constructs inserted into both Modified Vaccinia (Ankara) (MVA) and Fowl Pox (FP).
b) Dosage is $10^8 - 10^9$ pfu which is in an acceptable range for this type of vector.
c) 16 patients are proposed for JHU. No placebos will be used in the study which may be a concern for the IRB.
d) No problems have been noted in studies of Macaques so far.
e) A question was raised regarding immunocompromised patients and their tolerability of viral-based vaccines. It was pointed out the the proposed patients have pretty high CD4 counts so the viral vectors do not get out of control. The question was then asked what would happen if the patients lost viral control—CD4 goes down. It was noted that MVA has been used a lot in HIV+ people and is not expected to persist.

The Committee motioned to allow a subgroup consisting of Dr. Dahl, Dr. Hayward, Dr. Maouyo and Dr. Margolick, to meet and vote once sufficient answers are received from Dr. [redacted].
The IBC moved to vote:

For Approval:	8
Disapproval:	0
Abstain:	0

OLD BUSINESS:

1) IBC Policy Update
Dr. Dahl distributed a draft copy of the updated policy for IBC review. Dr. Dahl stated a final copy must be available by the August Joint Committee Meeting. IBC members raised questions regarding Responsibility of the Principle Investigators, database maintenance, online access to registration forms and posting any educational information on the website. Dr. Dahl will inform the Committee once final Draft is complete.

2) Electronic Submissions
IBC members discussed the feasibility of establishing electronic IBC registration submissions. The IBC recommended an effective date of January 2006 for all registrations being presented for IBC approval to be completed electronically.

The IBC moved to vote:

For Approval:	8
Disapproval:	0
Abstain:	0

3) Meeting Time
Dr. Dahl stated consensus had not been made in reference to changing the meeting time. Dr. Hayward suggested the meeting remain on the third Monday of every month but switching the start time to 2:45 instead of 3:00. Committee members were in favor.

4) Appeal of BSL3 Assignment for M. bovis, BCG
IBC members are awaiting clarification from the CDC in reference to level of containment. IBC members discussed housing facilities for the rabbits and the question regarding cross-contamination of other animals in same housing units. The IBC will hold voting until further information is received.

5) Biographical Sketches
Dr. Dahl proposed sharing biographical sketches amongst IBC Committee members. The IBC members were in favor and packets will be distributed with materials for next month's full IBC meeting.

Recombinant DNA/Pathogen Research Registrations
12 research registrations were presented for IBC consideration. 10 were approved and 2 were held for additional information (see next page).

The meeting was adjourned at 5:03 pm

Institutional Biosafety Committee Registrations
July 18, 2005 Meeting
Registrations from 6/11/05 -- 7/15/05

Title	IBC#	BSL	ABSL	Yes	No	Abstain
Yellow Fever Vaccine Epitope Discovery Sequences of Env, NS1, Ns2, NS3, NS5, capsid and pre-M & M from yellow fever virus will be sub-cloned into plasmid vector and injected into mice DN--Uses plasmid-based recombinant DNA to sub-clone fragment from yellow virus and inject into animals. *Supporting Document-Pathogen registration for Yellow fever virus*	**DN0507070101** *P0504060101*	**2**	**1**	**8**	**0**	**0**
Retroviral Regulatory Sequences Rous sarcoma virus will be used to infect cells. *Pathogen registration for Rous sarcoma virus*	**P0506210101**	**2**	**NA**	**8**	**0**	**0**
Retroviral Regulatory Sequences Avian leukosis virus will be used to infect cells. *Pathogen registration for Avian leukosis virus*	**P0506210201**	**2**	**NA**	**8**	**0**	**0**
Carcinogens in Biosolids as Determinants of Human Morbidity and Mortality Individual samples of biosolids will be homogenized, extracted and purified for analyzing the carcinogens in the samples. *Pathogen registration for Bio-sludge*	**P0507120101**	**2**	**NA**	**8**	**0**	**0**
Neurotrophin Protection of Hypoxic Ischemic Brain Injury Adeno-assocated viral vector will be used to transduce FGF-1 and NP1 into cultured cells and animals. DN--Uses recombinant DNA and viral vectors in cultured cells and animals *Supporting Document-Pathogen registration for adeno-associated virus (AAV)*	**DN0506240101** *P0506240101*	**2**	**2**	**8**	**0**	**0**
Hypothalamic Control of Food Intake	**DN0506240201**	**2**	**2**	**8**	**0**	**0**

Adenoviral and lentiviral vectors will be used to transduce CPT, SCD, MCD, ACC, LacZ and GFP into cultured cells and animals.						
DN--Uses recombinant DNA and viral vectors in cultured cells and animals						
Supporting Document-Pathogen registration for Adenovirus	*P0506240201*					
Supporting Document-Pathogen registration for Lentivirus	*P0506240301*					
Supporting Document-Human tissue registration	*B0506240101*					
Involvement of Fibroblast Growth Factor in the Development of Retinal Vasculature	**DN0507050101**	**2**	**NA**	**8**	**0**	**0**
Lentiviral vector will be used to transduce DNA repair enzymes, antioxidants, antiangiogenic proteins and their promoters into cultured cells.						
DN--Uses recombinant DNA and viral vectors in cultured cells.						
Supporting Document-Pathogen registration for Lentivirus	*P0507050101*					
Supporting Document-Human tissue registration	*B9212150113*					
Engraftment of Human CD34+ Hematopoietic Stem Cells in Immunodeficient RAG/IL2-Rgc Knockout Mice	**P0506270101**	**2**	**2**	**Hold for more information**		
Influenza virus H1N1 will be used to infect mice.						
Pathogen registration for Influenza virus						
Engraftment of Human Hepatocytes in Immunodeficient RAG/IL2-Rgc Knockout Mice	**P0506270201**	**2**	**2**	**Hold for more information**		
The serum from Hepatitis C virus (HCV) infected patients will be used to infect mice.						
Pathogen registration for Hepatitis C virus (HCV)						
Hepatitis C Recombination Incidence and Prevalence	**DN0507010101**	**2**	**NA**	**8**	**0**	**0**
Hepatitis C virus partial genomic segments obtained from human serum will be sub-cloned into plasmid vector.						
DN--Uses plasmid-based recombinant DNA to transfect hepatitis C virus partial genomic segments into E. coli DH5 alpha cells.						
Supporting Document-Pathogen registration for HCV	*P0507010101*					

Mouse Models of Human Granulocytic Anaplasmosis *Anaplasma phagocytophilum will be propagated in HL-60 cells and used to infect other cell cultures and mice.* *Pathogen registration for Anaplasma phagocytophilum*	**P0507060101**	**2**	**2**	**8**	**0**	**0**
Screening for Bioactive Molecules in Retinal Cell Culture Adeno-associated viral, sticky adenoviral, adenoviral and lentiviral vectors will be used to transduce GFP, cDNA of various neurotrophic factors (BDNF, CNTF, etc) and 2nd messenger signaling molecules into cells. DN--Uses recombinant DNA and viral vectors in cultured cells. *Supporting Document-Pathogen registration for Adeno-associated virus* *Supporting Document-Pathogen registration for Sticky Adenovirus* *Supporting Document-Pathogen registration for Adenovirus* *Supporting Document-Pathogen registration for Lentivirus* *Supporting Document-Human tissue registration*	**DN0507150401** *P 0507150101* *P 0507150201* *P 0507150301* *P 0507150401* *B9811020208*	**2**	**NA**	**8**	**0**	**0**

Johns Hopkins Institutional Biosafety Committee

JHU IBC Minutes for August 29, 2005
Room B-600, 2024 E. Monument Street Building

Members Present: Dr. Hayward, Chair; Dr. Adams, Dr. Borrello, Dr. Dahl, Dr. Kobrin, Ms. MacAuley, Dr. Margolick, Dr. Norris, Dr. Scott

Members Absent: Ms. Biedrzycki (Leave of Absence), Dr. Maouyo, Dr. Pan, Dr. Rade

Guests: Dr. [redacted]

The meeting was called to order at 11:27 pm.

APPROVAL OF MINUTES

The Minutes for July 2005 were unanimously approved.

Confidentiality Reminder

Dr. Dahl proposed the necessity of a form being created for distribution to Committee members to sign regarding confidentiality. The form will be drafted and distributed to Committee members for comment.

NEW BUSINESS:

1) [redacted] **Protocol GT0508290101,** "Phase I study to determine the safety, infectivity and tolerability of two doses of live attenuated recombinant cold passaged (cp) 45 parainfluenza type 3 virus vaccine, rHPIV3*cp*45, Lot PIV3 102A, delivered as nose drops to infants 6 to 12 months of age

Dr. [redacted] summarized and answered questions regarding the above submission.

--The study concerns a recombinant version of a previously studied, biologically-derived, attenuated virus.

