Yale University

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March 5, 2007

Edward Hammond, Director
The Sunshine Project
PO BOX 41987
Austin, TX 78704

Dear Dr. Hammond:

Enclosed please find copies of the University's Institutional Biosafety Committee's rDNA minutes requested in your October 12, 2006 letter. Minutes from the period 5/1/03 through 10/12/06 meetings are provided.

Sincerely,

Benjamin Fontes
Biosafety Officer

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Yale University Biological Safety Committee

Recombinant DNA Meeting Minutes

June 19, 2003

The Yale Biological Safety Committee rDNA meeting was held on June 19, 2003 in the Office of Environmental Health & Safety Conference Room, 135 College Street.

Attendance:
Members: Chairman Dean Rupp, Tina Agentis, Susan Compton, Rick Martinello, Erol Fikrig, Ben Fontes, Elan Gandsman, Brigitte Griffith, Robert Heimer, Paul Kowalski, Jim Macy, Sara Rockwell, Shirley Tirrell, Dorothy van Rhijn. Guest: Maryjo Lanzillotta.

Absent: Jonathan Clune, Katherine Goodbody, Karen lamb, Elisabetta Ullu, Ann Yoder.

Chairman's Report:
The minutes of the April 24, 2003 rDNA meeting were distributed for review. Chairman Rupp asked members to submit comments on the minutes to Ben or Joy. The meeting was called to order at 1:12 PM.

Old Business

Human Gene Transfer Subcommittee Report
Dr. [redacted] Protocol (#02-36)
Dr. [redacted] has withdrawn her human gene transfer protocol for activation at Yale related to reports of toxicity in the protocol at other locations. A copy of the Subcommittee's review and Investigator response were distributed to the Committee.

New Business

New Protocols:

Protocol #03-05: Dr. [redacted]
Title: "Study of Epstein Barr Virus & Kaposi Sarcoma Virus (HHV) Activation."
Description: An update of existing registered experiments, Dr. [redacted] will continue to study the role of various genes in the activation of viral replication in these two agents.
Comments: Dr. [redacted] laboratory has extensive experience with EBV, EBV-transformed cell lines, and related viruses. The OEHS Safety Advisor for [redacted] has found the existing facilities in conformity with BL2 requirements (NIH, CDC, Yale). Personnel have completed laboratory safety training and have consistently demonstrated proficiency with required safety work practices.

Protocol #03-06: Dr. [redacted]
Title: "Neurogenetic Processes"
Description: Dr. [redacted] will use an attenuated Pseudorabies virus containing green fluorescent protein to tag neurons in rodent brains to determine functional neuronal connections.
Comments: Dr. [redacted] laboratory has prior BL2 registrations for defective retroviral and adenoviral vectors. The lead researcher, Dr. [redacted] has completed required safety training and has also met with Dr. [redacted] (who also used a Pseudorabies vector in animals), to review procedures. Dr. [redacted] written safety procedures for using the virus were in good order and the experiment is in compliance with the NIH Guidelines at BL2 for in vitro and in vivo experiments. Biosafety and Dr. [redacted] Safety Advisor met with the group to review biosafety requirements and found their proposed facility and work practices appropriate for the proposed work. Animal experiments are recommended for approval at ABL2 with the requirement of a start up meeting with the researchers, Biosafety and the Yale Animal Resources Center (YARC) before initiation.

Protocol #03-07: Dr. [redacted]
Title: "Stem Cell Regulation and Neuronal Patterning in the Forebrain"
Description: Dr. [redacted] proposes the use of defective retroviral and lentiviral vectors to generate mutations in neural cells in culture and in animals to study genes involved in the regulation of brain development.
Comments: Dr. [redacted] has prior experience with BL2 vectors in cell culture and in animals from previous experiments in Dr. [redacted] laboratory. He has previously met with Biosafety and Dr. [redacted] Safety Advisor to review BL2 work practice and facility requirements, and his proposed lab space was found in conformity with BL2 requirements. The new elements of his protocol have not been clearly outlined. It is not clear which lentiviral vector will be used and more information is needed to review the proposed experiments in birds with a lentiviral vector. Dr. Jim Macy informed the Committee that YARC is still working with the laboratory to identify appropriate locations and containment equipment for this experiment. Committee discussion led to a recommendation for approval of the retroviral experiments at this time, but to place a hold on the proposed lentiviral work in vitro and in vivo until further information is provided.

Protocol #03-08: Dr. [redacted]
Title: "Cloning of Malarial MIF Homologue"
Description: Dr. [redacted] will express the MIF gene from Plasmodium falciparum in E. coli to determine if its properties are similar in function human MIF gene, which in involved in modulating the human immune response.
Comments: The proposed work is BL1 as less than 50% of the malarial genome will be used in these experiments. The [redacted] Safety Advisor has reported compliance with BL1 and BL2 requirements on her inspections of Dr. [redacted] laboratory. The lead researcher has attended required trainings and has BL2 work experience. The experiment is exempt from the NIH Guidelines. BL1 containment will be required for the experiment.

Protocol #03-09: Dr. [redacted]
Title: "Cloning and Expression of the SARS Spike Glycoprotein Gene"
Description: Dr. [redacted] will receive non-viable extracted RNA from the CDC, from which he will try to generate a complete cDNA clone of the SARS spike glycoprotein gene. He will then perform studies to determine if the protein is retained in the Endoplasmic Reticulum or the Golgi complex.
Comments: Safety information regarding laboratory research with the SARS virus from the CDC requires BL3 for experiments with viable material. Work with inactivated or non-viable SARS can be performed at a lower biosafety level as determined by the site biosafety committee. As this is the first SARS protocol received by the Committee, its review was deferred to the BL3 Subcommittee.

The Committee unanimously approved the Chair's proposal to approve the recommendations formulated for the protocols reviewed. The Committee's summer recess was initiated following meeting adjournment at 1:36 PM. The next scheduled meeting is September 18, 2003.

Respectfully submitted,

Benjamin Fontes
Biosafety Officer

Yale University

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Yale University Biological Safety Committee

Recombinant DNA Meeting Minutes

September 18, 2003

The Yale Biological Safety Committee rDNA meeting was held on September 18, 2003 in the Office of Environmental Health & Safety Conference Room, 135 College Street.

Attendance:
Members: Chairman Dean Rupp, Virginia Chapman, Jon Clune, Ben Fontes, Paul Forscher, Elan Gandsman, Brigitte Griffith, Robert Heimer, Paula Kavathas, Karen Lamb, Jim Macy, Sara Rockwell, Shirley Tirrell, Dorothy van Rhijn. Guests: Maryjo Lanzillotta.

Absent: Tina Agentis, Susan Compton, Louise Dembry, Katherine Goodbody, Paul Kowalski, Elisabetta Ullu.

Chairman's Report:
The meeting was called to order at 8:44 PM. Chairman Rupp welcomed the Committee's new members, Drs. Paula Kavathas and Paul Forscher, and continued with introduction of existing members. He then presented a brief history and overview of the Committee responsibilities and the split meeting structure (rDNA and other biosafety issues). A copy of the Committee mandate was distributed to Committee members. Chairman Rupp then discussed the recent regulations within the State of Connecticut that require the University to register BL3 laboratories and all research involving human pathogens. He explained that registration triggers periodic inspection by the State Department of Public Health. The State also meets annually with the Committee to review the campus BL3 safety program.

The minutes of the June 19, 2003 rDNA meeting were distributed for review. Chairman Rupp asked members to submit comments on the minutes to Ben Fontes or Joy Sherman of OEHS. Chairman Rupp then proceeded to old business.

Old Business

Dr. [redacted] Protocol (#03-07)
Since the last meeting, Dr. [redacted] has worked with the Yale Animal Resources Center (YARC) staff to identify an appropriate location, housing and proposed work practices for his experiment with a defective lentiviral vector in parakeets. The experiment will be conducted in [redacted] a negative pressure containment laboratory. Animal BL2 practices and personal protective equipment will be required for the experiment. The

work was approved administratively by the Biosafety Office at Animal BL2 with the requirement that start up meeting be held with YARC, Biosafety, and the PI to finalize the safe operating procedures for the animal portion of the experiment.

Dr. [redacted] Protocol (#03-09)
The BL3 Subcommittee of the Yale Biological Safety Committee met to review Dr. [redacted] protocol and determined that BL1 is adequate containment for Dr. [redacted] proposed experiments involving the cloning of individual non-virulent SARS Coronavirus genes in bacteria or animal cells. The standard criteria from the NIH Guidelines based on the percentage of the genome served as the foundation for the Committee's recommendations. Those experiments involving cloning of <50% of the genome may be conducted at BL1, provided the genomic sequence does not code for virulent or toxic subunits of the agent. The Subcommittee also agreed that the default level for inactivated genetic material that exceed 50% of the genome would be BL2. Again, each protocol will also be reviewed to assess the biohazard potential of the genetic elements.

New Business

New Protocols:

Protocol #03-10: Dr. [redacted]
Title: "Coronavirus Protein Microarray."
Description: Dr. [redacted] will express SARS Coronavirus proteins and protein fragments in yeast and E. coli to create microarray for the virus.
Comments: All of the proposed fragments received by Dr. [redacted] are well under 50% of the genome. Using the criteria established for Dr. [redacted] SARS protocol (#03-09 above), the project may be conducted at BL1. Dr. [redacted] laboratory has sufficient prior BL1 experience and his facility meets conformity with these requirements.

Protocol #03-11: Dr. [redacted]
Title: "Biochemical Dissection of Recombination Pathways"
Description: Dr. [redacted] will utilize the Baculovirus expression system to express and assay proteins involved in DNA repair.
Comments: The researchers have prior BL1 experience with this vector and the facility and his work practices were recently found to meet BL1 requirements by the [redacted] Safety Advisor.

Protocol #03-12: Dr. [redacted]
Title: "Lentiviral Expression of deltaFosB and MC-33"
Description: The protocol involves the use of defective lentiviral vector to express genes involved in osteoblast differentiation.
Comments: Dr. [redacted] laboratory has previously worked with viral vectors requiring the same containment as this new vector. The laboratory supervisor, Dr. [redacted] who oversaw the previous research with defective adenoviral and retroviral vectors, is still managing the lab. Biosafety and the [redacted] Safety Advisor met with [redacted] and

the researchers who will work with the new vector to review required BL2 work practices. They will utilize the same self-contained facility used for the previous work, which is also in conformity with BL2 requirements.

Protocol #03-13: Dr. [redacted]
Title: "Production of Adenovirus and Purification, Infection of Mouse Osteoclasts"
Description: Dr. [redacted] will use a replication defective adenovirus to transfect mouse osteoclasts with the Pyk2 gene (to determine its role in osteoclast function).
Comments: This lab has previous approval to work with defective retroviral vectors and amphotropic packaging cell lines. Biosafety Training for the lead researcher, Ms. [redacted] was provided in the field during the lab inspection with the [redacted] Safety Advisor. BL2 practices with additional precautions for work with defective adenovirus were reviewed. The first set of experiments will be conducted with the assistance of BL2 researchers in Dr. [redacted] laboratory, who have prior experience with the defective adenovirus vector proposed in this experiment. The work will also be conducted in Dr. [redacted] BL2 lab (as discussed above). Once Ms. [redacted] is comfortable with the required BL2 practices, she may consider moving the experiment back to Dr. [redacted] BL2 facility, which was also found in compliance with BL2 requirements during the inspection.

Protocol #03-14: Dr [redacted]
Title: "Lentivirus-Vector-Mediated RNA Interference in the Immune System"
Description: The lentiviral vector pLL3.7 (same as proposed by Dr. [redacted] under old business) will be utilized by Dr. [redacted] to block the activity of various genes involved in immunity.
Comments: Biosafety and the [redacted] – 5th floor Safety Advisor met with Dr. [redacted] Lab Manager, Dr. [redacted] and the proposed researchers to review the required BL2 practices for the experiment. Dr. [redacted] lab has numerous BL2 protocols on file with the Biosafety Committee. The proposed researchers have completed required Biosafety Training and have prior BL2 experience with related vectors or agents. Dr. [redacted] has an independent self-contained facility for all BL2 cell culture work. The lab was found in conformity with BL2 requirements.

Protocol #03-15: Dr. [redacted]
Title: "Regulation of T Cells by Ras Proteins"
Description: Dr. [redacted] will use a defective retrovirus to deliver Ras proteins into immune cells at various time points to determine the effect of this stimulation.
Comments: Dr. [redacted] lab has previous experience working with BL2 material ranging from human cells to human pathogens. The work described in her protocol will not extend the Biosafety Level of her current work. Her existing work practices and new cell culture facility are in compliance with the BL2 requirements for this work. All new researchers joining the protocol will be required to complete all relevant biosafety training classes and will be trained by experienced researchers in Dr. [redacted] laboratory.

Protocol #03-16: Dr. [redacted]
Title: "Production of Lentivirus for RNAi Experiment"
Description: Dr. [redacted] will also use the pLL3.7 vector to silence genes involved in synaptic membrane trafficking.
Comments: Dr. [redacted] laboratory has prior experience at BL2 and BL2+ with experiments ranging from low LD50 toxins of biological origin, defective vectors, and human pathogens. His BL2 self-contained facility in BCMM was inspected by Biosafety and the [redacted] Safety Advisor and found in conformity with BL2 requirements. The written safety protocol for the experiment was reviewed in the field with the lead researcher and augmented to require BL2+ practices as the facility now has multiple BL1 users. The researcher was asked to schedule the room in advance and restrict access to other users, or to utilize BL2+ work practices while working within the room.