--Purpose of this study is to confirm the recombinant virus behaves like the original.

-- Vaccine is manufactured by the NIH.

Dr. [redacted] stated that there were no expected problems with the study, but that the appearance post-innoculation of symptoms such as wheezing would be one reason for them to reconsider the trial.

The IBC moved to approve protocol **GT0508290101**:

For Approval: 9
Disapproval: 0
Abstain: 0

2) [redacted] **Protocol GT0508290201,** "Phase I Inpatient Study of the Safety and Immunogenicity of Live Influenza A Vaccine H5N1 (6-2) AA ca Recombinant (A/VietNam/1203/2004 x A/AnnArbor/6/60 ca), a

Live Attenuated Virus Vaccine Candidate for Prevention of Avian Influenza H5N1 Infection in the Event of a Pandemic"

Dr. [redacted] summarized and answered questions regarding the above submission.

-- Dr. [redacted] provided details regarding the unfortunate incident that occurred with her previously-approved study in the inpatient facility at [redacted]. An unruly patient became agitated and required police intervention. 5 does of Tamiflu were definitely taken due to it being given when they came n for check-ups. They were asked to take another pill at home, but it is not known if they complied with the request.

-- Three patients of the previous H9N2 study shed small amounts of virus $0.75 - 1.0 \times 10^1$ Those who had viral titer were pcr negative so this method needs to be made more robust. By concentration of nasal washings. Infective dose for humans of H9N2 is 10^4.

--H5N1 has same backbone as the H9N2 study. Multibasic cleavage site of H5N1 was removed (source of high pathogenicity due to allowing cleavage by other cellular enzymes) The virus derives all of its internal genes from AnnArbor

-- Study would start in the spring post flu season, April 1.

-- Dr. [redacted] indicated she would delay start if flu season was continuing past this date.

The IBC indicated the protocol would be approvable pending receipt of written statement regarding duration of flu season being April – September. That an extended flu season would delay the start of the study, that staff who may contract the vaccine strain from the patients be offered the opportunity to stay in the facility if they wished until the Tamiflu had a chance to take effect (2-4 days), and the suggestion that staff be sent home with N95 respirators or masks for protection of family members if they so desired. Further discussion regarding protection of family members will be discussed at next month's meeting.

The IBC moved to hold approval of protocol **GT0508290201**:

For Hold of Approval:	9
Disapproval:	0
Abstain:	0

3) BSL3 SOP

Dr. Dahl handed out a rough draft of a template to be used for Standard Operating Procedures for BSL3/ABSL3 Laboratories on campus. Dr. Dahl stated that certain details are missing and specifics are still needed. Committee members were asked to email questions and/or issues to Dr. Dahl. BSL3 SOPs are required annually from PIs working in BSL3 facilities.

OLD BUSINESS:

1) [redacted] Protocol

Subcommittee will meet to discuss protocol. Invitation will be made to Dr. [redacted] to attend.

2) [redacted] ABSL3 dilemma/update

The Committee motioned to convene a subgroup consisting of Dr. Dahl, Dr. Adams and Dr. Hayward with an invitation to Dr. [redacted] and Dr. [redacted] to discuss submission. The IBC moved to vote:

For Approval:	9
Disapproval:	0
Abstain:	0

3) Malawi Protocol Update

The Committee discussed forming a meeting to discuss Hopkins stance on outside IBC. Malawi protocol will be tabled for further discussion.

Recombinant DNA/Pathogen Research Registrations

8 research registrations were presented for IBC consideration. 7 were approved and 1 was approved pending confirmation of ATCC number.

The meeting was adjourned at 1:45 pm

Institutional Biosafety Committee Registrations
August 29, 2005 Meeting
Registrations from 7/16/05 – 8/29/05

Title	IBC#	BSL	ABSL	Yes	No	Abstain
Aerosol Mouse Model of Pneumococcal pneumonia Infectious aerosol containing Streptococcus pneumoniae will be used to infect mice. *Pathogen registration for Streptococcus pneumoniae*	P0507250101	3	3	9	0	0
Murine Aerosol Model of Pneumococcal pneumonia Infectious aerosol containing Bacteroides fragilis will be used to infect mice. *Pathogen registration for Bacteroides fragilis*	P0507280101	3	3	9	0	0
Manipulation of Autoimmune Disease in Mouse Models	P0508010101	2	2	9	0	0

Wild-type and attenuated Listeria monocytogenes will be used to infect mouse. *Pathogen registration for Listeria Monocytogenes*						
Alternative Lengthening of Telomeres Lentiviral vector from Invitrogen will be used to transduce GFP or a shRNA into cultured cells and mouse. *Pathogen registration for Lentivirus*	**P0508010201**	**2**	**2**	**9**	**0**	**0**
The Effect of LPS, TG, non-methylated CpG, and Bacterial Injection in the Prostate of MSR1 Knockout Mice Methylopilus methylotrophus from ATCC will be cultured, killed by paraformaldehyde and injected into mice. *Pathogen registration for Methylophilus methylotrophus*	**P0507190201**	**1**	**1**	**9**	**0**	**0**
Cell Biology of Immune Interaction Retroviral vector will be used to transduce the genes that encode signaling proteins into cultured cells. DN--Uses recombinant DNA and viral vectors in cultured cells. *Supporting Document - Pathogen registration for Retrovirus*	**DN0508040101** *P0508040101*	**2**	**NA**	**9**	**0**	**0**
Neonatal Transfer Used to Eradicate Theiler's Mouse Encephalomyelitis Virus Theiler's Mouse Encephalomyelitis Viruses from ATCC will be used to infect mouse. Pathogen registration for Theiler's Mouse Encephalomyelitis Virus (TMEV)	**P0507260101**	**2**	**2**	**9**	**0**	**0**
Studies of the Roles of Cell Adhesion during Mouse Embryonic Development Adenoviral vector from Stratagene will be used to transduce alpha4 integrin into cultured cells. DN -- Uses recombinant DNA and viral vectors in cultured cells. *Supporting Document – Pathogen registration for Adenovirus* *Supporting Document – Human tissue registration*	**DN0507190101** *P0507190101* *B0309150102*	**2**	**NA**	**9**	**0**	**0**

Johns Hopkins Institutional Biosafety Committee

JHU IBC Minutes for September 19, 2005
Room B-600, 2024 E. Monument Street Building

Members Present: Dr. Hayward, Chair; Dr. Adams, Dr. Dahl, Dr. Kobrin, Ms. MacAuley, Dr. Margolick, Dr. Norris, Dr. Pan, Dr. Scott

Members Absent: Ms. Biedrzycki (Leave of Absence), Dr. Borrello, Dr. Maouyo, Dr.Rade

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The meeting was called to order at 3:05 pm.

APPROVAL OF MINUTES

The Minutes for August 2005 were unanimously approved.

NEW BUSINESS:

1) Biosafety Cabinet Policy

Dr. Dahl distributed Biosafety Cabinet thimble waiver request from [redacted]. [redacted] would like to use a BCS that is not thimbled in a BSL2 animal room. Dr. Dahl asked the Committee for opinions regarding non-thimbled biological safety cabinets. At present the decision is at the discretion fo the Biosafety Officer to allow or deny waiver requests. Dr. Dahl stated that traditionally Hopkins has thimbled all biological safety cabinets. However, with the construction of the Broadway Research Building, only one of the three BSCs in the culture rooms is a thimbled cabinet. Dr. Dahl noted that neither CDC nor NIH routinely thimbles BSL2 BSCs. The question was asked if we should relax the standard for people working only with human tissues but not pathogens or viral vectors. Dr. Dahl suggested that [redacted] should contact [redacted] in Facilities to determine if there is enough exhaust air to thimble the BSC. If so, it should be thimbled. He also mentioned that every cabinet should be stickered as to which are thimbled and which are not and volatiles should not be used in the non-thimbled BSCs. Dr. Dahl will follow-up and inform the committee as needed.

2) Dengue exposure via needlestick

A staff member of Research Animal Resources suffered a needle-stick injury while performing contract work for an investigator working with Dengue virus in mice. There apparently was some confusion as to the proper response to the injury and some feelings of inadequate response from Occupational Health. Dr. Dahl stated that the Biosafety office was not initially notified of the incident. A meeting of all involved parties resolved some issues regarding the marking of cages and the importance of the principal investigator to take better responsibility for the safety of the work they choose to undertake.

3) HSE 302 Lab inspection addition

Dr. Dahl distributed copies of HSE 302 with attached Biosafety Information Sheet for Committee review. The Biosafety Information sheet contains questions that will be asked of lab members during inspection. The completed sheet will provided to the principle investigators and they will have to sign that they have seen the responses and agree/disagree with the information provided by their lab staff.. The BMBL requires a biosafety manual and an SOP for possible exposures and this addition to the inspections will help with compliance. Dr. Dahl asked the Committee to review and make any suggestions to him.

4) Monkey Cells, LPS

Dr. Dahl handed out information from ATCC and asked the committee for consensus on registering COS cells. Our current database does not have a history of registering monkey cells. Nothing is listed in the policy. Dr. Dahl stated that if we designate BSL-2 level for monkey cells, we must register them. The policy should state this recommendation. Dr. Dahl also raised the question as to whether we should register lipopolysaccharide as a biological toxin. Biological toxins are referenced in HSE 500 however it is not on any mandated lists nor is it regulated. The committee moved to vote to require the registration of non-human primate-derived cell lines.

For Approval: 9
Disapproval: 0
Abstain: 0

The committee then moved to vote to not register lipopolysaccharide as a biological toxin:

For Approval: 9
Disapproval: 0
Abstain: 0

OLD BUSINESS:

1) [redacted] Protocol

Dr. Dahl informed the committee that Dr. [redacted] had filed an annual report with the IBC covering the period 6-29-04 through 6-29-05 The IBC moved to accept the report as the annual renewal of registration:

For Approval: 9
Disapproval: 0
Abstain: 0

2) [redacted] Protocol

Dr. Dahl informed the Committee that Dr. [redacted] had filed an amendment and annual report with the IBC. DSMB was also provided but not required. Two adverse events were also noted. The IBC moved to accept the report as the annual renewal of registration and approve the amendments therein:

For Approval: 9
Disapproval: 0
Abstain: 0

3) HSE 500

Dr. Dahl informed the Committee HSE 500 has been passed out to the Joint Committee for review. He also suggested that all biosafety policies should be reviewed by the IBC membership for comments.

4) Confidentiality Statement

Dr. Dahl distributed a Statement of Confidentiality and informed Committee members that it has been sent to Clyde Bernett in JHU Legal for approval/comments.

Recombinant DNA/Pathogen Research Registrations

15 research registrations were presented for IBC consideration. 8 were approved and 7 were held pending receipt of additional information.

The meeting was adjourned at 4:30 pm

Institutional Biosafety Committee Registrations
September 19, 2005 Meeting
Registrations from 8/30/05 – 9/15/05

Title	IBC#	BSL	ABSL	Yes	No	Abstain
Hedgehog signaling in development and disease Adenovirus will be used to express oncogenes, marker genes and shRNAs into cultured cells and mice *Pathogen registration for Adenovirus*	**P0508290101**	**2**	**NA**	**Hold for more information**		
Hedgehog signaling in development and disease Lentivirus will be used to express oncogenes, marker genes and shRNAs into cultured cells and mice *Pathogen registration for Lentivirus*	**P0508290201**	**2**	**NA**	**Hold for more information**		
Hedgehog signaling in development and disease Replication-competent Avian Retrovirus will be used to express oncogenes, marker genes and shRNAs into cultured cells and mice *Pathogen registration for Replication-competent Avian Retrovirus*	**P0508290301**	**2**	**NA**	**Hold for more information**		
Effect of [redacted] on Rat Neuroma Pain Low doses of [redacted] (0.1 to 4 ug/kg) will be administered systematically to rats. *Toxin registration for [redacted]*	**T0508310101**	**2**	**2**	**9**	**0**	**0**

Effect of [redacted] on Rat Neuroma Pain Low doses of [redacted] (0.1 to 4 ug/kg) will be administered systematically to rats. *Toxin registration for [redacted]*	**T0508310201**	**2**	**2**	**9**	**0**	**0**
Diagnostics for neorickettsiosis Neorickettsia helminthoeca will be cultured and studied to derive a pcr screen for the organism. *Pathogen registration for Neorickettsia helminthoeca*	**P0508230101**	**2**	**2**	**9**	**0**	**0**
Selenoprotein Expression in Prostate Cancer Lentiviral vector will be used to transducer shRNAs into human cell lines. DN—Uses recombinant and viral vectors in cultured cells *Supporting Document – Pathogen registration for Lentivirus* *Supporting Document – Human Tissue registration*	**DN0509150101** *P0509150101* *B0504080101*	**2**	**NA**	**9**	**0**	**0**
The functional effect of PDE5 and Rho kinase on cardiac myofilament contractility Adenoviral vector will be used to transducer cultured cardiac myocytes DN -- Uses recombinant DNA and viral vectors in cultured cells. *Supporting Document – Pathogen registration for Adenovirus*	**DN0508220101** *P0508220101*	**2**	**NA**	**9**	**0**	**0**
Assay development for identifying anti-viral compounds Influenza strains H1N1, H3N2, and B-type virus will be cultured on MDCK cells and used to develop an assay for screening therapeutics. *Pathogen registration for Influenza virus*	**P0508250101**	**2**	**NA**	**Hold for more information**		
Development of an *In Vitro* Model for Visualizing Motoraxon Pathfinding Adenoviral vector from Stratagene will be used to transducer GFP into cultured cells and rats. DN—Uses recombinant DNA and viral	**DN0509090101**	**2**	**2**	**9**	**0**	**0**

vectors in cultured cells and animals. *Supporting Document – Pathogen registration for Adenovirus* *Supporting Document – Human tissue registration*	*P0509090101* *B0509090101*					
Effect of [redacted] on Rat Neuroma Pain Low doses of [redacted] (0.1 to 4 ug/kg) will be administered systemically to rats. *Toxin registration for [redacted]*	**T0508310301**	**2**	**2**	**9**	**0**	**0**
Cationic Steroid Antimicrobials in Treatment of Sepsis *Pseudomonas aeruginosa* from ATCC will be cultured and applied on the scalded area of animals. *Pathogen registration for Pseudomonas aeruginosa*	**P0509120101**	**2**	**2**	**Hold for more information**		
Cationic Steroid Antimicrobials in Treatment of Sepsis *S. aureus* from ATCC will be cultured and applied on the scalded area of animals. *Pathogen registration for S. Aureus*	**P0509120201**	**2**	**2**	**Hold for more information**		
Cationic Steroid Antimicrobials in Treatment of Sepsis Lipopolysaccaride (LPS) from Sigma will be used to treat animals. *Toxin registration for Lipopolysaccaride (LPS)*	**T0509120101**	**2**	**2**	**Hold for more information**		
Effect of [redacted] on Rat Neuroma Pain Low doses of [redacted] (0.1 to 4 ug/kg) will be administered systemically to rats. *Toxin registration for [redacted]*	**T0508310401**	**2**	**2**	**9**	**0**	**0**

Johns Hopkins Institutional Biosafety Committee

JHU IBC Minutes for October 17, 2005
Room B-600, 2024 E. Monument Street Building

Members Present: Dr. Hayward, Chair; Dr. Adams, Dr. Dahl, Dr. Kobrin, Ms. MacAuley, Dr. Margolick, Dr. Norris, Dr. Pan

Members Absent: Ms. Biedrzycki (Leave of Absence), Dr. Borrello, Dr. Maouyo, Dr.Rade, Dr. Scott

Guests: Dr. [redacted] (by phone), Dr. [redacted], Dr. [redacted]

The meeting was called to order at 2:41 pm.

APPROVAL OF MINUTES

The Minutes for September 2005 were unanimously approved.

OLD BUSINESS:

BCG Project

Dr. Dahl summarized an overview of Dr. [redacted] protocol. The strain of BCG that Dr. [redacted] works on is the Pasteur strain from ATCC, strain #35734. ATCC lists the organism as BSL3. Dr. Dahl also provided references from Ft. Meade indicating that a communication from Dr. [redacted] of the NIH suggested that NIH recommends BSL3 for handling BCG and that this is what Ft. Meade uses for the organism. The BMBL allows BCG in mice and rats, but specifically excludes rabbits. Dr. [redacted] via teleconference, noted the CDC TB guidance suggests BSL2, but Dr. Dahl pointed out that this reference is for handling the material in a diagnostic setting. The same document goes on to say that laboratories asked to attempt culture of BCG should handle the material as they would TB and thus follow BSL3 containment. The question then is whether inoculation of an animal is "culturing'. Dr. [redacted] stated that the organism does grow in the animal. Is this a culture? The Committee asked whether anyone's PPD has converted in the [redacted] Lab. Dr. [redacted] stated one had but it was due to a non-lab strain of tuberculosis. There were 3 needlesticks with NTB. Dr. [redacted] was requested to send BCG protocols for evaluation. Dr. Dahl will check with other Facilities as to what their levels are when working with BCG.