Protocol #03-17: Dr. [redacted]
Title: "The Secretory Pathway of Ovarian Cancer Cells as a Therapeutic Target"
Description: Dr. [redacted] will utilize a defective adenoviral vector with the del32 gene to determine its effect on ovarian tumor cells in vivo.
Comments: Dr. [redacted] laboratory has prior BL2 experience with human cells but have not previously worked with the adenoviral vector. Biosafety and the [redacted] Safety Advisor met with Dr. [redacted] and her staff to review the required BL2 cell culture procedures for this work, provide additional biosafety training, and to inspect the proposed facility. They found the facility and the proposed work practices adequate for the proposed experiment. Dr. [redacted] also completed the required Yale Animal Resources Center start-up meeting to outline the Animal BL2 procedures for her proposed work with this vector in mice.

The Committee unanimously approved the Chair's proposal to approve the recommendations formulated for the protocols reviewed during the meeting. The meeting was adjourned at 9:13 AM. The next scheduled meeting is October 16, 2003.

Respectfully submitted,

Benjamin Fontes
Biosafety Officer

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Yale University Biological Safety Committee

Recombinant DNA Meeting Minutes

November 20, 2003

The Yale Biological Safety Committee rDNA meeting was held on November 20, 2003 in the Office of Environmental Health & Safety Conference Room, 135 College Street. The meeting was called to order at 8:40 AM.

Attendance:
Members: Chairman Dean Rupp, Tina Agentis, Susan Compton, Virginia Chapman, Louise Dembry, Ben Fontes, Paul Forscher, Elan Gandsman, Katherine Goodbody, Paula Kavathas, Karen Lamb, Jim Macy, Sara Rockwell, Shirley Tirrell, Dorothy van Rhijn.
Guests: Maryjo Lanzillotta.

Absent: Jon Clune, Brigitte Griffith, Robert Heimer, Paul Kowalski, Elisabetta Ullu.

Chairman's Report:
The minutes of the September 18, 2003 rDNA meeting were distributed for review. Chairman Rupp asked members to submit comments on the minutes to Ben Fontes or Joy Sherman of OEHS. Chairman Rupp then proceeded to old business.

New Business

New Protocols:

Protocol #03-18: Dr. [redacted]
Title: "Cytokine Signaling in Vascular System"
Description: Dr[redacted] will use defective retroviral, adenoviral and lentiviral vectors to study the effect of effect of various genes on signal transmission across the cell membrane.
Comments: Dr.[redacted] has previously worked with all three vectors at the University of [redacted] prior to coming to Yale. The[redacted] Safety Advisor and Biosafety met with Dr.[redacted] to inspect his proposed cell culture facility and to review his written set of standard operating procedures. His lab,[redacted] is in full compliance with BL2 requirements and is a self-contained cell culture lab. His work practices were also well established and were in conformity with BL2 requirements. OEHS recommended the use of dilute bleach (1- 10%) in addition to ethanol for his decontamination procedures, as ethanol is not effective against adenovirus. The proposed work in animals is approved at ABL2 with the contingencies that Dr.[redacted] obtain an approved YACUC protocol and

complete the required start-up meeting with YARC and Biosafety to develop an SOP for the animal protocol.

Dr. [redacted] requested identification of the individual cloned by Dr. [redacted] and Ben Fontes agreed to contact the lab to obtain this information.

Protocol #03-19: Dr. [redacted]
Title: "Campylobacter jejuni Cell Shape"
Description: Dr. [redacted] will knock out various cytoskeletal genes in Campylobacter jejuni to determine their role in shape and structure of the organism.
Comments: Dr. [redacted] will serve as the lead researcher for the project. Dr. [redacted] has previous BL2 experience with Candida albicans at another institution. All work with viable C. jejuni will be conducted with personnel from Dr. [redacted] laboratory in [redacted]. Dr. [redacted] laboratory is currently registered with the Biosafety Committee and the State of CT Dept. of Public Health for work with the agent. Dr. [redacted] staff will provide Dr. [redacted] with direct training in handling the agent. All work with viable C. jejuni will be conducted in [redacted] the laboratory of Dr. [redacted] The [redacted] and [redacted] Safety Advisors met with Dr. [redacted] and lab personnel from Dr. [redacted] laboratory to review BL2 procedures with the group and to inspect the proposed BL2 laboratory. The facility and proposed work practices were found in conformity with BL2 requirements. Cloning individual C. jejuni genes in E. coli can be conducted at BL1. The [redacted] Safety Advisor indicated that Dr. [redacted] laboratory remains in full conformity with BL1 requirements.

Protocol #03-20: Dr. [redacted]
Title: "Survivin Regulation of Lung Fibrosis"
Description: Dr. [redacted] will use a defective adenoviral vector to examine the role of the surviving and its pathway in lung injury.
Comments: Dr. [redacted] will lead the project and has prior BL2 experience. Biosafety and the Dr. [redacted] Safety Advisor inspected the proposed cell culture facility and found the facility and proposed work practices in compliance with BL2 requirements. The proposed animal work can also be approved at ABL2 with the contingencies of prior YACUC approval and the requisite start up meeting with YARC and Biosafety. Biosafety will require any aerosol generating procedures, such as intra-tracheal inoculation of virus, to be conducted within primary containment. Since the in vitro work may not be initiated for an indeterminate time period, the approval letter will include a requirement for a biosafety review of the safety procedures with representatives from OEHS before starting this work.

Protocol #03-21: Dr. [redacted]
Title: "Study of Peptides That Might Inhibit HIV-1 Fusion"
Description: Dr [redacted] will express a very short piece of HIV-1 gp41 (100 base pairs) in E. coli. The segment of the gp41 studied by the group is involved in its shape change that allows it to infect the cell. She will subsequently test the ability of synthesized peptides in binding this portion of the molecule.

Comments: This is the first rDNA protocol for the laboratory. They are also interested in pursuing a research project with Listeria monocytogenes in the future. . Researchers from the group are attended Yale Biosafety Training. Biosafety and the [redacted] Department Safety Advisor inspected the proposed space and reviewed the required BL1 work practices. They are in the process of retrofitting an existing lab to meet BL1 and BL2 facility requirements for this experiment and possible future work at BL2. Biosafety and the [redacted] Department Safety Advisor will work with Dr. [redacted] to ensure the facility is completed and inspected for BL1 and BL2 compliance.

Protocol #03-22: Dr. [redacted]
Title: "Role of TGF-B in Memory T Cell Development"
Description: Update of existing experiment from [redacted] involving a defective adenoviral vector. Here, the adenoviral vector will be used to prime an immune response and generate memory T cells.
Comments: Dr. [redacted] has previous experience with a VSV vector at BL2 and related BL2 cell lines. The graduate student also has prior work experience with adenoviral vectors at another institution. Both have completed required Biosafety Training. Biosafety and the [redacted] floor Safety Advisor visited the laboratory to review the proposed registrations, work area, and work practices. All were well in conformity with BL2 requirements. The lab has existing approval to work with defective adenovirus through the Biosafety Committee and a variety of human pathogens through the State of CT Dept. of Public Health. Many protocols with similar vectors at BL2 are already in progress within the facility. Animal work may be approved with the requirement of an approved YACUC registration and a satisfactory start up meeting with YARC and Biosafety prior to the initiation of any work in animals.

Protocol #03-23: Dr. [redacted]
Title: "Use of Recombinant Listeria monocytogenes to Study Memory T Cell Development"
Description: Dr. [redacted] will utilize a recombinant Listeria monocytogenes containing the ovalbumin gene in a study of the developmental stages of memory T cells.
Comments: As above for 03-22 – same two researchers and proposed biosafety work practices.

The Committee unanimously approved the Chair's proposal to approve the recommendations formulated for the protocols reviewed during the meeting. The meeting was adjourned at 9:01 AM. The next scheduled meeting is December 18, 2003.

Respectfully submitted,

Benjamin Fontes
Biosafety Officer

Yale University

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Yale University Biological Safety Committee

Recombinant DNA Meeting Minutes

December 18, 2003

The Yale Biological Safety Committee rDNA meeting was held on November 20, 2003 in the Office of Environmental Health & Safety Conference Room, 135 College Street. The meeting was called to order at 8:36 AM.

Attendance:
Members: Chairman Dean Rupp, Virginia Chapman, Jon Clune, Louise Dembry, Ben Fontes, Elan Gandsman, Brigitte Griffith, Katherine Goodbody, Robert Heimer, Paula Kavathas, Paul Kowalski, Karen Lamb, Jim Macy, Sara Rockwell, Shirley Tirrell, Dorothy van Rhijn. Guests: Maryjo Lanzillotta.

Absent: Tina Agentis, Susan Compton, Paul Forscher.

Chairman's Report:
The minutes of the November 20, 2003 rDNA meeting were distributed for review. Chairman Rupp asked members to submit comments on the minutes to Ben Fontes or Joy Sherman of OEHS. Chairman Rupp then proceeded to old business.

Old Business

Dr. [redacted] Proposal (#03-18). An update on the nomenclature of Dr. [redacted] protocol was provided to the Committee. ASK stands for Apoptosis signal kinase and Etk represents Endothelial tyrosine kinase.

New Business

New Protocols:

Protocol #03-24: Dr. [redacted] rDNA Proposal
Title: "HIV-1 Reverse Transcriptase Project"
Description: Dr. [redacted] laboratory will use the baculovirus expression system to express human proteins and non-conjugative E. coli to express the reverse transcriptase gene of HIV-1. The group is involved in studying compounds that inhibit replication of HIV-1 in cell culture.
Comments: The protocol was incomplete (a full summary of the protocol was not provided). Dr. [redacted] will be requested to provide additional information to the

Biosafety Office to complete the protocol. Biosafety is authorized to administratively approve once the description is obtained. Dr. [redacted] lab group has extensive experience working at BL1, BL2, and BL2+ from previous experiments.

Protocol #01-14: Update of Dr. [redacted] rDNA Protocol
Title: "West Nile Virus (WNV) Immunization"
Description: Dr. [redacted] would like to add rabbits to his previously approved rDNA protocols. Rabbits will be immunized with a vaccine containing a single WNV envelope gene to elicit antibodies to West Nile Virus.
Comments: The protocol will not involve work with or challenge with live West Nile Virus, but only a recombinant vaccine provided to rabbits to obtain antibodies. The work is a continuation of an existing project in rodents. The work may be handled at Biosafety Level 1 for generation of the vaccine and Animal Biosafety Level 1 for immunization of rabbits.

The Committee did not approve Dr. [redacted] protocol, #03-24, at the meeting, but authorized the Biosafety Office to approve once the full project summary is received if in order. The Committee unanimously approved the Chair's proposal to approve the recommendations presented for the update of #01-14. The meeting was adjourned at 9:07 AM. The next scheduled meeting is January 15, 2004.

Respectfully submitted,

Benjamin Fontes
Biosafety Officer

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Yale University Biological Safety Committee

Recombinant DNA Meeting Minutes

February 19, 2004

The Yale Biological Safety Committee rDNA meeting was held on February 19, 2004 in the Office of Environmental Health & Safety Conference Room, 135 College Street. The meeting was called to order at 9:11 AM.

Attendance:
Members: Chairman Dean Rupp, Tina Agentis, Virginia Chapman, Susan Compton, Louise Dembry, Ben Fontes, Elan Gandsman, Robert Heimer, Katherine Goodbody, Paula Kavathas, Paul Kowalski, Karen Lamb, Jim Macy, Sara Rockwell, Dorothy van Rhijn. Guests: Maryjo Lanzillotta.

Absent: Paul Forscher, Brigitte Griffith, and Shirley Tirrell.

Chairman's Report:
The minutes of the December 18, 2003 rDNA meeting were distributed for review. Chairman Rupp asked members to submit comments on the minutes to Ben Fontes or Joy Sherman of OEHS.

NIH IBC Training Conference
Chairman Rupp informed the Committee that the presentations from the NIH IBC conference that he attended in 2003 were now available on line at the NIH OBA website. The link, www4.od.nihi.gov/oba/IBC/IBC_conf_links.htm, was provided to Committee members.

New Business

Sunshine Project Request:
The Committee then reviewed a request from the Sunshine Project for copies of the two most recent meetings of the Yale IBC, pursuant to the NIH Guidelines for Research Involving rDNA Molecules. Biosafety contacted the NIH OBA Office, who confirmed their awareness of the group and its request. The General Counsel's Office is assisting the Biosafety Office with the response to the Sunshine Group. Committee members offered suggestions for Biosafety and General Counsel for preparing the response.

New Business

<u>New Protocols:</u>

Protocol #04-01: Dr. [redacted]
Title: "Adenoviral Vector Injection into Dorsal Root Ganglion of Rat"
Description: Use of a defective adenoviral vector carrying GFP and potassium channel proteins to alter neuronal excitability as part of experiments involving the effects of nerve injury.
Comments: This laboratory has previous experience with human cell lines, non-human primates (NHP's), and tissues and cells from NHP's at BL2. They have not worked with adenoviral vectors previously, but have prior BL2 work experience. Biosafety and the [redacted] Safety Advisor conducted on-site Biosafety Training for the Principal Investigator and his research staff. In addition, all proposed work locations were toured to review the proposed procedures in animals (from injection of Ad vectors, transport of animals to and from the animal facility, behavioral testing chambers, electrophysiology, and necropsy). Biosafety requirements for each of these applications were reviewed on site. Also, the investigator has YACUC approval for the experiment. Work in animals will also require a start-up meeting with YARC, Biosafety, and the research group prior to initiation. The final Animal BL2 SOP will be developed at this meeting.

Protocol #04-02: Dr. [redacted]
Title: "Radixin Gene Silence and Functional Characterization"
Description: The investigator will use a defective adenoviral vector to knockout an anchor protein in the plasma membrane of liver cells to examine its role in hepatic excretory function.
Comments: The lab has previous experience with human cells and tissues at BL2. The lead researcher has completed applicable Biosafety courses at OEHS for this work. The OEHS Safety Advisor has met with the group to inspect the proposed work and found the proposed facility and work practices to be in conformity with BL2 requirements. Work in animals requires YACUC approval and a start-up meeting with YARC, Biosafety and the research group before initiation of work to outline required ABL2 procedures.

Protocol #04-03: Dr. [redacted]
Title: "Characterization of NHE8"
Description: The lab will utilize a defective adenoviral vector for expression of the NHE8 (Na+ - H+ isoforms in kidney) in different cell lines to study its function.
Comments: The lab has prior experience with human material and Vaccinia virus at BL2. The Lab Supervisor has demonstrated consistent compliance with BL2 requirements on OEHS and State or CT laboratory inspections. The lead researcher has completed all required Biosafety Trainings. The lab has previously been found in compliance with BL2 requirements. The OEHS Safety Advisor met with the lab supervisor and the lead researcher, to review BL2 containment procedures for work with the defective adenovirus. The cell culture facility in [redacted] is updated and well in conformity with BL2 requirements. No work in animals has been proposed in this protocol.

Protocol #04-04: Dr. [redacted]
Title: "Use of Recombinant VEGF in Mice with Ischemic Kidney Injury"

Description: The lab will use a defective adenoviral vector to deliver vascular endothelial growth factor (VEGF) to mice to examine protective effects from ischemic injury.
Comments: The investigator's staff has prior work experience with human materials retroviral vectors and amphotropic packaging cell lines at BL2. The group also has prior experience with these agents in animals at BL2. The group's new cell culture facility in [redacted] is in full conformity with BL2 requirements and adequate for dilution of virus (which will be sent to his lab already containing VEGF from Boston). The animal studies involving the vector will require YACUC approval and a start-up meeting with YARC, Biosafety and his lab prior to initiation of the experiment to outline the work location and to finalize the ABL2 SOP.

Protocol #04-05: Dr. [redacted]
Title: "Mutational Analysis of RtsM Homologs in Pseudomonas syringae Pathovars"
Description: The lab will study the effect of a signaling protein in Pseudomonas syringae by knocking it out.
Comments: The investigator has extensive work experience with BL2 bacterial pathogens. All personnel involved in training have sufficient BL2 work experience and have completed all required OEHS Biosafety Training courses. The group's new cell culture facility in [redacted] is well in conformity with BL2 containment. The proposed work practices as described in the attached protocol were exemplary. The Biosafety inspection confirmed full conformity with BL2 requirements. Receipt of the agent required a USDA permit, which has been received by the lab. No work with plants is planned. If required, vectors will be shipped to the University of [redacted] for research in plants. Dr. S.P. Dinesh-Kumar, assisted with the review and indicated that the proposed practices are sufficient to contain the organism.

Protocol #04-06: Dr. [redacted]
Title: "Therapeutic Vaccines against Papillomavirus"
Description: The investigator will utilize a defective adenovirus and attenuated Salmonella typhimurium as vectors to express Papilloma virus antigens as part of a Papilloma virus vaccine study.
Comments: The investigator has extensive experience with human material and Human Papilloma virus at BL2 and Animal BL2. The lab has also collaborated on experiments involving lab strains of VSV with another Yale investigator. The group also has prior experience with Vaccinia virus in cell culture. All Biosafety Training courses have been confirmed as part of the renewal registration process. Ben Fontes and [redacted] from OEHS and [redacted] and [redacted] from YARC, have worked to retrain Dr. [redacted] laboratory in relevant in vitro and in vivo BL2 and BL2+ practices. The proposed in vitro facility, [redacted], is well in conformity with BL2 requirements. Work in animals will require YACUC approval. The proposed animal BL2 research location for work in rabbits will be assigned by YARC at the required start up meeting for all of her BL2 experiments. OEHS and YARC will also monitor progress with Dr. [redacted] compliance efforts with both in vitro and in vivo experiments upon initiation and periodically thereafter.

Protocol #04-07: Dr. [redacted]
Title: "Therapeutic Vaccines against Papillomavirus"
Description: Similar to 04-06, but use of a laboratory strain VSV vector to express Papilloma virus antigens. Vaccinia virus will also be used to help enhance expression.
Comments: As above for #04-06.

A draft approval letter for Protocols #04-06 and #04-07 was distributed for Committee review. Additional requirements were requested from the Committee. Biosafety agreed to add the information and distribute to Committee members via email for review.

The Committee unanimously approved the Chair's proposal to approve the recommendations formulated for protocols #04-01, #04-02, #04-03, #04-04, and #04-05. Protocols #04-06 & #04-07 were not approved at the meeting. The Committee may attempt an email vote on the updated approval letter for these protocols prior to the next meeting. The meeting was adjourned at 9:50 AM. The next scheduled meeting is March 18, 2004.

Respectfully submitted,

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Yale University Biological Safety Committee
Recombinant DNA Meeting Minutes
March 18, 2004

The Yale Biological Safety Committee rDNA meeting was held on March 18, 2004 in the Office of Environmental Health & Safety Conference Room, 135 College Street. The meeting was called to order at 9:27 AM.

Attendance:
Members: Chairman Dean Rupp, Virginia Chapman, Susan Compton, Ben Fontes, , Brigitte Griffith, Jim Macy, Shirley Tirrell, Dorothy van Rhijn. Guests: Maryjo Lanzillotta, Joy Sherman.

Absent: Tina Agentis, Louise Dembry, Paul Forscher, Elan Gandsman Katherine Goodbody, Robert Heimer, Paula Kavathas, Paul Kowalski, Karen Lamb, Brigitte Griffith, Sara Rockwell.

Chairman's Report:
The minutes of the February 19, 2004 rDNA meeting were distributed for review. Chairman Rupp asked members to submit comments on the minutes to Ben Fontes or Joy Sherman of OEHS.

Old Business

Sunshine Project Request:

Ben Fontes reported that the University has submitted copies of the two most recent rDNA meeting minutes to the Sunshine Project. The submission was reviewed and approved by the General Counsel's Office.

Dr. [redacted] rDNA Protocols (#04-06 & #04-07)

The approval letters for Dr. [redacted] protocols were updated to reflect the comments from the previous Committee meeting. Detailed Standard Operating Procedures shall be required for each aspect of her biohazard work and Biosafety and the Yale Animal Resources Center (YARC) will work together to monitor her experiments periodically. Each new experiment must have a start-up meeting with Biosafety and YARC prior to initiation. The experiments were approved by the Committee through an email ballot.

New Protocols:

Protocol #04-08: Dr. [redacted]
Title: "Characterization of Proteins that Guide Axons in the Vertebrate Nervous System."
Description: Dr. [redacted] will use standard cloning vectors to study the function of various cell surface receptors and ligands involved in axonal transport.
Comments: Dr. [redacted] has prior BL2 experience with Adenoviral and Retroviral vectors at another institution. She will submit a BL2 experimental protocol involving non-exempt rDNA work in the near future. Her staff has completed all required Biosafety training. Dr. [redacted] has a self-contained BL2 cell culture laboratory equipped with biosafety cabinet, incubator, and small bench top centrifuge. A below-counter freezer and refrigerator will be installed in the near future along with a larger bench top centrifuge equipped with safety buckets for secondary containment. Biosafety reviewed BL1 work practices for her rDNA studies and BL2 work practices for her cell culture experiments with Dr. [redacted]

Protocol #04-09: Dr. [redacted]
Title: "Use of Recombinant DNA for Studies of Gene Function."
Description: Dr. [redacted] will utilize both ecotropic and amphotropic retroviral vectors to study the role of hypoxia-regulated genes on metabolism and tumor development.
Comments: Dr. [redacted] has worked with retroviral vectors and transgenic animals at another institution. His staff has completed all applicable biosafety training classes. Dr. [redacted] and his lead researcher demonstrated strong conformity with BL2 work practice requirements during the start up biosafety inspection of his laboratory.

Protocol #04-10: Dr. [redacted]
Title: "Molecular Analysis of CD8, MHC Class I Interaction."
Description: Dr. [redacted] will use an amphotropic retroviral vector to express a cell surface protein from human CD8+ T lymphocytes in a murine T cell hybridoma cell line.
Comments: Dr. [redacted] has previous BL2 experience with infectious agents here at Yale, and is up to date with required Biosafety training. Dr. [redacted] has a dedicated self-contained BL2 cell culture laboratory that was previously inspected and found in conformity with biosafety requirements.

Protocol #04-11: Dr. [redacted]
Title: "Generation of Langerhans Cell Deficient Mice."
Description: Dr. [redacted] will use the Diptheria toxin A-Chain to generate a line of transgenic lacking dendritic cells, to study the role of dendritic cells in immune regulation.
Comments: Dr. [redacted] lab has prior experience at BL1 and BL2 containment. A prior Committee precedent [redacted] 1994) utilizing the Diptheria A toxin in plant cells and plants that was approved at BL1 served as the principle reference for this review. The toxicity of the A chain only is substantially reduced in the absence of the Binding or B toxin subunit. The protocol can be approved at BL1 provided that Diptheria B Toxin is not present in the laboratory.

Protocol #04-12: Dr. [redacted]

Title: "Analysis and Study of RNA Band Regulatory Elements in A. Tumefaciens."
Description: Dr. [redacted] protocol involves the cloning of RNA elements from Agrobacterium tumefaciens in E. coli.
Comments: Dr. [redacted] staff has prior BL1 work experience. This protocol is exempt from the NIH Guidelines and does not require Committee review. Biosafety also met with the lab Supervisor and determined that the project will not involve the use of live plants.

The Committee did not have a quorum present at the meeting and did not vote on the protocols presented. The Biosafety Office will either administratively approve the protocols or submit a postal ballot to the full Committee for approval. The meeting was adjourned at 9:47 AM. The next scheduled meeting is April 15, 2004.

Respectfully submitted,

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Yale University Biological Safety Committee
Recombinant DNA Meeting Minutes
May 20, 2004

The Yale Biological Safety Committee Biological Safety meeting was held on March 18, 2004 in the Office of Environmental Health & Safety Conference Room, 135 College Street. The meeting was called to order at 8:38 AM.

Attendance:
Members: Chairman Dean Rupp, Susan Compton, Ben Fontes, Elan Gandsman, Katherine Goodbody, Robert Heimer, Paula Kavathas, James Macy, Shirley Tirrell, Dorothy van Rhijn. Guests: Deborah Ferry, Maryjo Lanzillotta, Joy Sherman.

Absent: Tina Agentis, Virginia Chapman, Louise Dembry, Paul Forscher, Brigitte Griffith, Paul Kowalski, Karen Lamb, Sara Rockwell.

Chairman's Report:
The minutes of the March 18, 2004 Biological Safety Committee meeting were distributed for review. Chairman Rupp asked members to submit comments on the minutes to Ben Fontes or Joy Sherman of OEHS. Chairman Rupp also indicated that the NIH Office of Biotechnology Activities (OBA) has issued a guidance document for IBC minutes. NIH OBA developed the document in response to the numerous questions they received in response to the Sunshine Project's request for minutes from the IBC's registered with the NIH. The document was distributed to Committee members at the meeting.

Old Business

The protocols that were presented at the 3/18/04 meeting: #04-08, Dr. [redacted] Protocol; #04-09, Dr. [redacted] Protocol; #04-10, Dr. [redacted] Protocol; #04-11, Dr. [redacted] Protocol; and #04-12, Dr. [redacted] Protocol, have been administratively approved by the Biosafety Office. They were presented once again to the Committee as there was not a quorum present at the meeting.

New Protocols:

Protocol #04-13: Dr. [redacted] Protocol
Title: "Cloning of the ITSI or rrn Operon from Mycobacteria."

Description: A 400 to 500 base segment of M. tuberculosis, M. bovis, or M. smegmatis will be cloned in E. coli to investigate the difference in cleavage sites in ribosomal RNA's between slow and fast growing Mycobacteria.
Comments: Dr. [redacted] has worked at BL2 and BL1 in Dr. [redacted] laboratory, and has completed required Biosafety training. Dr. [redacted] laboratory has annually demonstrated compliance with BL2 requirements on State of CT and/or Yale Biosafety lab inspections. The proposed work will be carried out using the lab's existing protocol that was established for handling BL2 human pathogens.

Protocol #04-14: Dr. [redacted]
Title: "Role of Brg Complex in T Cell Development."
Description: An exempt rDNA experiment. The transgenic knockout mice will be produced by Yale core facility for Dr. [redacted]. Mice and will lack BRG gene to study its role in T Cell development.
Comments: Dr. [redacted] is in new lab space in the [redacted] building, and has access to both cell culture and wet lab bench space. All facilities are well in conformity for BL1 experiments.

Protocol #04-15: Dr. [redacted] Protocol
Title: "Pathogenesis of SARS Virus in Rats."
Description: Use of plasmids that contain SARS Virus S and N genes for screening of fixed tissues from SARS inoculated Rats.
Comments: Dr. [redacted] has prior BL3 and BL2 work experience. Although the rDNA portion of the experiment will only require BL2, Dr. Compton's protocol is currently under review by the Yale BSC BL3 Subcommittee for proposed cell culture and animal experiments with live SARS virus.