NEW BUSINESS:

1) [redacted] Protocol, GT0510170101,

Dr. [redacted] has submitted a proposal for a study involving recombinant viral vector vaccine for HIV (canary pox vector) in infants in Uganda. The IBC noted that the NIH guidance for recombinant studies in foreign countries had recently been discussed with Mr. Alan Shipp at the NIH. The NIH Guidelines require IBC oversight of the foreign country's IBC if one exists or the establishment of an IBC that reflects the membership requirements of the NIH Guidelines. This could be accomplished by establishing an IBC *de novo* in the country or the addition of two outside members from Uganda to the JHU IBC. The Committee discussed assembling an IBC and questioned whether two IBC's should be established? Dr. [redacted] reported they generally they have hundreds of serious adverse events which may or may not be related. A local IBC is possible, but they can not deal with all the paperwork of being the "IBC of record". Dr. Dahl stated that a

discussion with Dean Sharon Krag of the BSPH indicated that the PI establishing a local IBC and the JHU IBC providing oversight would be the preferred way to go. Other options being JHU IBC as the IBC of record or the possibility of using Western IBC. Dr. Dahl noted that the problem with the paperwork had not been discussed and stated he would look into this.

Dr. [redacted] study will initially involve 40 patients. There will be 4 injections of vaccine times at birth, 1 month, 2 months and 3 months. It was noted that this trial would never be done in the USA because we don't have significant breast-feeding transmission of HIV in this country. Uganda does. The Committee questioned Dr. [redacted] about the use of anti retroviral therapy (ARV). Dr. [redacted] stated that ARV is not the current general standard therapy in Uganda but it is coming. There is a 9000 person wait-list for ARV therapy. Because of anticipated severe adverse events in this patient population it will be very hard to track events in Phase I due to low patient numbers. Phase II hopefully will be much larger and adverse events should be more prominent. Dr. Margolick stated the issue that there was an IRB issue here in that the vaccine is directed at a B-E clade and Uganda has A-D clade virus so there is questionable benefit for the patients. Project looks OK for now. The Committee voted to approve pending IBC of record decision.

For Approval:	8
Disapproval:	0
Abstain:	0

2) [redacted] Protocol, GT0510170201,

Dr. [redacted] distributed a handout which summarized the project. The project involves the use of Clostridium novyi-NT spores as a treatment for patients afflicted with solid tumor malignancies. This treatment has not been performed in humans with this agent though some studies in the 1950s and 60s using Clostridium butyricum. There were toxicity issues with this treatment. The current agent under review is an attenuated form that lacks the synthesis of alpha toxin. The spores are expected to germinate and grow in hypoxic tissue areas such as found in certain tumor masses. Animal studies have been done in mice with some toxicity attributed to dosing. Studies in rabbits showed no toxicity. Both animal models suggested a 25-30% "cure" rate. The mechanism is thought to be inflammatory response plus proteases and lipases of the bacteria itself. Trial population will have exhausted all other options. The protocol has been submitted to the FDA. The IBC queried Dr. [redacted] on the longevity of the spores in the system, the nature of the alpha toxin gene and potential for recovery of the lost gene, and infection control issues given the desire to perform the study in the Weinberg Oncology center which houses many immunocompromised individuals. Dr. [redacted] noted that JHH Infection Control would be contacted. He also indicated that some spores could circulate for months. There will be a six month period between the patient's last chemotherapy and introduction to drug if enrolled in the study. Dr. [redacted] will distribute FDA results as soon as they are received.

3) [redacted] **Protocol, GT0510170301,** "Protective efficacy of orally delivered bovine milk immunoglobulin (BIgG) specific for the minor CFA/I fimbrial adhesion CfaE against challenge with H10407 enterotoxigenic E. coli (ETEC) strain expressing CFA/I"

Dr. [redacted] protocol involves the us of bovine milk immunoglobulins as a food-based antidiarrheal supplement with activity against ETEC, the predominant cause of traveler's diarrhea. The IBC has previously approved Dr. [redacted] use of H10407 as a challenge strain of ETEC for inpatient studies. The H10407 strain is susceptible to ciprofloxacin, bactrim, and ampicilin/amoxicillin. The challenge dose of 1x 10^9 cfu protocol is the same as in the previously approved study. The protocol includes bleaching of stools and all patients must have two negative stool cultures prior to discharge from the inpatient unit. The IBC asked about monitoring of the study staff for diarrhea. The committee moved to approve the study:

For Approval:	8
Disapproval:	0
Abstain:	0

OLD BUSINESS:

1) [redacted] Protocol Update

Dr. Dahl informed the committee of Dr. [redacted] response to the questions raised by the IBC at the September meeting. Dr. [redacted] is willing to provide PPE to the staff working on her project if they show signs of influenza and wish to have the masks for use at home. Dr. [redacted] prefers to not offer space in the inpatient unit for staff that show flu symptoms because she is concerned that their flu (which she considers most likely to be from the outside) will confound her study's results. The Committee moved to approve with the additional responses from Dr. [redacted]:

For Approval:	8
Disapproval:	0
Abstain:	0

2) BRB Vivarium Update

Dr. Dahl reported on the outcome of the certification of the BRB BSL3 vivarium. Dr. Dahl noted that a handful of items need to be corrected prior to certification:

-- Exhaust HEPA Bag-in/Bag-out units need to be certified.
-- An interlock needs to be installed to shut down the supply air in case of total exhaust failure.

Facilities Construction and Design is working with the Biosafety Office to make these modifications. The facility will reschedule certification for early December.

Recombinant DNA/Pathogen Research Registrations

3 research registrations were presented for IBC consideration. 2 were approved and 1 was held pending receipt of additional information.

The meeting was adjourned at 4:45 pm

Institutional Biosafety Committee Registrations
October 17, 2005 Meeting
Registrations from 9/16/05 – 10/06/05

Title	IBC#	BSL	ABSL	Yes	No	Abstain
Combinatorial Vaccination Strategies for Breast Cancer Treatment	P0509260101	2	2	8	0	0

Listeria-based vaccines will be injected into mice. *Pathogen registration for Listeria monocytogenes*						
HIV Pathogenesis	**DN0509230101**	**2**	**NA**		**Hold for additional info**	
Plasmid vectors will be used to transfect tat, env, HIV proviral DNA, GFP, and venus into cultured cells. DN—Uses plasmid and proviral DNA-based recombinant DNA in cultured cells. *Supporting Document – Pathogen registration for HIV*	*P0305150303*					
Differences in Quasispecies Between Responders and Null-responders...ML17756	**DN0509290101**	**2**	**NA**	**8**	**0**	**0**
Hepatitis C virus partial genomic segments obtained from human serum will be sub-cloned into plasmid vector. DN—Uses plasmid-based recombinant DNA to transfect hepatitis C virus partial genomic segments into E. coli DH5 alpha cells. *Supporting Document – Pathogen registration for HCV* *Supporting Document – Human tissue registration*	*P0507010101* *B9811110208*					

Johns Hopkins Institutional Biosafety Committee

JHU IBC Minutes for November 21, 2005
Room B-600, 2024 E. Monument Street Building

Members Present: Dr. Hayward, Chair; Dr. Adams, Dr. Dahl, Dr. Kobrin, Ms. MacAuley, Dr. Maouyo, Dr. Margolick, Dr. Norris, Dr. Pan, Dr. Rade, Dr. Scott

Members Absent: Ms. Biedrzycki (Leave of Absence), Dr. Borrello

Guests: Dr. [redacted]

The meeting was called to order at 2:50 pm.

APPROVAL OF MINUTES

The Minutes for October 2005 were unanimously approved.

NEW BUSINESS:

1) [redacted] **Protocol, GT0511210101,** Phase I study of the safety and immunogenicity of rDEN4delta30-200, 201, a live attenuated virus vaccine.

This protocol involves a live, attenuated Dengue fever vaccine with a DEN4 base and Δ30-200, 201 point mutations in the NS5 (RNA Polymerase) gene to ameliorate adverse events observed in vaccinees receiving the rDEN4 Δ30 vaccine previously approved by the IBC. Adverse events included neutropenia, rash, and mild ALT (alanine aminotransferase) elevation. Dr. [redacted] presented a summary of the project for the IBC and discussed the results seen with the rDEN4 Δ30 study. Dr. [redacted] Expects to enroll 84 volunteers in three groups of 28. These three groups will receive 10^5, 10^3, and 10^1 PFU respectively. Volunteer participants are not used in any additional projects.

--Dr. [redacted] was queried on the nature of the RNA Polymerase mutations contained in the new vaccine and whether studies had been done to examine the effect of these mutations on enzymatic activity. Dr. [redacted] stated that these biochemical studies have not been done.
--Dr [redacted] was asked about FDA approval and noted that for virus stability reasons they had decided to switch from PBS to L15 for their vaccine suspensions. FDA has requested QC information on these L15 lots.
--Dr. [redacted] was asked about the potential for compensating mutations that could rescue the point mutations in the new vaccine. Dr. [redacted] indicated that these have not been seen in the animal studies, but have not been thoroughly investigated.