Protocol #04-16: Dr. [redacted]
Title: "Lentivirus-Vector-Mediated RNA Interference in Lymphocytes."
Description: Dr. [redacted] will utilize a defective lentiviral vector to knock out the function of genes in various immune cells at different stages of activation.
Comments: Dr. [redacted] and her staff have extensive experience with BL2 agents, including human pathogens and defective viral vectors. Researchers have completed applicable biosafety training. Dr. [redacted] new cell culture in the [redacted] building facility has been previously inspected by OEHS and found in conformity with Bl2 requirements. She also has a dedicated BL2 cell culture room for the experiments.

Protocol #04-17: Dr. [redacted]
Title: "Infection of Mice with Recombinant Viruses and Bacteria."
Description: Dr. [redacted] will utilize recombinant strains of viruses and bacteria (Vaccinia, VSV-NJ, Listeria, and an attenuated Influenza virus that contain a glycoprotein from LCM for study of T-cell responses to the protein in mice after infection.
Comments: Dr. [redacted] has previously worked with these BL2 agents and LCMV at [redacted] University. She has also attended all applicable Biosafety training classes since arriving at Yale. Dr. [redacted] also has previous work experience with infected animals. Dr. [redacted] BL2 cell culture facility and her work practices were inspected by Biosafety

and found in conformity with BL2 requirements. Biosafety is working with Dr. [redacted] to develop a dedicated self-contained cell culture room solely for her research, which would eliminate traffic from other research groups. A start up meeting for animal work was held with YARC management and facility staff to outline required BL2 and BL2+ procedures for each of the agents on this protocol.

Protocol #04-18: Dr. [redacted]
Title: "Regulation of Mitochondrial Gene Expression."
Description: This exempt project involves expression of human and yeast genes into E. coli, yeast, and human cells to study mitochondrial gene expression and function.
Comments: The OEHS Safety Advisor for Dr. [redacted] found his lab and cell culture work practices in conformity with BL1 and BL2 requirements.

Protocol #04-19: Dr. [redacted]
Title: "Functional Characterization of Soluble EGFR Isoforms and EGFR Mutants."
Description: Dr. [redacted] will use Rous Sarcoma virus and standard cloning vectors in her research on early growth factor proteins on normal and tumor cell regulation.
Comments: The lab has prior experience with the vector system and materials listed in the protocol. The lab group has completed applicable Biosafety training. The lab is currently in the [redacted] Street [redacted] research labs, but has not initiated the work. The Safety Advisor assigned to the group has verified that the space is adequate for the work and meets BL2 criteria. Biosafety and/or [redacted] Safety Advisor will inspect the laboratory to review BL2 work practices prior to the initiation of BL2 rDNA experiments.

Protocol #04-20: Dr. [redacted]
Title: "DNA Immunization of Mice."
Description: Use of glycoprotein DNA from LCMV for immunization in mice. Mice will be subsequently challenged with LCMV to determine the level of protection and effect on memory T Cells from DNA injections.
Comments: As above for 04-17. The creation of DNA immunization and injection of Mice with DNA can be approved with requisite YARC start up meetings as applicable. The BSC BL3 Subcommittee will determine the biosafety level for challenge of these mice with LCMV and the location of the work.

Protocol #04-21: Dr. [redacted]
Title: "Lentiviral Transduction of Primary Mouse Splenocytes."
Description: Dr. [redacted] will use a defective lentiviral vector to examine the effect of various genes on the development of memory T Cells.
Comments: As above for 04-17. The proposed laboratory was inspected by Biosafety and Dr. [redacted] Safety Advisor and was found in conformity with BL2 requirements.

Protocol #04-22: Dr. [redacted]
Title: "Heterotrimeric G Protein Control of Centrosome Function."

Description: Use of baculovirus vector to express genes from C. elegans to study the mechanism of signaling in G proteins. Will also generate transgenic C. elegans, and cloning work in E. coli may exceed large-scale limits (> 10 liters).
Comments: Dr. [redacted] and his lab staff have training and experience applicable to BL1 experiments. Dr. [redacted] laboratory has previously been inspected for BL1 procedures and his lab facility is in conformity with BL1 criteria. Biosafety will revisit the lab prior to the initiation of large-scale E. coli experiments to review Good Large Scale Practices and ensure that appropriate containment and spill control supplies are in place.

Protocol #04-23: Dr. [redacted]
Title: "Zebrafish Ribbon Synapse Physiology."
Description: Dr. [redacted] will label neurotransmitter proteins with GFP in transgenic zebrafish to help study their function and localization.
Comments: The lab group has prior experience with human cells and transgenic zebrafish and has completed applicable training classes. The [redacted] Safety Advisor has conducted a start up lab inspection for the work and identified the facility in conformity with BL1 and BL2 requirements. Biosafety and/or Dr. [redacted] Safety Advisor will conduct a follow-up visit to review basic guidelines for work with transgenic zebrafish and precautions to control microbial growth in the tanks.

Protocol #04-24: Dr. [redacted]
Title: "A Putative Rnase P RNA from Camelpox Virus."
Description: Dr. [redacted] lab will obtain a chemically synthesized fragment of Camelpox virus RNA to determine if it has RnaseP activity.
Comments: As above for #04-13.

Protocol #04-25: Dr. [redacted]
Title: "FeoB Characterization."
Description: Dr. [redacted] will clone the iron-binding protein FeoB from BL2 bacteria to study mechanism of uptake. The sequences are not pathogenic and represent much < 50% of the genome.
Comments: Dr. [redacted] has prior BL1 work experience and applicable biosafety training. Dr. [redacted] Safety Advisor on the most recent lab inspection found the facility in conformity with BL1 requirements.

With the exception of #04-15, the Committee unanimously approved the non-exempt rDNA protocols presented at the meeting. The meeting was adjourned at 9:20 AM. The next scheduled meeting is June 17, 2004.

Respectfully submitted,

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Yale University Biological Safety Committee
RDNA Minutes
September 30, 2004

The Yale Biological Safety Committee Biological Safety meeting was held on September 30, 2004 in the Office of Environmental Health & Safety Conference Room, 135 College Street. The meeting was called to order at 8:38 AM.

Attendance:
Members: Chairman Dean Rupp, Jon Clune, Susan Compton, Ben Fontes, Elan Gandsman, Katherine Goodbody, Robert Heimer, Douglas Kankel, Paula Kavathas, Karen Lamb, Mark Solomon, Dorothy Van Rhijn Guests: Maryjo Lanzillotta, Kevin Charbonneau, Joy Sherman.

Absent: Tina Agentis, Linda Buonocore-Buzzelli, Louise Dembry, James Macy, Sara Rockwell, George Zdru

Chairman's Report:
The minutes of the May 20, 2004 Biological Safety Committee meeting were distributed for review. Chairman Rupp asked members to submit comments on the minutes to Ben Fontes or Joy Sherman of OEHS.

Chairman Rupp welcomed new members and provided an overview of the Biosafety Committee responsibilities, which is divided equally into recombinant DNA and Biosafety (all other biohazard) issues. Following the introduction, Dr. Robert Heimer asked if the Committee is required to ensure that the experiments submitted are scientifically sound, like the IRB. Chairman Rupp responded by stating the Committee is generally concerned with safety, not solely good science. Karen Lamb reported that protocols involving animals or humans are looked at by the IRB and IACUC, which takes scientific justification into account. The Committee's Human Gene Transfer Subcommittee does discuss the scientific validity of HGT experiments when submitted. Dr. Douglas Kankel, a new member, also asked if members could be held legally responsible in their capacity as Committee members. Jon Clune, from the Office of the General Counsel, indicated that most lawsuits would be filed against the University, not individuals, and that in most circumstances state law and University policy would provide indemnification for Committee members carrying out their responsibilities in good faith.

Chairman Rupp briefly discussed the NIH IBC Policy Conference in Bethesda that he attended in September. Recombinant experiments involving SARS and Influenza viruses were prominently addressed at the meeting. Committee members were also shown key biosafety references and provided with a few handouts to help facilitate their participation

in the review of biohazard protocols. The existing Committee mandate was also distributed to members for review and evaluation. Dr. Elan Gandsman recommended that a few Committee members form a Subcommittee to review, and if necessary, rewrite the document. Members were asked to inform Chairman Rupp of their interest in updating the mandate.

New Protocols

Protocol (#04-08): Dr. [redacted]
Title: "Characterization of Proteins that Guide Axons in the Vertebrate Nervous System."
Description: Dr. [redacted] will add a defective lentivirus vector to her existing research experiments exploring the function of various cell adhesion proteins and cell ligands involved in neuronal signaling.
Comments: Dr. [redacted] has worked with a variety of defective viral vectors at [redacted] prior to coming to Yale. Upon arrival at Yale a year ago, she has been setting up a BL2 cell culture facility and training her new staff in BL2 cell culture procedures. The previous OEHS inspection found her [redacted] cell culture lab and existing work practices to be in full conformity with BL2 requirements.

Protocol (#04-26): Dr. [redacted]
Title: "Retroviral Reconstitution of CD45-Deficient Mice."
Description: Dr. [redacted] will use defective retroviral vectors with both ecotropic and amphotropic packaging cell lines to examine the function of CD45-1 gene
Comments: Dr. [redacted] has prior research and clinical experience at BL2, along with experience utilizing universal precautions in the laboratory setting. The annual OEHS biosafety inspection by the OEHS Safety Advisor assigned to [redacted] has found Dr. [redacted] laboratory in conformity with NIH/CDC BL2 requirements. The animal portion of this experiment will not involve direct injection of defective vector into the animal, but the placement back of cells that have been transfected ex-vivo, and can be handled at Animal BL1. This will not require an Animal Biohazard start up meeting.

Protocol (#04-27): Dr. [redacted]
Title: "Genetically Encoded Reporters and Effectors of Neuronal Function"
Description: In a study that will analyze functional neural circuits in the mammalian brain, he will use a defective lentiviral vector to generate rDNA molecules encoding ion channels and fluorescent marker proteins for testing in cell culture and in animals (mice and drosophila).
Comments: Dr. [redacted] and his staff have prior BL2 experience with all of the proposed experimental procedures from previous experiments at the [redacted] (his previous lab location). His entire laboratory has completed the required OEHS Biosafety trainings. Dr. [redacted] laboratory space in [redacted] was inspected by the [redacted] Safety Advisor and found in conformity with NIH BL2 requirements. His lab will be moving within [redacted] to renovated lab space in the near future. The [redacted] Safety Advisor will work with the lab to set up the new space to meet BL2 requirements. Animal BL2 experiments with Lentivirus are approved

contingent upon a start-up meeting with YARC, the research group and Biosafety to establish the site-specific safety protocol.

Protocol (#04-28): Dr. [redacted]
Title: "Gene Expression and Regulation During Neural Development"
Description: Use of defective adenovirus and retrovirus vectors in vitro and in vivo for study of genes involved in molecular mechanism of development of retina and visual cortex.
Comments: Dr. [redacted] has prior work experience with both vectors at BL2 and has completed all relevant Biosafety training classes within OEHS. The OEHS Safety Advisor, assigned to [redacted], has inspected the proposed laboratories and found them in conformity with NIH/CDC BL2 requirements. The space was inherited from Dr. [redacted], who previously performed BL2 work in this location. An Animal BL2 Biohazard start-up meeting will be required with the PI, Biosafety and YARC representatives prior to the initiation of experiments in animals involving either defective vector.

Protocol (#04-29): Dr. [redacted]
Title: "The Effects of Macrophage Inhibitory Factor on Endothelial Cells"
Description: Use of defective retroviral vector and amphotropic packaging cell line for study of effect of Macrophage Inhibitory Factor on endothelial cells.
Comments: Dr. [redacted] and his staff have prior work experience at BL2 and he is currently registering his lab for work with human pathogens with the State of Connecticut Department of Public Health. Dr. [redacted] new cell culture facility in [redacted] has been found to be in compliance with BL2 requirements. His work practices were also found in conformity by the [redacted] floor Safety Advisor during her inspection of his laboratory

Protocol (#04-30): Dr. [redacted]
Title: "Inhibition of Cell-Cell Fusion with Beta-Peptides"
Description: Dr. [redacted] will utilize recombinant cells containing the HIV env, tat, and rev genes in her protocol to examine the ability of Beta-peptides to inhibit HIV cell fusion
Comments: Infectious HIV will not be used in this protocol. Dr. [redacted] staff has worked with OEHS to establish a BL2 cell culture facility in the [redacted] Laboratories. The lab manager has prior BL2 cell culture experience and will train the post-doctoral researcher who will be performing this work. All researchers have attended applicable biosafety training classes in preparation for this experiment. OEHS has assisted with the design of the cell culture lab and inspected the facility previously for BL2 work practices. A follow-up inspection was conducted with the lead researcher who exhibited knowledge of the BL2 facility requirements, and the proposed work area was also found in conformity with NIH/CDC BL2 requirements.

Protocol (#04-31): Dr. [redacted]
Title: "Choroid Plexus Morphogenesis and Cerebrovascular Development"

Description: This project will use in utero electroporation to deliver various signaling and receptor genes into developing embryos as part of a protocol researching the development of the mammalian brain.
Comments: Dr. [redacted] is familiar with the proposed technique and has prior experience handling animals at the BL1 level. The annual audit of Dr. [redacted] laboratory (within Professor [redacted] lab space) found the facility to meet BL1 criteria.

Protocol (#04-32): Dr. [redacted]
Title: "Translational Studies of Psychiatric Genetics"
Description: This protocol will employ a defective Adeno-Associated Virus vector for expression of genes involved in neuronal development in vitro and in vivo.
Comments: The two lead researchers performing this work have prior experience at BL2 from work at their former institution. The OEHS Safety Advisor assigned to the [redacted] has audited the proposed space and reviewed the proposed biosafety work practices and reported that the facility meets BL2 requirements. An Animal BL2 biohazard start-up meeting will be required with responsible research staff, Biosafety, and representatives from YARC Regulatory and Safety Services prior to initiation of animal work.

The Committee voted to unanimously approve the protocols presented at the meeting. The meeting was adjourned at 9:27 AM. The Committee will not meet in October unless needed. The next scheduled meeting is November 11, 2004, which will accommodate the schedules of Committee members. Following the November meeting, the Committee will resume its standard 3rd Thursday of the month meeting time.

Respectfully submitted,

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Yale University Biological Safety Committee
RDNA Minutes
December 16, 2004

The Yale Biological Safety Committee Biological Safety meeting was held on December 16, 2004 in the Office of Environmental Health & Safety Conference Room, 135 College Street. The meeting was called to order at 8:38 AM.

Attendance:
Members: Chairman Dean Rupp, Tina Agentis, Jon Clune, Susan Compton, Louise Dembry, Ben Fontes, Elan Gandsman, Katherine Goodbody, Douglas Kankel, Paula Kavathas, Paul Kowalski, Karen Lamb, James Macy, Mark Solomon, Dorothy Van Rhijn, George Zdru
Guests: John Murphy, (St. of Ct), Maryjo Lanzillotta, Rob Klein, Carlos Torres-Viera, Joy Sherman.

Absent: Linda Buonocore-Buzzelli, Robert Heimer, Sara Rockwell

Chairman's Report:
The minutes of the September 30, 2004 Biological Safety Committee meeting were distributed for review. Chairman Rupp asked members to submit comments on the minutes to Ben Fontes or Joy Sherman of OEHS.

Human Gene Transfer (HGT) Subcommittee Report
Dr. [redacted] Human Gene Transfer Protocol (#04-33)
Dr. [redacted] HGT protocol involves the use of Vaccinia and Fowlpox viruses for use in patients with late stage metastatic cancer of the pancreas. The protocol has been reviewed by the HGT subcommittee and a list of questions from this review has been provided to Dr. [redacted] A copy of the HGT subcommittee questions were provided to the Committee at the meeting. Maryjo Lanzillotta has also had a preliminary meeting with potential clinical staff in Medical Oncology regarding the protocol. Since Vaccinia virus is involved, the HGT subcommittee has required that any staff handling the vector be provided with a medical consult for the Vaccinia virus immunization. Dr. Louise Dembry indicated that it may be difficult to obtain the vaccine. The medical consults will be handled by Dr. van Rhijn for Yale employees and Drs. Dembry and [redacted] for YNHH employees.

New rDNA Protocols

Protocol (#04-34): Dr. [redacted]
Title: "Inhibition of HBV and HCV by Interferon"

Description: Dr. [redacted] will employ two BL2 vectors (Vaccinia virus, defective adenovirus) and transformed murine cell lines that contain the HBV and HCV genomes to study how interferon inhibits HBV and HCV replication.
Comments: Dr. [redacted] has prior work experience with HBV, HCV and HTLV at BL2+/BL3. He has completed all applicable OEHS training classes and has registered with the State of CT for work with human pathogens. OEHS is helping Dr. [redacted] prepare for his initial state lab inspection later this month (December 2004). Biosafety and the OEHS Safety Advisor for the PI met with Dr. [redacted] to inspect his proposed cell culture research laboratory. The lab was recently built for the Pathology Department and easily met BL2 requirements. Dr. [redacted] work practices exceeded standard BL2 requirements (BL2+ work practices are followed by his lab). All of the three new biosafety cabinets in the cell culture room were recently certified and ready for use.

In a response to Dr. [redacted] question regarding the requirement vs. recommendation of Hepatitis B Virus vaccination, the Committee agreed that the free offer of immunization and requirement for a medical consultation with Employee Health to discuss the vaccine should remain in place. Employees who refuse the vaccine will be required to sign the HBV declination form as required by the OSHA Bloodborne Pathogen Standard.

Protocol (#04-35): Dr. [redacted]
Title: "Interaction of Yersinia with dendritic cells"
Description: An extension of previous work, Dr. [redacted] will insert the ovalbumin gene in Yersinia pseudotuberulosis and Salmonella typhimurium to study role of dendritic cells in immune response.
Comments: Dr. [redacted] has been previously approved for similar work. Dr. [redacted] the post-doctoral associate who will be performing the work has completed all required OEHS training and previously worked with BL2 pathogens at another institution. The OEHS Safety Advisor assigned to Dr. [redacted] indicated that the laboratory's most recent laboratory inspection demonstrated full compliance with the required BL2 work practices. Dr. [redacted] BL2 cell culture facility in [redacted] is also in conformity with BL2 requirements.

Protocol (#04-36): Dr. [redacted]
Title: "Examination of Murid Herpesvirus 68 gene function"
Description: Dr. [redacted] will utilize a Murid Herpesvirus 68 (MHV-68) as a model for the study of Human Herpes Virus –8 (HHV-8, Kaposi's Sarcoma Associated Herpesvirus). Various genes will be deleted to study viral lifecycle and their role in pathogenecity.
Comments: Drs. [redacted] and [redacted] have prior BL3/BL2+ research experience in vitro and in vivo with HIV, SIV, and work with non-human primates. They have completed all relevant OEHS safety classes. The OEHS Safety Advisor, assigned to the PI met with Drs. [redacted] and [redacted] for a lab inspection for the proposed work and found their work practices to also exceed NIH/CDC BL2 requirements. They are employing BL2+ precautions for their cell culture experiments. They will be sharing research space with Dr. [redacted] in the new cell culture facility described above for 04-34.

Protocol (#04-37): Dr. [redacted]
Title: "Examination of Herpesvirus saimiri gene function"
Description: Similar to 04-36 but involves the use of Herpesvirus saimiri (HV-S). Genes from Kaposi's Sarcoma Associated Herpes Virus will also be inserted into HV-S.
Comments: As above for 04-36

Protocol (#04-38): Dr. [redacted]
Title: "Examination of Kaposi's sarcoma-associated herpesvirus gene function"
Description: Study of pathogenesis of HHV-8, by examining the role of various genes in human and murine cell lines.
Comments: As above for 04-36

Protocol (#04-39): Dr. [redacted]
Title: " Mitochondrial DNA mutations in mice"
Description: Generation of transgenic mice carrying mutations in the mitochondrial chromosome for use as an animal model for the study of the mechanism of mitochondrial disorders.
Comments: The lab has prior BL1 work experience. This protocol is an extension of Yale BSC protocol #04-18, which generated the mutations in mitochondria. The lab has previously demonstrated compliance with BL1 requirements on the annual OEHS lab inspection.

Protocol (#04-40): Dr. [redacted]
Title: "Influence of Gap Junction Expression and DNA-PK Function on Cisplatin Response in Vivi"
Description: Use of standard cloning vectors to generate a mouse model to examine the role of gap junctions and Ku80 in tumor sensitivity to cisplatin.
Comments: Dr. [redacted] laboratory has prior work experience with human tumor cells at BL2. Applicable OEHS training has been completed and the most recent OEHS biosafety inspection has found the lab in conformity with BL1 and BL2 lab safety requirements.

Protocol (#04-41): Dr. [redacted]
Title: "Development of VSV/HPV Recombinants as HPV Vaccines"
Description: Dr. [redacted] will use a lab strain of Vesicular Stomatitis Virus to develop a vaccine containing Human Papilloma virus oncoproteins (HPV E6 & E7) against cervical cancer.
Comments: Dr. [redacted] and his staff have prior experience with BL2 pathogens and have completed all required OEHS and YARC training requirements. Dr. [redacted] has been working with these agents on a collaborative effort on the protocols of Dr. [redacted] and Dr. [redacted] for the past few years. Dr. [redacted] researchers have been trained on the safe handling of VSV in Dr. [redacted] lab, and will continue to work with the agent in Dr. [redacted] cell culture laboratory. Animal work will be conducted in an approved BL2/BL2+ facility in BCMM. Dr. [redacted] has obtained YACUC approval and has already met with YARC staff for the required protocol start-up meeting.

Protocol #04-42, was withdrawn by Dr. [redacted]

The Committee voted to unanimously approve the protocols presented at the meeting. The meeting was adjourned at 9:00 AM.

Respectfully submitted,

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Yale University Biological Safety Committee
Recombinant DNA Meeting Minutes
February 17, 2005

The Yale Biological Safety Committee rDNA meeting was held on February 17, 2005 in the Office of Environmental Health & Safety Conference Room, 135 College Street. The meeting was called to order at 8:39 AM.

Attendance:
Members: Chairman Dean Rupp, Tina Agentis, Sarah K. Biran(for J.Clune), Susan Compton, Louise Dembry, Ben Fontes, Elan Gandsman, Douglas Kankel, Paul Kowalski, Sara Rockwell, Mark Solomon, Dorothy van Rhijn, George Zdru Guests: Maryjo Lanzillotta, Rob Klein, Carlos Torrel-Viera, taking notes Joy Sherman.

Absent: Katherine Goodbody, Robert Heimer, Paula Kavathas, James Macy, Karen Lamb

Chairman's Report:
The minutes of the December 16, 2004 rDNA meeting were distributed for review. Chairman Rupp asked members to submit comments on the minutes to Ben Fontes or Joy Sherman of OEHS.

Old Business

Human Gene Transfer Subcommittee
Ben Fontes provided a brief update on Dr. [redacted] human gene transfer protocol. Postal ballot responses were unanimous for approval. The project is awaiting final HIC approval of the amended protocol. As the protocol involves employees from Yale and Yale New Haven Hospital, each institution will participate in training and providing medical consultation where needed. Training for individuals involved in the protocol will begin shortly.

New Business

<u>New Protocols:</u>

<u>Protocol #05-01</u>: Dr. [redacted]
<u>Title:</u> "Role of GILT in the immune response to melanoma"
<u>Description:</u> Dr. [redacted] will use a recombinant Vaccinia virus vector expressing different melanoma antigens in cell culture and in mice to study their role in potential immunity to melanoma.

Comments: [redacted] lab has been previously registered with the State of CT Dept. of Public Health for experiments involving Human Pathogens at BL2 and with the Yale IBC for multiple rDNA experiments at BL2. The lead researcher has completed all required training and has prior BL2 experience with human cells in culture. However, she has not worked with Vaccinia Virus previously. Dr. [redacted] will work with an authorized Vaccinia virus researcher in Dr. [redacted] lab to perform an internship to learn safe procedures for working with this agent. Dr. [redacted] cell culture is in conformity with BL2 requirements and his proposed work practices are also in compliance as identified on previous OEHS and State of CT Dept. of Public Health lab inspections. OEHS Biosafety will meet with the lead researcher after documentation by Dr. [redacted] lab of her successful internship to schedule a start up inspection for BL2 cell culture work. Dr. [redacted] protocol will also require YACUC approval and a start up meeting with Biosafety, YARC, and applicable researchers to develop the site-specific Animal BL2 protocol for the experiment.

The Committee briefly discussed the difficulty in obtaining the vaccinia virus immunization. Dr. van Rhijn and Dr. Dembry discussed the possibility of working with the State Department of Public Health to obtain the vaccine for researchers, which may be difficult, as it has been allocated for medical response teams.

Protocol #05-02: Dr. [redacted]
Title: "Role of ASC and NALP3/Cryopyrin in Regulation of Inflammation"
Description: Dr. [redacted] protocol involves the use of a defective retroviral vector and amphotropic packaging cell line for expression of signaling molecules in cell culture and in animals.
Comments: Dr. [redacted] has existing BL2 registrations for BL2 human pathogens, defective rDNA vectors, including an existing defective retroviral vector protocol. His staff has completed required Biosafety trainings and has prior experience handling similar research vectors at BL2. Dr. [redacted] has an independent BL2 cell culture facility that has been found in conformity by OEHS and the State of CT Dept. of Public Health on previous lab inspections.

Protocol #05-03: Dr. [redacted]
Title: "Expression of recombinant proteases in insect cells"
Description: Dr. [redacted] protocol will employ the baculovirus expression system to study the metalloproteinases (ADAM) and its activity against peptides and protein substrates.
Comments: Dr. [redacted] has completed all required OEHS trainings his proposed research. He also has prior research experience with BL1 and BL2 agents. Dr. [redacted] laboratory is currently being set up. The OEHS Safety Advisor has met with Dr. [redacted] to review BL1 and BL2 lab set up and will return to conduct an inspection of Dr. [redacted] laboratory when he is up and running and ready to initiate BL1 and BL2 experiments to review applicable biosafety work practices.

Protocol #05-04: Dr. [redacted]
Title: "Expression of MKK proteins in mouse macrophages"

Description: Dr. [redacted] will use a defective lentiviral vector to express various Mitogen Activated Protein Kinases (MKK's) in mouse macrophages to study their role in cell survival.
Comments: Dr. [redacted] has prior experience with this vector at another institution. He has completed all required OEHS training classes for the proposed work. OEHS will meet with Dr. [redacted] to inspect his proposed cell culture facility to verify conformity with required BL2 facility needs and work practices. Dr. [redacted] OEHS Safety Advisor has been actively working with Dr. [redacted] to help set up his laboratory and will document the lab inspection once the lab has been set up and ready for the proposed work. The protocol is recommended for approval upon a satisfactory lab inspection.