It was noted that Dr. [redacted] had not included the IBC on the list of recipients of Severe Adverse Events. Dr. [redacted] stated that the oversight would be corrected and the IBC would be included.
Dr. [redacted] was thanked for her presentation and left the IBC meeting.
The IBC moved to approve protocol **GT0511210101.**

For Approval:	11
Disapproval:	0
Abstain:	0

2) [redacted] - [redacted] **Protocol GT0511200201,** A phase I, dose-escalation study of CRS-100 in adult subjects with carcinoma and liver metastases.

Dr. [redacted] had originally indicated that he could make a presentation to the IBC at this meeting, but was not able to appear. The study involves the administration of live, attenuated Listeria to patients with carcinoma with hepatic metastases . The Listeria were attenuated through excision of specific virulence factor genes *actA* and *internalin B.* Though not technically "recombinant" by NIH guidelines, the manner in which the excisions were performed may result in recombinant material left in the Listeria genome and should be proven to not be the case. Concerns raised by the IBC Members included where the project is being done, handling and disposal, whether hospital infection control has weighed in on the study and QC information for the agent to be administered.

The Committee motioned to approve pending satisfactory answers to safety issues. The motion was tabled for a subsequent presentation by Dr. [redacted] at the next IBC meeting.

3) [redacted] **Protocol Amendment to GT0504180101,** A phase 2, randomized, double-blind, placebo-controlled, parallel-group, multicenter, dose-selection study of Ad2/Hypoxia Inducible Factor (HIF)-1α/VP16 in patients with intermittent claudication (IMPROVE) with amendment 1, dated 6 December 2004.

This protocol was previously approved at the April 18, 2005 IBC meeting.
The changes in the protocol include:
1) Improvements in bulk processes to yield increased product purity and stability
2) Changes in the Human Use section to include updated patient information from the PAD Phase 1 studies and the current status of the phase I trials conducted with Ad2/HIF-1α/VP16 in patients with coronary artery disease as an adjunct to coronary artery bypass graft surgery.
3) Acronym has been changed from IMPROVE to WALK

The IBC moved to approve the amended protocol **GT0504180101.**
The Committee voted to approve:

For Approval:	11
Disapproval:	0
Abstain:	0

OLD BUSINESS:

1) [redacted] Protocol

Dr. Dahl presented the IBC committee with an update of the project. Dr. [redacted] will secure two people in Uganda to serve as outside, non-affiliated ad hoc members of the IBC. This will also serve as a "test" for how to handle outside committee members from sites in other countries via conference call with IBC. Resumes of these outside members will have to be submitted to IBC and presented to the Dean.

2) Historic Pooling of Pathogen Registrations

Dr. Dahl questioned whether the IBC membership should review all submitted pathogen registrations as individual registrations. The current system includes the pathogen information with any co-submitted recombinant DNA registration(s). Pathogen registrations that are not submitted with a recombinant DNA registration form are the only ones that are presented individually to the IBC. The decision was made that Dr. Dahl will continue to pool the pathogens with any submitted/related recombinant DNA forms as currently performed.

3) Biological Safety Cabinet Issues

Dr. Dahl mentioned to the IBC that [redacted] from animal resources has contacted [redacted] regarding thimble-connection of Biosafety cabinets in the vivariums. Currently, many buildings and areas can not support the previously stated expectation that all BSL2 BSCs be thimble-connected. Dr. Dahl also noted that Dr. [redacted] has requested a waiver for similar reasons. It was noted that there is no CDC requirement for thimble-connection of BSCs at BSL2. This is a JHU requirement. Dr. Dahl thinks this position should be reconsidered. One problem noted by Dr. Dahl is that people are accustomed to vented BSCs and, unfortunately, have been permitted in the past to use small amounts of volatile chemicals in these units. Dr. Dahl thinks this is a dangerous precedent. Non-thimbled BSCs should be labeled absolutely no volatiles and any use of these chemicals in BSCs should be discouraged. The IBC agreed that both waivers should be granted due to physical plant limitations.

Recombinant DNA/Pathogen Research Registrations

There were 9 research registrations presented for IBC consideration. All were approved
The meeting was adjourned at 4:40 pm

Institutional Biosafety Committee Registrations
November 21, 2005 Meeting
Registrations from 10/7/05 -- 11/07/05

Title	IBC#	BSL	ABSL	Yes	No	Abstain
Genetic Analysis of Congenital Anomalies in Humans	**P0511100101**	**2**	**NA**	**11**	**0**	**0**
Epstein-Barr virus (EBV) will be used to immortalize human B-cells.						
Pathogen registration for EBV virus						
Clinical Validation of Molecular-Based Assay IDI-VRE for the Direct Detection of Vancomycin Resistance in Rectal and Stool Specimens	**P0511110101**	**2**	**NA**	**11**	**0**	**0**
Vancomycin resistant enterococci from sponsor will be used as a control strain for assay validation.						
Pathogen registration for Vancomycin resistant enterococci						
Influence of Cardiac Gene Transfer on Right Ventricular Function	**DN0511070101**	**2**	**2**	**11**	**0**	**0**
Adenoviral vector will be used to transducer RhoA, rho kinase and PDE5A into mice.						
DN—Uses recombinant DNA and viral vectors in mice.						
Supporting Document – Pathogen registration for Adenovirus	*P0511070101*					
Molecular Genetics of the HSV-1 Virion	**P0510270101**	**2**	**NA**	**11**	**0**	**0**
Baculovirus will be used to express herpes simplex virus type 1 protein *in vitro.*						
Pathogen registration for Baculovirus						

Intravenous Testing of M. tuberculosis Complex Strains in Rabbits The wild type and mutant strains of *M. tuberculosis* and *M. bovis* will be injected into rabbit. DN – Uses recombinant *M. tuberculosis* and *M. bovis* to infect rabbit *Supporting Document – Pathogen registration for M. tuberculosis* *Supporting Document – Pathogen registration for M. bovis*	**DN0511010101** ***P0003140506*** ***P0511010101***	**3**	**3**	**11**	**0**	**0**
Intravenous Testing of M. tuberculosis Complex Strains in Rabbits The wild type and mutant strains of *M. tuberculosis* and *M. bovis* will be injected into rabbit. *Pathogen registration for M. bovis*	**P0511010101**	**3**	**3**	**11**	**0**	**0**
Mechanism of Neonatal Immune Modulation by Maternal Schistosomiasis Mice infected with Schistosoma mansoni will be obtained from NIAID and used to study how infant immune responses are modulated by maternal schistosomiasis *Pathogen registration for mice infected with Schistosoma mansoni*	**P0511020101**	**2**	**2**	**11**	**0**	**0**
Alpha 1 Antitrypsin as an Apoptotic Agent in Emphysema Adeno-associated viral vector will be used to transducer alpha 1 antitrypsin gene into mice. *Pathogen registration for Adeno-associated virus*	**P0510280101**	**2**	**2**	**11**	**0**	**0**
Effectiveness of ClO2 Gas, H2O2 Vapor and Time on Infectivity of Aspiculuris Tetraptera Eggs The ability of chlorine dioxide gas (ClO2) and hydrogen peroxide vapor (H2O2) to destroy Aspiculuris Tetraptera (Pinworm) Eggs in shoebox cages that have been inhabited by pinworm-infected mice will be tested using nude or other immunosuppressed mice. *Pathogen registration for Aspiculuris Tetraptera Eggs*	**P0510270201**	**2**	**2**	**11**	**0**	**0**

Johns Hopkins Institutional Biosafety Committee

JHU IBC Minutes for December 13, 2005
Blalock 1024B

Members Present: Dr. Hayward, Chair; Dr. Adams, Dr. Dahl, Dr. Kobrin, Ms. MacAuley, Dr. Maouyo, Dr. Norris, Dr. Pan, Dr. Rade, Dr. Scott

Members Absent: Ms. Biedrzycki (Leave of Absence), Dr. Borrello, Dr. Margolick

Guests: Dr. [redacted], Ms. [redacted], Ms. [redacted]

The meeting was called to order at 11:07 am.

Investigator Presentation, [redacted] protocol #GT051120201, A phase I, dose-escalation study of CRS-100 in adult subjects with carcinoma and liver metastases.

Dr. [redacted] provided a brief summary of the study and its goals. The study will be performed in the GCRC and uses attenuated Listeria as a treatment for liver cancer. Listeria does not "attack" the tumor, rather it targets the liver and increases the immune response to the organ resulting in a more robust anti-tumor response in situ. The initial study involves the potential for 60 patients, but will be performed in a dose-escalation manner with 3 subjects per cohort with the potential for a maximum of 6 subjects per cohort. There is no recombinant component to this particular trial but future trials may include recombinant organisms.

IBC Members asked questions including:

Q: Are there any potential safety issues?
A: Virulence is about 1,000 times less than wild type. Standard precautions are used but not much more than that.