The Committee unanimously approved rDNA Protocols #05-02 and #05-03. Protocols #05-01 and #05-04 were not approved at this time, but may be approved administratively by the Biosafety Officer once all requirements are satisfied as detailed above.

The meeting was adjourned at 9:10 AM. The next scheduled meeting is March 17, 2005.

Respectfully submitted,

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Yale University Biological Safety Committee
Recombinant DNA Meeting Minutes
April 21, 2005

The Yale Biological Safety Committee rDNA meeting was held on April 21, 2005 in the Office of Environmental Health & Safety Conference Room, 135 College Street. The meeting was called to order at 8:40 AM.

Attendance:
Members: Chairman Dean Rupp, Tina Agentis, Susan Compton, Louise Dembry, Ben Fontes, Katherine Goodbody, Robert Heimer, Douglas Kankel, Paula Kavathas, Paul Kowalski, James Macy, Dorothy van Rhijn, Guests: Maryjo Lanzillotta, David Willihite, Leta Bradford, taking notes-Joy Sherman.

Absent: Jonathan Clune, Elan Gandsman, Karen Lamb, Sara Rockwell, Mark Solomon, George Zdru

Chairman's Report
Minutes from the Feb. 17, 2005 meeting were distributed to the members for review. Chairman Rupp polled members in attendance on the recent distribution of Adobe PDF versions of the rDNA Registrations. Committee members endorsed the new format, but requested that all the forms be sent at once, and not one at a time upon receipt by OEHS. Discussion of a possible web page for the Committee followed. Current links to the Committee stem from the OEHS web site. Committee members were in favor of a web page, complete with a basic overview, policies, registration forms, and links to relevant resources. Dr. Macy suggested that OEHS refer to the home page of the Yale Institutional Animal Care and Use Committee (Yale IACUC) for ideas. Ben Fontes agreed to work with OEHS ITS personnel to create a sample home page for review by the Committee in the future.

Old Business

Dr. [redacted] Protocol (#04-33)
Dr. [redacted] has received full authorization from the HIC for her human gene transfer protocol, #04-33. Prior to initiation of the protocol, Dr. [redacted] will identify the full roster of Yale and Yale New Haven Hospital employees who will be assigned to the study. The Employee Health Offices of both institutions must provide a confidential medical consultation with each employee for the Vaccinia virus immunization. A meeting with the sponsor, [redacted] has been scheduled for April 26, 2005 to review any remaining questions on the protocol

Dr. [redacted] rDNA Protocol (#05-04)
Dr. [redacted] BL2 laboratory has been completed and the lab and Dr. [redacted] practice were audited with no major findings by OEHS. Based on the successful lab inspection, Dr. [redacted] was issued an approval letter his work as discussed at the last Committee meeting.

Dr. [redacted] rDNA Protocol (#05-01)
Dr [redacted] protocol remains on hold as the lead researcher for this project has not completed her internship yet in Dr. [redacted] laboratory to gain experience with the safe handling of Vaccinia virus. She will notify her OEHS Safety Advisor for a start up lab inspection once she has completed the safety and experience internship.

New Business

Protocol #05-05: Dr. [redacted]
Title: "Recombinant retrovirus production and infection of mouse cell lines"
Description: Dr. [redacted] will utilize a replication defective retrovirus and amphotropic packaging cell line carrying to inhibit the expression of mouse Filamin A (using short hairpin RNA methodology).
Comments: Dr. [redacted] laboratory has prior BL2 lab research experience and has attended relevant biosafety training classes for BL2 work. The lab inspection conducted by OEHS has found the lab and the proposed work practices to be in compliance with CDC/NIH and Yale BL2 requirements. The protocol is recommended for approval at BL2.

Protocol #05-06: Dr. [redacted]
Title: "Cloning and expression of rodent parvovirus & corona virus proteins"
Description: Use of the baculovirus expression system for cloning individual viral proteins from mouse parvovirus or corona virus.
Comments: Dr. [redacted] and her staff have prior work experience and training adequate for the proposed experiment. Dr. [redacted] laboratory is annually inspected for general biosafety requirements through the OEHS Safety Advisor program. The lab has maintained compliance with BL1 requirements in previous laboratory inspections.

Protocol #05-07: Dr. [redacted]
Title: "Neuronal tracking in the rat brain using a LacZ-expressing herpes virus"
Description: Dr. [redacted] laboratory will use the Herpes Simplex virus to carry the LacZ gene in various regions of the rat brain to examine neuronal connections.
Comments: Dr. [redacted] has multiple BL2 rDNA and infectious agent protocols. The staff assigned to this protocol has completed required biosafety training. Dr. [redacted] and Dr. [redacted] are the lead researchers for the protocol and each has recently demonstrated compliance with BL2 lab biosafety work practices on a recent inspection with OEHS. Dr. [redacted] written biosafety SOP for BL2 work with this virus was one of the most detailed and comprehensive safety protocols ever received by the Biosafety Office. Their [redacted] research cell culture facility is also in conformity with BL2 requirements. Animal work is approved at Animal BL2 with the requirement of an

approved YACUC registration and YARC BL2 start-up meeting to review ABL2 practices prior to the initiation of work in rats.

Protocol #05-08: Dr. [redacted]
Title: "Lentiviral Transduction of Hippocampal Neurons"
Description: Dr. [redacted] will utilize a replication defective lentiviral vector for cell culture experiments designed to develop a fluorescent voltage-sensitive probe in rat hippocampal cells.
Comments: Dr. [redacted] lab has prior work experience with human cell lines at BL2. The lead researchers have completed biosafety training and two other researchers are scheduled to complete biosafety training at an upcoming course. The OEHS Safety Advisor has met with lead researchers to review work practices and inspect the proposed work location and found both to be in conformity with BL2 requirements.

Protocol #05-09: Dr. [redacted]
Title: "Delivering RNA through VIRM infection.
Description: Dr. [redacted] will utilize a replication defective retroviral vector and an amphotropic packaging cell line to down regulate the DM1 gene in ovarian cancel cells to further examine its function.
Comments: Dr. [redacted] lab has extensive experience working with human tissue and human cell culture. The lead researcher has attended all required Biosafety Training classes and will be responsible for training new personnel on the protocol. The OEHS Safety Advisor for [redacted] lab did not identify significant issues on the last BL2 facility inspection in 2004. The Safety Advisor has been asked to conduct a follow-up for this work and will report back to the Biosafety Officer. Once the inspection has been complete and work practices and facility requirements are recertified, a BL2 approval letter will be granted.

Item F. on today's rDNA Agenda was a typographical error. Dr. [redacted] rDNA Protocol (#05-10) was inadvertently listed twice.

Following the presentation of the summary of rDNA protocols by the Biosafety Officer, the Committee voted unanimously to approve the recommendations for approval presented at today's meeting (Protocol #05-09 will be approved following a successful lab inspection by the OEHS Safety Advisor assigned to Dr. [redacted] laboratory).

Proposed MTA from [redacted] for Dr. [redacted]
Ben Fontes reported that Dr. [redacted] had alerted OEHS of a requirement from [redacted] that work with genetically altered mice expressing Hepatitis B Virus be conducted at full Biosafety Level 3. Dr. [redacted] concern is that with the paucity of Animal BL3 space on campus, it would be difficult to initiate this work at Yale. He also indicated that previously, this work was conducted at Animal BL2+ (BL3 work practices in a BL2 lab) at [redacted]. There is also a requirement on the MTA that all those who handle the HBV animals obtain the HBV immunization and demonstrate an adequate titre. OEHS will work with Dr. [redacted], Grants and Contracts within the School of Medicine, Yale

Employee Health, Yale Animal Resources Center, and representatives from [redacted] to review and hopefully change the proposed MTA.

Vaccinia Virus Needle stick – [redacted] Hospital
Tina Agentis distributed a letter to the NIH Office of Biotechnology Affairs from Dr. [redacted], a [redacted] PI, who experienced a needle stick while working with animals on his Vaccinia virus protocol. Dr. [redacted] letter provides a summary of the incident and outlines his plan to minimize the potential for accidents in the future. Corrective actions include placement of a sharps container in the immediate vicinity of use (inside the biosafety cabinet) for prompt disposal of sharps, consideration of safe sharps devices (such as the vanishpoint retractable needle for inoculations); and prompt reporting of accidental exposures to the [redacted] Biosafety Officer and the [redacted] Employee Health Physician.

Dr. Louise Dembry reported that the incident was not reported until 5 days following the incident, when a localized infection from the accident had developed. There was also a secondary bacterial infection of the wound that required additional attention by the hospital. The initial call from the PI was made directly to the U.S. Centers for Disease Control and Prevention, who in turn called Yale New Haven Hospital, who provided the information to the [redacted] Employee Health Office. The incident raised concerns over researchers working with infectious agents and not reporting accidents, exposures, spills or near misses. Every effort should be made to inform researchers working with hazardous biological materials of their responsibility to report incidents to their supervisors, and relevant safety and employee health professionals at their institutions.

The meeting was adjourned at 9:30 AM. The next scheduled meeting is May 19, 2005.

Respectfully submitted,

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Yale University Biological Safety Committee
Recombinant DNA Meeting Minutes
May 19, 2005

The Yale Biological Safety Committee rDNA meeting was held on May 19, 2005 in the Office of Environmental Health & Safety Conference Room, 135 College Street. The meeting was called to order at 8:38 AM.

Attendance:
Members: Chairman Dean Rupp, Jon Clune, Susan Compton, Ben Fontes, Elan Gandsman, Douglas Kankel, Paul Kowalski, Paula Kavathas, James Macy, George Zdru

Absent: Tina Agentis, Linda Buonocore-Buzzelli, Louise Dembry, Katherine Goodbody, Robert Heimer, Karen Lamb, Sara Rockwell, Mark Solomon, Dorothy van Rhijn

Chairman's Report:
The minutes of the April 21, 2005 rDNA meeting were distributed for review. Chairman Rupp asked members to submit comments on the minutes to Ben Fontes.

Old Business

Human Gene Transfer Subcommittee
Ben Fontes provided a brief update on Dr. [redacted] human gene transfer protocol (#04-33). [redacted], the sponsor of the proposed protocol, organized an in-service training session for the research team, study nurses, and pertinent representatives from Yale and Yale-New Haven Hospital (YNHH). Most of the discussion related focused on whether or not Yale and YNHH would require or recommend the Vaccinia virus immunization for those with direct contact with [redacted] or patients who could be shedding the virus. Representatives from [redacted] provided documentation that immunization was not required, as their drug has been based on an attenuated strain of Vaccinia. Employee Health physicians from each hospital requested information about employee immunization rates and patient shedding data at other sites enrolled in the study. Once this information has been obtained and evaluated, a final decision will be made regarding the immunization. Other sites that do not require the immunization make available a private consultation to discuss the risks and benefits of immunization (a practice currently established by Yale's Employee Health Office for those conducting research with Vaccinia virus).

New Business

New Protocols:

Protocol #05-10: Dr. [redacted]
Title: "Lentiviral Introduction of Fluorescent Molecules in Cells"
Description: Dr. [redacted] will use a defective lentiviral vector containing the VSV-G protein to insert mouse adaptor proteins labeled with green fluorescent protein to localize these molecules in real time within the cell. No animal work is associated with this project.
Comments: Dr. [redacted] and her staff have a strong background with experiments involving infectious agents up to BL2+ (SIV) and commonly work with Herpes Simplex Virus-2 in the laboratory at BL2. They have also previously worked with VSV vectors and a variety of replication defective vectors, and have completed all required OEHS training. Dr. [redacted] has recently moved into a new dedicated self-contained cell culture facility in [redacted] that was assigned solely to her laboratory. No other research groups will use this space. The lab space successfully passed the State of Connecticut Department of Public Health's lab inspection and was approved for BL2 work. Laboratory biosafety work practices were found in conformity with BL2 requirements by biosafety office representatives on the annual inspection. The BL2 containment level with the additional precautions required for work with defective viral vectors are suitable for this experiment.

Protocol #05-11: Dr. [redacted]
Title: "Influence of the Immunoproteasome on CTL Specificity to Hepatitis B virus (HBV)"
Description: Dr. [redacted] latest rDNA protocol continues his study of HBV proteins (core, polymerase, and envelope) on the immune response in mice.
Comments: Dr. [redacted] was previously authorized to perform biohazard experiments in his cell culture laboratory and with animals with HBV. In addition to completing all required biosafety training classes, he has previous experience with BL2, BL2+, and BL3 pathogens and commensurate biosafety practices from previous institutions. His cell culture room has been inspected and found in conformity with BL2 and BL2 enhanced (BL2+) work practices. Research space for the animal experiments work will be assigned by the Yale Animal Resources Center (YARC) in conjunction with previously approved experiments. Dr. [redacted] has met with YARC, Biosafety and Veterinary Care Services representatives to develop Animal BL2 and BL2+ safety procedures for his HBV work in animals. Cloning of individual genes from HBV and inoculation into mice can be conducted at Animal BL1. Inoculation of Vaccinia virus into mice will require Animal BL2 containment, with the requirement that all researchers and YARC staff who have contact with the animals have a medical consult with Employee Health for the Vaccinia virus immunization. Dr. [redacted] currently requires that all of his employees also document HBV immunization. Note: Information on mice expressing HBV listed in the meeting protocol matrix was not considered as part of this protocol as it was not on the rDNA registration form. This research has been reviewed on a separate protocol.