Q: Will Stool be tested before releasing patients?
A: Yes. Patients are sent home after five days in the GCRC and commence a 10 day regimen of amoxicillin treatment. Their stay in the hospital will be monitored until they are released. The IBC suggested discharge papers state standard precautions or hygiene sheet.

Q: Listeria can cross into the brain, any chance of meningitis?
A: Risk of CNS infection is very small. Meningitis is possible, but not likely.

Q: Are there risks to immunocompromised patients already in GCRC?
A: Yes. These patients will not share rooms or interact with other patients unless they are on the same project.

Q: Are there any clean-up or disinfection procedures for rooms following patient discharge?
A: No. The IBC recommended providing SOP for clean-up of spills.

Q: Has JHH infection control been consulted on this study?
A: Dr. [redacted] has contacted and discussed infection control issues with HEIC.

Q: Will staff on floor be aware of project? What about housekeeping?
A: Absolutely, the floor staff will be aware. GCRC staff will receive a clinical trial inservice. It is not known about housekeeping, but Infection Control works with housekeeping and Dr. [redacted] will look into this.

Q: Has vaccine been tried inactivated?
A: No.

The IBC made the following requests of Dr. [redacted]:

1) The IBC is concerned about the method used to produce the attenuated Listeria strains and the subsequent potential for exogenous DNA to be present in the agent. Please demonstrate the absence of exogenous DNA in the Listeria intended for human use. This could be done by PCR for plasmid and AmpR gene sequences or by Southern blot. It is important to demonstrate that there is no residual nucleic acid from the genetic manipulation. This is also touched on in the letter from NIH/OBA

2) Please generate and submit standard operating procedures (SOPs) for spills involving the agent that may occur at the bedside, during transport of the agent in the hospital, and at the pharmacy during preparation of the agent.

3) Please prepare a set of hygiene precautions/instructions for the released research participants. The IBC expressed concern for families that may have young, aged, or immunocompromised individuals in the participant's household.

4) Please demonstrate that you have received approval for your study by Johns Hopkins Hospital Infection Control.

5) Please provide QC data on the formulation destined for human use.

6) Please provide any FDA correspondence regarding approval when received.

7) Out of concern for the safety of other individuals in the GCRC at the time of the study, the IBC requests that sharing of rooms between participants and non-participants should not be permitted.

The Committee voted for approval pending FDA approval:

For Approval:	8
Disapproval:	0
Abstain:	0

NEW BUSINESS:

1) [redacted] **Protocol, Amendment to GT0504180101,** "Randomized Trial of Early Versus Late Vaccination with a GM-CSF Secreting Allogeneic Tumor Cell-based Vaccine, KGEL/GM-CSF/LMP-2, in Patients with High Risk Chronic Lymphocytic Leukemia."

The protocol is a phase II trial that uses the KGEL cell line (K562 cells that secrete human GM-CSF) to treat Chronic Lymphocytic Leukemia (CLL). The primary objectives are to determine efficacy and toxicity from administering rituximab and cyclophosphamide to high-risk CLL patients and determine preliminary efficacy and toxicity from early and delayed administration of the CLL Vaccine (KGEL cells) following rituximab and cyclophosphamide. The study will also compare the magnitude of the T cell response to the CLL Vaccine given early vs. late and correlate the responses with the extent of immune reconstitution.

42 Patients with high risk untreated CLL will be treated with rituximab and cyclophosphamide. Four weeks following the last treatment, 30 of the patients that showed a remission response will be randomly assigned to the early or late treatment arm and receive a series of 6 intradermal vaccine cycles, every 3 weeks, consisting of an admixture of $1x10^8$ irradiated, autologous tumor cells with $2x10^7$ KGEL vaccine cells. The early treatment arm will receive the vaccine starting on week 2 post-remission evaluation. The late arm will receive the vaccine starting on week 20 post-remission evaluation.

The IBC discussed the status of patients in remission. Since patients have to be in remission to participate in the study the IBC also questioned whether there was any chance patients could "pop" out of remission by participating in the proposed study. It was noted that CLL patients always come out of remission eventually. The IBC moved to approve protocol GT0504180101:

For Approval:	8
Disapproval:	0
Abstain:	0

[redacted], **GT0512130301,** K562/GM-CSF Vaccination in Patients with Myelodysplastic Syndrome"

The protocol will use the K562/GM-CSF tumor cell vaccine to treat patients afflicted with myelodysplastic syndrome (MDS). The primary objective is to determine if vaccination with the K562/GM-CSF vaccine is safe and can induce a hematologic or cytogenetic response in MDS patients. Secondary objectives are to determine if the vaccine induces an immune response to WTI-1, survivin, or proteinase-3 (all common myeloid antigens). Study subjects will receive a total of 5 vaccinations containing $1x10^8$ cells/dose. Vaccination will occur at weeks 0, 3, 6, 9, and 17.

The IBC noted that this was a Standard GVAC project, similar to many that have previously been submitted for review. No additional safety concerns were noted. The IBC membership moved to approve protocol GT0512130301:

For Approval:	7
Disapproval:	0
Abstain:	1

Recombinant DNA/Pathogen Research Registrations

There were 5 research registrations presented for IBC consideration. All were approved, see table on next page. The meeting was adjourned at 12:38 pm.

Institutional Biosafety Committee Registrations
December 13, 2005 Meeting
Registrations from 11/7/05 – 12/08/05

Title	IBC#	BSL	ABSL	Yes	No	Abstain
Functional Analysis of WASP and WIP using an RNAi Approach in C2C12 Cells Lentiviral and retroviral vectors will be used to knock down the expression of WASp and WIP in C2C12 cells. DN – Uses viral vectors in cultured cells *Supporting Document – Pathogen registration for Lentivirus* *Supporting Document – Pathogen registration for Retrovirus*	DN0512060101 *P0512060101* *P0512060201*	2	NA	8	0	0
Overcoming Tolerance Through Intratumoral Vaccination Adenoviral vector will be used to transduce herpes simplex thymidine kinase and b-galactosidase into cultured cells and mice DN – Uses recombinant DNA and viral vectors in cultured cells and mice. *Supporting Document – Pathogen registration for Adenovirus*	DN0512010101 *P0512010101*	2	2	8	0	0
Knock Down of AR & RB in Prostate Normal and Cancer Cells The retrovirus expressing siRNA will be used to knock down RB expression in cultured cells. *Pathogen registration for Adenovirus*	P0511290101	2	NA	8	0	0
AR Expression in Prostate Cancer Cells CRE recombinase-expressing adenovirus will be used to excise AR transgene out of 957E/hTERT cells *Pathogen registration for Adenovirus*	P0511290201	2	NA	8	0	0
Growth Hormone (GH) Gene Therapy in GH-deficient Mice Adeno-associated viral vector will be used to transducer GFP or GH into mice. *Pathogen registration for Aspiculuris Tetraptera Eggs*	P0512070101	1	1	8	0	0

Johns Hopkins Institutional Biosafety Committee

JHU IBC Minutes for January 17, 2006
. Blalock 1024B, 11:00 am

Members Present: Dr. Hayward, Chair; Dr. Adams, Dr. Dahl, Dr. Kobrin, Ms. MacAuley, Dr. Maouyo, Dr. Pan, Dr. Scott (arrived late for last four research registration votes)

Members Absent: Ms. Biedrzycki (Leave of Absence), Dr. Borrello, Dr. Margolick, Dr. Rade

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The meeting was called to order at 11:20 am.

APPROVAL OF MINUTES

The Minutes for November 2005 were unanimously approved.

OLD BUSINESS:

1) JHU Singapore Update

Dr. Dahl distributed a registration of research with human tissue, infectious agents, pathogens, oncogenes or toxins obtained from [redacted] of the [redacted] Lab. He informed the IBC he was working with Clyde Bernett to resolve JHU Singapore issues.

NEW BUSINESS:

1) Research Registration and Gene Therapy Sub-Group Meetings

Dr. Hayward discussed combining the Research Registration and the Gene Therapy Sub-Group meetings. Currently the two sub-groups are scheduled to meet on the second Monday and second Tuesday of the month to look for issues that could be resolved prior to the full IBC meeting which is held on the third Monday of the month. Since neither meeting tends to last through the full 2 hours scheduled it was suggested that one meeting date and time be established to handle all the triage issues. The meeting will be held on the second Tuesday of the month at 11:00 am. The location will be Blalock 1024B. The IBC motioned to approve a single triage meeting to discuss registration issues.

For Approval:	7
Disapproval:	0
Abstain:	0

2) Gene Therapy Protocols

The IBC was presented with two Gene Therapy submissions; a new submission for Dr. [redacted] and another for Dr. [redacted]. The Committee decided to hold review of both submissions until the next meeting. The Committee also decided to invite Dr. [redacted] to the next meeting to discuss her new project.

At this point in the meeting, Dr. Dahl excused himself due to illness. The IBC meeting continued with a quorum of 6 members.

3) [redacted] **Protocol GT0601170101,** "A single-site, Phase 1, Double-blind, Safety and Immunogenicity Trial of a Bivalent Alphavirus Replicon Vaccine Expressing Botulinum Neurotoxin Heavy Chain Fragments (AVX401) in Healthy Volunteers"

The protocol proposes to study the immunogenicity of AVX401 which is comprised of two virus-like replicon particles (VRP); one expressing the nontoxic carboxy-terminal portion of the heavy chain of botulinum neurotoxin serotype A (BoNT/A) and the other expressing the heavy chain fragment of botulinum neurotoxin serotype B (BoNT/B). Both VRPs of AVX401 are derived from an attenuated strain of Venezuelan equine encephalitis virus. The VRPs derived from the system do not contain VEE structural genes and thus are defective in their ability to form new infectious virus-like particles.

Two groups of 20 healthy volunteer study participants (40 total for the study) will be enrolled. In group 1, 8 volunteers will receive the vaccine intramuscularly (IM), 8 volunteers will receive the vaccine sub-cutaneously (SC), 2 volunteers will receive placebo IM and 2 volunteers will receive placebo SC. Each participant will receive a total of 4 injections of vaccine or placebo. Those receiving the actual vaccine will receive 0.5ml containing $1x10^7$ IU of each VRP above. Group 2 will begin after safety analysis of Group 1. Group 2 will be handled as Group 1 only Group 2 volunteers will receive 0.5ml containing $1x10^8$ IU of each VRP above.

The IBC discussed the submission of Dr. [redacted]. Members noted all oversight committees are in place and pre-clinical justifications seem to be good. The project has gone through animal toxicity. There are no issues other than QC issues. We are requesting QC issues be submitted to the IBC. Dr. Hayward motioned to approve on condition QC issues be forwarded to IBC.

For Approval:	6
Disapproval:	0
Abstain:	0

Recombinant DNA/Pathogen Research Registrations

9 research registrations were presented for IBC consideration. 5 were approved, 3 were conditionally approved pending receipt of additional information. The registrations and the vote tally are found on the next page.

The meeting was adjourned at 12:25 pm.

Institutional Biosafety Committee Registrations
January 17, 2006 Meeting
Registrations from 12/07/05 – 1/09/06

Title	IBC#	BSL	ABSL	Yes	No	Abstain
Anti-viral Mechanisms Induced by Granzymes Adenovirus will be used to infect cultured cells. *Pathogen registration for Adenovirus*	**P0512140201**	**2**	**NA**	**6**	**0**	**0**
Stem Cell Derived Motoneurons in Adult Mammalian CNS and in Motor Neuron Diseases Pseudorabies virus will be propagated in pig kidney epithelial cells and injected into rats. *Pathogen registration for pseudorabies virus*	**P0601090101**	**2**	**2**	**0**	**6**	**0**
Isolation of T. violaceum and T. Soudanense from Cultures of Skin, Hair and Nails at Johns Hopkins Hospital Dermatophyte will be subcultured and tested in the Clinical Microbiology Laboratory. *Pathogen registration for dermatophytes*	**P0512140101**	**2**	**NA**	**6**	**0** Approval based on co-signature requirement	**0**
Lentiviral Vectors in the Study of Murine Autoimmune Myocarditis Lentiviral vector from Invitrogen will be used to transducer caspase 8 into cultured cells. DN – Uses viral vectors in cultured cells. *Supporting Document – Pathogen registration for Lentivirus*	**DN0512290101** *P0512290101*	**2**	**NA**	**6**	**0**	**0**
Pertussis Toxin in the Study of Murine Autoimmune Myocarditis Pertussis toxin will be injected with Complete Freund's Adjuvant (CFA) into mice to induce myocardial inflammation. *Toxin registration for pertussis toxin*	**T0512290101**	**2**	**2**	**6**	**0**	**0**
Does habitat Fragmentation Increase Transmission Between Forest and Human-dwelling Rodents? The blood samples will be collected from various Tanzanian rodents for diagnostic testing. *Pathogen registration for blood from various Tanzanian rodents*	**P0601090201**	**2**	**2**	**7**	**0** Approval conditional upon USDA BSL 2 approval	**0**

Liposomal Delivery of High LET Emitters to Cell Nuclei Cyan fluorescent protein will be transfected into cultured cells and mice. DN—Uses recombinant in cultured cells and animals	**DN0512280101**	**2**	**1**	**7**	**0**	**0**
Cerebral Malaria Recombinant Proteins The plasmodium proteins identified in the study will be sub-cloned into plasmid vector and expressed in E. coli. DN -- Uses plasmid-based recombinant DNA to transfect plasmodium proteins into E. Coli cells. *Supporting Document – Pathogen registration for Plasmodium Falciparum*	**DN0512230101** *P0505020101*	**2**	**2**	**7**	**0**	**0**
C/EBPbeta Isoform Function and Regulation by Tyrosine Kinase Retroviral vector will be used to transducer the CCAAT/Enhancer binding protein beta (C/EBP-beta) into cultured cells. *Pathogen registration for retrovirus*	**P0512230101**	**2**	**NA**	**7**	**0**	**0** **Approved pending clarification and answers of size of culture being used.**

Johns Hopkins Institutional Biosafety Committee

JHU IBC Minutes for February 20, 2006
Room B-600, 2024 E. Monument Street Building

Members Present: Dr. Hayward, Chair; Dr. Adams, Dr. Dahl, Dr. Kobrin, Dr. Maouyo, Dr. Margolick, Dr. Pan

Members Absent: Ms. Biedrzycki (Leave of Absence), Dr. Borrello, Ms. MacAuley, Dr. Norris, Dr. Rade, Dr. Scott

Guests: Dr. [redacted], Dr. [redacted]

The meeting was called to order at 3:05 pm.

APPROVAL OF MINUTES

The Minutes for December 2005 and January 2006 were unanimously approved.

INVESTIGATOR PRESENTATION – Dr. [redacted], "Phase I study of the safety and immunogenicity of rDEN4 Δ30-4995, a live attenuated virus vaccine candidate for the prevention of Dengue serotype 4"

Dr. [redacted] provided a brief summary of the study and its goals.
The study is designed to evaluate the safety, infectivity and immunogenicity of the live attenuated rDEN4 Δ30-4995 virus vaccine in seronegative adult volunteers. The ultimate goal is to determine the agent's suitability for inclusion in a tetravalent dengue vaccine formulation.

Virus has attenuating mutations in the RS3 gene which is a protease/helicase. Previous study involved mutations in the NS5 gene. Additional trials are being performed because 5 volunteers of the previous study had elevated liver enzyme reaction to the vaccine.

There will be 3 groups of 28 volunteers (20 vaccinees and 8 placebos). The study will start with a 10^5 dose for group 1, group 2 will involve 10^3, and group 3 will receive 10^1. The goal is to find the lowest infectious/immunogenic dose of the virus. The virus titer of the innoculum batch is tested every time prior to vaccination.

A viremia of 103 will be the trigger for the investigator to stop the study and discuss with the IBC restrictions, such as time of year, for the study to continue.

INVESTIGATOR PRESENTATION - Dr. [redacted]: Project Entitled, "Cancer Immunotherapy Using Attenuated Measles Virus Vectors"

Dr. [redacted] study proposes to use the attenuated strain of measles vaccine virus (Edmonston B strain) as a vector for transducing immune-regulatory molecules into tumor cells in mice. Dr. [redacted] distributed a sheet that summarized his project. Dr. [redacted] proposes changing the tropism of the virus from the human CD46 molecule to mutating the virus H protein. He will also add a targeted tropism by including a gene encoding a single-chain antibody to human epidermal growth factor receptor or a particular MHC/peptide comples (mouse MHC Kb linked with OVA epitope). The project will be performed at strict BSL2 containment. Dr. [redacted] states that a titer of 10^3 or 10^4 pfu will be inoculated into the mice. He indicated tumor cells are being targeted

and no molecules are oncogenes. The IBC membership recommended Dr. [redacted] verify the measles vaccination status of all laboratory staff and recommended restriction of pregnant staff. Dr. [redacted] is also to prohibit use of other viral vectors during the manipulation of the measles strain and surface decontamination of the biosafety cabinet prior and after work on the virus.

OLD BUSINESS:

1) [redacted] Trial, GT0511200201

Dr. Dahl distributed the response received from [redacted] and provided a chronological order of events leading to the response. The IBC noted the mention of a final amended protocol in the current documents as well as a statement regarding IRB approval. Members also asked to confirm the location of the GCRC.

The IBC moved to approve protocol GT0511200201 pending receipt of the final amended protocol and confirmation of location.