Protocol #05-12: Dr. [redacted]
Title: "Molecular Basis of Host/Pathogen Interaction"

Description: Dr. [redacted] experiments involve the examination of the role that various genes from Chlamydia, Shigella, and Listeria play in pathogenesis. The role of specific genes will be examined in human and drosophila cell lines. Subsequent studies will involve the use of silencing vectors to knockout these genes in the bacterial pathogens.
Comments: Dr. [redacted] and his staff have prior work experience with these pathogens at another institution. All required OEHS and applicable trainings for these experiments have been completed. Dr. [redacted] will notify OEHS when renovation of his laboratory is completed to schedule a lab inspection to review the facility and his proposed work practices. Based on prior work experience, the research may be administratively approved by the Biosafety Office pending a successful laboratory inspection. Note: no work in drosophila will be conducted as noted in the meeting protocol matrix.

Protocol #05-13: Dr. [redacted]
Title: "Host-Pathogen Interactions and the Innate Immune System"
Description: Dr. [redacted] will use standard cloning vectors and the Baculovirus expression system to examine the roles of proteins in the innate immune system.
Comments: Dr. [redacted] and his lab staff have prior BL1 work experience. As a new faculty member, he is currently establishing a laboratory in the [redacted] Building. The OEHS Safety Advisor has been working with him on laboratory registrations and will return to inspect his laboratory once all of the equipment is in place.

Protocol #00-08: Dr. [redacted]
Title: "Development of Immunizations based on Vesicular Stomatitis Virus (VSV)"
Description: Dr. [redacted] has submitted an update of his existing rDNA experiments involving recombinant VSV (lab strains) and Vaccinia virus vectors. The VSV used in Dr. [redacted] lab are not exotic strains and thus do not require registration as Select Agents with the USDA or CDC. A summary of Dr. [redacted] vaccine related experiments were provided to the Committee along with the new experiments using the toxins from Bacillus anthracis, Protective Antigen (PA), Lethal Factor (LF), and the combination (PA/LF). Although Bacillus anthracis is regulated as a Select Agent, the toxins produced by the organism are not regulated as Select Agents, thus additional registration is not required. The toxin will not be grown in the laboratory but will be required from the NIH and a commercial source. Researchers will inoculate research animals with the toxin to determine the protective effect of a VSV vaccine targeted against the toxic effects of B. anthracis.
Comments: Dr. [redacted] researchers have completed requisite training and have prior experience with biohazards up to BL2+ (for work with VSV laboratory adapted strains, Vaccinia virus, Dengue virus, HIV, and SIV). VSV experiments in animals have a dedicated Animal BL2+ protocol that has been developed for compliance with USDA requirements for work with the agent. All prior biohazardous experiments in animals have Yale IACUC approval. Commensurate with the requirement for Yale IACUC approval, the proposed work in toxins (once approved) will require a safety start-up meeting with representatives from the laboratory, the biosafety office, Yale Animal Resources Center (YARC), and Veterinary Care Services (VCS). The final SOP will be developed at this meeting. Preliminary review of the proposed work indicates that the

existing enhanced BL2 animal and cell culture safety protocols established for Dr. [redacted] experiments are adequate for containment of the toxin experiments.

The Committee unanimously approved rDNA Protocols #05-10, #05-11, #05-12, and #05-13 with the corrections noted in the discussion above. Protocol #00-08 was not approved at this meeting and will be reviewed by the BL3 Subcommittee at its next session.

The meeting was adjourned at 9:16 AM. The next scheduled meeting is June 16, 2005.

Respectfully submitted,

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Yale University Biological Safety Committee
Recombinant DNA Meeting Minutes
September 15, 2005

The Yale Biological Safety Committee rDNA meeting was held on September 15, 2005 in the Office of Environmental Health & Safety Conference Room, 135 College Street. The meeting was called to order at 8:43 AM.

Attendance:
Members: Chairman Dean Rupp, Jon Clune, Susan Compton, Ben Fontes, Elan Gandsman, Douglas Kankel, Paul Kowalski, James Macy, Mark Solomon, George Zdru, Herbert Yu, and Dorothy van Rhijn. Guests: John Dalto, Deborah Ferry, Rob Klein, and Maryjo Lanzillotta.

Absent: Tina Agentis, Linda Buonocore-Buzzelli, Abe Colon, Louise Dembry, Karen Lamb, Sara Rockwell, and Craig Roy.

Chairman's Report:

Chairman Rupp welcomed the new members and guests in attendance, including Ms. Linda Mouning who will be assisting with administrative management of the Committee. Ms. Mouning requested updated copies of CV's from members for inclusion in the annual report filed with the NIH Office of Biotechnology Activities. Chairman Rupp then provided an overview of Committee operation and function, explaining the rDNA meeting session, which is traditionally followed by a separate discussion of all other relevant biosafety topics. Minutes are maintained for each session. The existing mandate for the Committee was distributed to Committee members. Ben Fontes, Jon Clune, Karen Lamb will assist Chairman Rupp in updating the mandate in the near future.

A list of useful websites and reference links related to rDNA experiments and work with biohazard was also provided to Committee members as part of their meeting packet. Members were informed that these references are helpful in the review of experiments registered with the Committee. Reference information included the web page of the NIH Office of Biotechnology Activities, frequently asked questions related to human gene transfer experiments, a similar site for IBC's, and the web site for the newly created National Science Advisory Board on Biosecurity (NSABB), which will have oversight for dual use research at federally funded locations. In addition to the references, Committee members were provided with a presentation on Risk Assessment and Risk Management, and the flow of experiments from registration to approval.

[redacted], the assistant Biosafety Officer, and Manager of the Clean Air Device program at Yale, reported that the University had recently entered into a contract to bring a new vendor, Technical Safety Services (TSS), to campus to provide Yale with testing, certification and repair services for biological safety cabinets, exhaust HEPA filters, and related devices. OEHS worked in conjunction with staff from the Yale Animal Resources Center and Yale Purchasing in the selection of the new vendor. [redacted], a regional manager for TSS was introduced to Committee members.

[redacted] also provided a PowerPoint presentation of a draft of the new homepage for the Committee. Other relevant regulatory committee websites at Yale and around the country were reviewed for format and content and used to establish the new Yale IBC homepage. The draft has been provided to [redacted], the OEHS ITS manager for implementation into the OEHS website.

The minutes of the May 19, 2005 rDNA meeting were distributed for review. Chairman Rupp asked members to submit comments on the minutes to Ben Fontes.

Old Business

Dr. [redacted] Human Gene Transfer Protocol (#04-33)
The Yale Biological Safety Subcommittee on Human Gene Transfer has completed its review of the protocol and issued a formal approval for the project. [redacted], the sponsor of the protocol, provided an in service training session to all personnel on the protocol. Dr[redacted] is still awaiting final HIC approval before initiating the experiment.

Dr. [redacted] rDNA Protocol Update (#00-08)
Dr. [redacted] request to add the toxins Lethal Factor and Protective Antigen from Bacillus anthracis was formally approved by the BL3 Subcommittee at Biosafety Level 2+ for work in cell culture and also for work in animals. The toxins from B. anthracis do not require registration as a Select Agent. The toxins will not be produced within the laboratory, but obtained from a source outside the University for use in their experiments. Both the lab inspection and Animal Care start-up meetings have been held to review the procedures required for the experiments. Dr. [redacted] lab has prior experience with BL2+ and BL3 agents. A copy of the approval letter was provided to the Committee in the packet.

Dr. [redacted] Laboratory
Ben Fontes reported that health and safety issues in Dr. [redacted] laboratory have improved greatly and since the last meeting. The OEHS Safety Advisor assigned to Dr. [redacted] lab will continue to monitor the lab periodically until further notice.

New Business

<u>New Protocols</u>

<u>Protocol #05-14</u>: Dr. [redacted] Protocol

Title: "Probing the Molecular Basis of Information Processing in the Mouse Brain."
Description: Dr. [redacted] will use Herpes simplex Virus 1 and Pseudorabies virus for labeling and localizing experiments in the mouse brain, targeting olfactory receptor neurons. The synaptic connectivity of neuronal cells will also be evaluated.
Comments: The lab has prior BL2 research experience and the lead researcher has attended relevant biosafety training classes for BL2 work. Dr. [redacted], the postdoctoral researcher who will be performing the work has decided to use these agents in place of Rabies virus as initially proposed. A lab inspection conducted by the OEHS SA has found the lab and the proposed work practices to be in compliance with CDC/NIH and Yale BL2 requirements. The cell culture laboratory has been recently renovated to meet BL2 criteria. As the lab is off a main traffic corridor, the SA worked with Project Management to ensure that the lab was under negative pressure in relation to the corridor. Work in animals will require IACUC approval and YARC BL2 start up meeting before initiation.

Protocol #05-15: Dr. [redacted] Protocol
Title: "Megalin Function in Normal and Diseased Kidney"
Description: Dr. [redacted] will use a transgenic mouse model to study the role of megalin in protein absorption and gene regulation in the proximal tubule of the kidney.
Comments: The group has BL1 research experience. Dr. [redacted] lab and work practices have been reviewed by the OEHS SA as part of the annual inspection program and meet BL1 requirements. Transgenic animal work does not represent a hazard and can be conducted at Animal BL1. A YARC hazard start up meeting is not required.

Protocol #05-16: Dr. [redacted] Protocol
Title: "Treatment of Lung Cancer in K-ras Mutant Mice by Let-7 Overexperssion Using Nasal Administration of Adenoviral Vectors"
Description: Dr. [redacted] will use defective adenoviral vectors as part of a study to determine if the Let-7 gene acts as a tumor suppressor.
Comments: : The lead researcher for the project has completed all required OEHS training, but did not have direct experience working with defective viral vectors. Dr. [redacted] has completed a safety internship in Dr. [redacted] laboratory to learn the BL2 techniques. The lab has been inspected by the OEHS SA and the proposed BL2 practices and facility are in conformity with CDC/NIH and Yale requirements for BL2 research. The work will require IACUC approval and a YARC BL2 start up meeting with Biosafety, the research group, and VCS personnel. The work will likely be assigned to the [redacted] BL2 facility. As the experiment involves intranasal inoculation – procedures will be confined to a Class II biosafety cabinet in a BL2 room.

Protocol #05-05-17: Dr. [redacted] Protocol
Title: "Lentiviral Transduction of Mouse Brain Tissue to Study the in vivo Expression of Genetically-Encoded Voltage-Sensitive Fluorescent Probes"
Description: Dr. [redacted] will use a defective lentiviral vector to express voltage sensitive fluorescent probes in the mouse brain.

Comments: Dr. [redacted] lab has prior work experience with this lentiviral vector at BL2 containment. Now that he has completed his cell culture experiments, he's prepared to move on to in vivo experiments involving mice. Dr. [redacted] laboratory was inspected and identified to meet BL2 requirements on the previous protocol in the spring of this year. No further inspections are required. The work in animals will require IACUC approval and a YARC BL2 start up meeting with Biosafety, VCS and lab personnel.

Protocol #05-18: Dr. [redacted] Protocol
Title: "Functional Analysis of Yeast and Human Proteins via Protein and DNA Microarrays and Mammalian Stem Cells"
Description: Dr. [redacted] will utilize a defective lentiviral vector to infect mouse stem cells as part of ongoing experiments to study novel human cDNA's and their effect on protein function and interaction.
Comments: Dr. [redacted] lab personnel have completed OEHS training classes and have prior research experience with defective viral vectors and human pathogens classed at BL2 (Epstein Barr Virus and Human Papilloma Virus). Dr. [redacted] laboratory has recently been registered with the State of CT for research with human pathogens at BL2. The OEHS safety advisor has worked with group to bring them into compliance with BL2 requirements. The lab has an existing Animal BL2 protocol and experience with YARC BL2 procedures in the [redacted] BL2 facility. The work will require IACUC approval and another YARC BL2 start-up meeting.

Protocol #05-19: Dr. [redacted] Protocol
Title: "Molecular Characterization of TRP Ion Channels in the Pain Pathway"
Description: Dr. [redacted] will study the structure and function of ion channel proteins that are expressed in pain-transducing neurons.
Comments: Dr. [redacted] has prior experience handling human and non-human primate cells and the lab has completed OEHS Biosafety Training. Dr. [redacted] laboratory and work practices were found to be in compliance with BL2 requirements during the lab inspection for this experiment by the OEHS SA.

Protocol #05-20: Dr. [redacted] Protocol
Title: "Which Chlamydia trachomatis Proteins are Exported via Type III Secretion Systems?"
Description: Dr. [redacted] will use a genetically modified Salmonella typhimurium that contains a fusion protein to examine whether a C. trachomatis protein is secreted by the Type III Secretion system of Salmonella.
Comments: Dr. [redacted] and her lab have prior work experience with BL2 and enhanced BL2 containment procedures for experiments with BL2 pathogens. She is registered with the State of CT Dept. of Public Health for other BL2 agents and her registration will be updated for this work. Dr. [redacted] has an established BL2 containment cell culture suite and both her facility and her work practices have been consistently identified in conformity with BL2 requirements on the annual OEHS lab inspections. This experiment will not expand the containment requirements of her existing lab experiments.

Protocol #05-21: Dr. [redacted] Protocol
Title: "Role of Growth Factors in Brain Development"
Description: Dr. [redacted] will employ defective retroviral and adeno-associated virus vectors in her experiments to study the effects of growth factors on brain development and reaction to hypoxia.
Comments: Dr. [redacted] lab has previously completed OEHS training for work with defective adenovirus experiments at BL2. Work with defective retroviral and adeno-associated virus can be safely handled at BL2 using her existing protocol. Dr. [redacted] laboratory has been previously inspected for work with defective adenovirus vectors in vitro and in vivo and is inspected annually to verify that she remains in conformity with BL2 practices. IACUC registration and approval is required for animal work and a YARC BL2 start up meeting will be required prior to initiation of work with these vectors in mice.