For Approval:	6	(Dr. Margolick was not present for the vote)
Disapproval:	0	
Abstain:	0	

2) Recombinant studies performed in Foreign Countries, [redacted] Protocol, GT0510170101

Dr. Dahl informed the Committee that JHU General Counsel's Office approved the registration of a joint Ugandan/JHU IBC for the purposes of Dr. [redacted] study. Dr. [redacted] will arrange for appropriate committee members from the community. The Joint Makerere University/Johns Hopkins University Research Collaboration IBC will meet via conference call to discuss the protocol after the NIH/OBA approves the IBC membership.

3) JHU Singapore

Dr. Dahl informed the Committee of conversations with Clyde Bernett. Dr. Hayward, Dr. Dahl and Ted Poehler will meet to discuss the issues surrounding the overlap of protocols and their oversight between the two institutions.

NEW BUSINESS:

[redacted] **Protocol, GT0602200101,** Phase I Study of the Safety and Immunogenicity of rDEN4-Δ30-4995, a Live, Attenuated Virus Vaccine Candidate for the Prevention of Dengue Serotype 4.

The Chair asked if there were any outstanding issues that needed to be discussed that were not covered during [redacted] presentation. There were none. The IBC moved to approve protocol GT0602200101

For Approval:	7
Disapproval:	0
Abstain:	0

[redacted] **Protocol, GT0602200201,** K562/GM-CSF Vaccination in Combination with Imatinib Mesylate as Booster for Chronic Myeloid Leukemia Patients Previously Vaccinated on Protocol J0345.

Dr. [redacted]'s protocol is similar to many that have been approved by the IBC involving the K562/GM-CSF reagent. Indeed, this protocol involves boosting previously vaccinated subject.

The study will involve the 19 patients who participated to date in the previous trial. The subjects will receive 4 doses, every 3 weeks, of $1x10^8$ irradiated K562/GM-CSF cells. Subjects will only be enrolled if they did not experience any dose-modifying toxicities.

The IBC moved to approve protocol GT0602200201 voted for approval:

For Approval:	6	(Dr. Margolick was not present for the vote)
Disapproval:	0	
Abstain:	0	

Recombinant DNA/Pathogen Research Registrations

20 research registrations were presented for IBC consideration. 17 were approved, 3 were places on hold pending receipt of more information. The registrations and the vote tally are found on the next page.

The meeting was adjourned at 4:50 pm.

Institutional Biosafety Committee Registrations
February 20, 2006 Meeting
Registrations from 1/10/06 – 2/10/06

Title	IBC#	BSL	ABSL	Yes	No	Abstain
Modifier Role of Nrf2 in Emphysema Pseudomonas aeruginosa will be cultured and used to infect mice. *Pathogen registration for Pseudomonas aeruginosa*	**P0602070101**	**2**	**2**	**7**	**0**	**0**
Modifier Role of Nrf2 in Emphysema Streptococcus pneumonia will be cultured and used to infect mice. *Pathogen registration for Streptococcus pneumonia*	**P0602070201**	**2**	**2**	**7**	**0**	**0**
Modifier Role of Nrf2 in Emphysema Respiratory syncytial virus (RSV) will be used to infect mice. *Pathogen registration for Respiratory syncytial virus (RSV)*	**P0602070301**	**2**	**2**	**7**	**0**	**0**
Modifier Role of Nrf2 in Emphysema Influenza A-WSN-33 (H1N1) will be used to infect mice.	**P0602070401**	**2**	**2**	**7**	**0**	**0**

Pathogen registration for Influenza A-WSN-33 (H1N1)						
DNA Damage Signaling in Human Cancer Cells Adenoviral vector will be used to transduce various human genomic fragments that involve in DNA damage responses into cultured cells. *Pathogen registration for Adenovirus*	**P0601130101**	**2**	**NA**	**7**	**0**	**0**
Role of Kv1.3 on Antigen-specific Effector T Cells Lentiviral vector FUGW will be used to transduce potassium channel Kv1.3 and green fluorescence protein into cultured cells. DN—Uses plasmid and viral vectors in cultured cells. *Supporting Document – Pathogen registration for lentivirus* *Supporting Document – Human tissue registration*	**DN0601300101** *P0602020101* *B0307220103*	**2**	**NA**	**7**	**0**	**0**
Use of shRNA to knockdown Mammalian Gene Expression Retroviral vector will be used to reduce expression of two human genes PGRMC1 and PGRMC2 that are potentially required for activity of cytochrome P450 enzymes. DN—Uses plasmid and viral vectors in cultured cells. *Supporting Document – Pathogen registration for Retrovirus* *Supporting Document – Human tissue registration*	**DN0602200101** *P0602200101* *B0212190204*	**2**	**NA**	**7**	**0**	**0**
Testing the Role of Alloimmunity in Retroviral Resistance Murine leukemia virus (MLV) from ATCC will be used to infect rats. *Pathogen registration for Murine leukemia virus (MLV)*	**P0601230101**	**2**	**2**	**7**	**0**	**0**
Mouse Model of the Role of Telomerase in Aplastic Anemia and Dyskeratosis Congenita Listeria monocytogenes will be used to infect mice. *Pathogen registration for Listeria monocytogenes*	**P0602030101**	**2**	**2**	**0**	**7**	**0**
Mouse Model of the Role of Telomerase in Aplastic Anemia and Dyskeratosis	**P0602030201**	**2**	**2**	**7**	**0**	**0**

Congenita Candida albicans will be used to infect mice. *Pathogen registration for Candida albicans*						
Molecularly Targeted Agents for Prostate Cancer Adenoviral vector will be used to transduce the newly identified targeting genes for prostate cancer therapy into culture cells and animals. DN—Uses plasmid and viral vectors in cultured cells and mouse. *Supporting Document – Pathogen registration for Adenovirus* *Supporting Document – Human tissue registration*	**DN0601170101** *P0601170101* *B0601300101*	**2**	**2**	**7**	**0**	**0**
Adeno-associated Viral Transfection of Cultured Neurons and Glia Adeno-associated viral vector from Applied Viromics will be used to transduce GFP into cultured neurons and glial cells. *Pathogen registration for Adeno-associated virus*	***P0601240201***	**2**	**NA**	**7**	**0**	**0**
Lentiviral Transfection of Cultured Neurons and Glia Lentiviral vector from SBI Biosystem will be used to transduce GFP into cultured neurons and glial cells. *Pathogen registration for Lentivirus*	**P0601240301**	**2**	**NA**	**7**	**0**	**0**
Effects of Toxoplasma Gondii on Brain and Behavior Development Toxoplasma gondii will be used to infect cultured cells and mice. *Pathogen registration for Toxoplasma gondii*	***P0601190101***	**2**	**2**	**0**	**7**	**0**
Effects of Herpes Simplex Virus-1 on Brain and Behavior Development HSV-1 will be used to infect cultured cells and mice. *Pathogen registration for Herpes simplex virus-1 (HSV-1)*	***P0601190201***	**2**	**2**	**0**	**7**	**0**
Growth Hormone (GH) Gene Therapy in GH-deficient Mice Adeno-associated viral vector will be used to transduce GFP or GH into mice. DN—Uses viral vectors in mice *Supporting Document – Pathogen registration for Adeno-associated virus*	**DN0601200101** *P0512070101*	**2**	**2**	**7**	**0**	**0**

Exploration of Regulatory Genes on Immune Responses to Self and Non-self Antigens Retroviral and lentiviral vectors will be used to transduce TNF and immunoglobulin superfamily molecules into cultured cells. DN—Uses viral vectors in cultured cells *Supporting Document – Pathogen registration for Retrovirus* *Supporting Document – Pathogen registration for Lentivirus* *Supporting Document – Human tissue registration*	**DN0601120101** *P0601180101* *P0601180201* *B0601120101*	**2**	**NA**	**7**	**0**	**0** **Recommendations will be emailed.**
Cancer Immunotherapy Using Attenuated Measles Virus Vectors The attenuated vaccine strain of measles virus (Edmonston B Strain) and mutant Edmonston B strain that will be generated by measles virus rescue system will be used as the shuttle vectors to deliver immune-regulatory genes into mice. *Supporting Document – Pathogen registration for measles virus* *Supporting Document – Human tissue registration*	**DN0601240101** *P0601120101* *B0601120101*	**2**	**2**	**7**	**0**	**0** **Ask to segregate experiments.**
Tissue Cultures Repository of MRRC genetic Core Epstein-Barr virus will be used to establish lymphoblast cell lines *Pathogen registration for Epstein-Barr virus*	**P0601240101**	**2**	**NA**	**7**	**0**	**0** **Confirm strain**
Study of GPI-Transamidase Complex Subunits as Putative Oncogenes in Breast Cancer Plasmid vector will be used to express transamidas complex subunits in cultured cells and mice. DN—Uses plasmid vectors in cultured cells and mice *Supporting Document – Human tissue registration*	**DN0601270101** *B0601270101*	**2**	**2**	**7**	**0**	**0**