Protocol #05-22: Dr. [redacted] Protocol
Title: "Neurotropic CMV During Immune Suppression and Vaccine Development"
Description: Dr. [redacted] will use VSV to express proteins from mouse- CMV in an attempt to develop a vaccine against human CMV. The vaccine will be tested in mice.
Comments: Dr. [redacted] has previous experience with lab-adapted strains of VSV from previous experiments with Dr. [redacted] and Dr. [redacted] He has completed all required OEHS training for the experiment. Dr. [redacted] has utilized BL2+ cell culture rooms in the Comparative Medicine Virology labs of Dr. [redacted] for his in vitro work and biohazard rooms in the [redacted] animal facility (assigned by YARC). He has YARC approval and has completed an ABL2+ start up meeting for this experiment.

Protocol #05-23: Dr. [redacted] Protocol
Title: "Use of Lentiviral Vectors in Cell Culture and Mice"
Description: Dr. [redacted] will utilize a defective lentiviral vector to introduce genes involved in blood development into mouse bone marrow cells and into mice.
Comments: Dr. [redacted] and her lab have prior BL2 work experience and OEHS Biosafety Training. The lead researcher, Dr. [redacted], is an OEHS approved BL2+/BL3 researcher for work with wild type HIV. Dr. [redacted] new lab has been inspected as part of her move to [redacted] and has been found in conformity with BL2 criteria. IACUC approval and a YARC BL2 start up meeting with the lab, VCS, and Biosafety personnel are required prior to the initiation of work in animals.

Protocol #05-24: Dr. [redacted]s Protocol
Title: "The Effect of Ngal on Renal Epithelial Cell Morphogenesis"
Description: Dr. [redacted] will use a defective retroviral vector to study the effect of Lipocalin-2 on cell growth and migration in cell culture and in mice.
Comments: Dr. [redacted] and his staff have prior work experience with defective viral vectors (retrovirus, adenovirus, and lentivirus), and have completed OEHS Biosafety training classes. Dr. [redacted] has recently moved into the [redacted], and has a modern BL2 approved cell culture suite for these experiments. He has previously satisfied all biosafety requirements for BL2 research and OEHS has found his new facility in conformity with BL2 requirements. His previous animal BL2 work was conducted in one

of the two animal BL2 rooms in [redacted]. IACUC approval is required for this experiment. A YARC BL2 start up meeting is also required for research staff, VCS and Biosafety personnel.

Protocol #05-25: Dr. [redacted] Protocol
Title: "Role of Neuregulin in Endothelial Cells"
Description: Dr. [redacted] will use a defective adenovirus vector to transfect endothelial cells with green fluorescent protein and to knock out the neuregulin gene to study its function.
Comments: Dr. [redacted] and her staff have prior BL2 work experience with BL2 materials and have completed OEHS safety training. Dr. [redacted] will use the existing cell culture suite that is shared with Dr. [redacted] an approved BL2 research Principal Investigator, who also has an approved adenovirus BL2 protocol. The laboratory inspection for the proposed cell culture experiment was conducted by the OEHS safety advisor who found the lab in conformity with BL2 requirements.

Protocol #05-26: Dr. [redacted] Protocol
Title: "Role of BAFF and April in the Maintenance of Lupus"
Description: Dr. [redacted] will use a defective adenovirus vector to express two cytokines in the mice as part of a study of the autoimmune disease lupus.
Comments: Dr. [redacted] will use a defective adenovirus vector to express two cytokines in the mice as part of a study of the autoimmune disease lupus. A collaborating laboratory will supply the vector. Dr. [redacted] lab will inoculate mice with the vector to express the desired proteins. Dr. [redacted] has existing Animal BL2 experiments. IACUC registration and approval and a YARC BL2 start up meeting will be required prior to initiation of the work.

Protocol #05-27: Dr. [redacted] Protocol
Title: "Functional Characterization of Soluble EGFR Isoforms and EGFR Mutants"
Description: Dr. [redacted] will clone various oncogenic proteins in a variety of human and animal cells using avian virus vectors.
Comments: Dr. [redacted] has prior work history with oncogenes and avian virus vectors. Her lab staff has completed required OEHS Biosafety training classes. Dr. [redacted] cell culture laboratory has been inspected by the OEHS Safety Advisor and was found in conformity with BL2 requirements.

Protocol #05-28: Dr. [redacted] Protocol
Title: "EGS Technology on CFTR, HSP Human Genes and Pseudomonas Genes"
Description: Dr. [redacted] will use conventional plasmids to insert synthetic EGS into Pseudomonas aeruginosa.
Comments: Dr. [redacted] lab has extensive BL2 research experience. The lead technician, [redacted] has demonstrated a very strong lab safety record in other BL2 protocols and has completed all required trainings. The OEHS Safety Advisor has conducted frequent audits of the laboratory for a variety of BL2 research protocols and has found the laboratory to be in conformity with BL2 requirements.

Protocol #05-29: Dr. [redacted] Protocol
Title: "Antiviral Adaptor: Construction of Zero Fitness Sinks Against HIV"
Description: Dr. [redacted] proposes to use Vaccinia virus and Vesicular Stomatitis Virus to express HIV proteins as part of an experiment designed to tag red blood cells with receptors designed to attract HIV. He will also use a defective HIV genome as part of a cell culture assay to determine the effectiveness of the approach.
Comments: Dr. [redacted] has extensive experience with human pathogens and defective vectors. The primary researcher is an undergraduate student who has gained basic BL2 work experience in Dr. [redacted] laboratory. The student has also completed all required training classes. Dr. [redacted] is in the process of arranging a BL2+ safety internship in the lab of Dr. [redacted] Ben Fontes and the OEHS Safety Advisor for [redacted] completed a biosafety inspection of Dr. [redacted] cell culture laboratory and reviewed BL2+ research requirements (BL3 practices in his BL2 laboratory). His cell culture room is two doors off of the main corridor.

The Committee discussed the potential risk of having an undergraduate participate in an experiment that could potentially generate a threat to an immunocompromised dorm mate. The student could possibly infect another student during the period following immunization if the vaccination site is not adequately covered. Dr. van Rhijn inquired if the lab could possibly work with a highly attenuated strain of Vaccinia. Ben Fontes agreed to ask Dr. [redacted] if he could switch strains on the protocol. Dr. Solomon recommended that a mentoring laboratory would be critical in this case and provide supervision for the student. Dr. Kankel asked the Committee to seek the counsel of the Dean's Science Advisor, [redacted] Ben Fontes agreed to notify [redacted] for further feedback on this issue. Dr. van Rhijn also agreed to continue to work with [redacted] the Student Health Physician on this issue. Review of the protocol was tabled until additional information can be obtained from these groups.

Protocol #05-30: Dr. [redacted] Protocol
Title: "Use of Defective HSV Vector in Rodents"
Description: Dr. [redacted] will use a defective Herpes virus vector to express signaling genes in the brains of rats and mice to determine their role in mediating the actions of antidepressants and other medications.
Comments: Dr. [redacted] is part of a group of researchers at [redacted] that have been using this vector system for the past decade. The OEHS SA has found Dr. [redacted] laboratory in conformity with BL2 requirements. IACUC registration and approval is required for this experiment and a YARC BL2 start up meeting will be required for the work if conducted at a Yale Animal research facility. If conducted at the [redacted] animal facility, existing Animal BL2 procedures will be followed for containment of the vector.

Protocol #05-31: Dr. [redacted] Protocol
Title: "Role and Regulation of iNOS in Human T Cells"
Description: Dr. [redacted] will utilize a 3rd generation lentiviral vector to knockout the iNOS (inducible nitric oxide synthase) gene in human T cells with a goal of identifying the gene promoter elements that regulate its transcription.

Comments: Dr. [redacted] lab has a solid BL2 laboratory research history encompassing defective BL2 vectors and human pathogens. The lead researcher has prior BL2 experience and has completed OEHS Biosafety Training. The OEHS Safety Advisor has met with the lead researcher to review BL2 requirements with the laboratory group. She found the group to be well in conformity with BL2 practices.

Protocol #05-32: Dr. [redacted] Protocol
Title: "Intracranial Delivery of DNA Plasmids and Oligos by In Utero Electroporation of Mouse Embryos"
Description: Will over express the Synaptic Adhesion molecule (SynCAM) in the developing mouse and rat brain.
Comments: Dr. [redacted] lab has experience with the techniques required for electroporation of embryos to insert the rDNA. The work will be conducted at Animal BL1 procedures. Existing YARC requirements for survival surgery satisfy Animal BL1 requirements. The lab has been inspected by YARC and by the OEHS Safety Advisor, who found them in conformity with BL1 procedures.

Protocol #05-33: Dr. [redacted] Protocol
Title: "Transgenic Tethered-Toxin Toolkit for In Vivo Neuropharmacology"
Description: Dr. [redacted] will clone toxins that are peptide ion channel blockers in E. coli and in Drosophila melanogaster. The toxins, Agatoxin and Atracotoxin, are spider venom toxins with a low LD50 value.
Comments: The Biosafety Office is in the process of developing a safety protocol for the cloning work and for containment of Drosophila. The PI reports that the amount of toxin expressed in the fly is not appreciable. As the safety protocol has not been finalized, a final protocol lab inspection has not been scheduled. Initial Biosafety review has focused on the use of the OEHS Biosafety Toxin guidelines at BL2 and BL1 containment of transgenic drosophila upon confirmation that the toxin is produced in very small quantities in the fly. The Committee deferred approval until the quantity of toxin involved in the experiment has been identified by the Principal Investigator.

Protocol #05-34: Dr. [redacted] Protocol
Title: "Genetics of Mental Disease"
Description: Dr. [redacted] will use Adeno-associated Virus, Epstein Barr Virus and other plasmids to introduce various genes from the central nervous system in human and animal cells and in mice or rats.
Comments: Dr. [redacted] has prior experience with the proposed vectors and agents at another institution. His lab is in the process of completing their OEHS required safety training classes. His research is also in the process of being registered with the State of CT Dept. of Public Health. Dr. [redacted] is a new PI who has occupied an unfinished laboratory in [redacted] Street. The OEHS Safety Advisor is working with Dr. [redacted] to ensure that an appropriate BL2 cell culture experiment. The protocol is on hold until the facility has been completed. Work in animals will require IACUC approval and a YARC Biosafety start up meeting. This protocol was not approved at the meeting, but may be approved by the Biosafety Office once the laboratory and proposed work practices have been evaluated and found in compliance.

Protocol #05-35: Dr. [redacted] Protocol
Title: "sh-RNA Mediated Knockdown in MDCK Cells"
Description: Dr. [redacted] will use a defective retroviral vector with short hairpin RNA sequences to reduce expression of various dog genes.
Comments: Dr. [redacted] lab has numerous approved BL2 protocols involving infectious agents and defective vectors. This registration covers the proposed retroviral vector work that has not been used in their lab previously. The OEHS Safety Advisor has reported that the lab has frequently been found in conformity with BL2 requirements on previous laboratory inspections and this work can be handled safely with the lab's existing BL2 safety protocols. The facility is a BL2+ laboratory, with many enhancements beyond standard BL2 labs.

Protocol #05-36: Dr. [redacted] Protocol
Title: "Investigation of miRNA Roles in Innate Immunity"
Description: Dr. [redacted] will inoculate wild type and mutant C. elegans with Pseudomonas aeruginosa and assay the killing rate as part of an experiment to identify which mini RNA's are potentially involved in
Comments: The lead researcher has prior research experience with both C. elegans and with Pseudomonas aeruginosa at another institution. She has also completed all required OEHS BL2 Trainings. The OEHS Safety Advisor has completed two BL2 laboratory inspections for Dr. [redacted] lab in the last 3 months (for this experiment and for the proposed Adenovirus vector work). He has found their laboratory to be in conformity with BL2 requirements.

Protocol #05-37: Dr. [redacted] Protocol
Title: "Invitrogen's plenty Viral Expression System"
Description: Dr. [redacted] will use a defective lentiviral vector to express genes involved in intracellular transport in rat primary neurons.
Comments: Dr. [redacted] laboratory has prior BL2 experience. The OEHS Safety advisor is in the process of determining that all personnel involved in the protocol have completed biosafety training. Dr. [redacted] has BL2 research space has previously been found in conformity with BL2 requirements. The OEHS Safety Advisor will confirm that the group's proposed work practices are in conformity with CDC/NIH and Yale BL2 requirements. The protocol was not approved at this meeting, but may be approved by the Biosafety Office once the lab has satisfied all requirements for approval.

Protocols #05-29 was not approved at this time and will require review by other University officials (Dean of Students and the Student Health Office). Protocols #05-34, #05-33, and #05-37 were not approved at this time, but may be approved by the Biosafety Office once the outstanding questions or issues have been addressed. The Committee unanimously approved the remaining rDNA protocols 9/15/05 rDNA agenda.

RDNA Training for Yale OEHS Safety Advisors
The Biosafety Office has created a 6 session training program in rDNA and the NIH Guidelines as part of the ongoing health & safety training for the Safety Advisors within

OEHS. Sessions cover an overview of the Guidelines, rDNA technology, a review of the rDNA Registration Process and Form, and a session each covering NIH Section III-A/III-B/III-C, Section III-D, and the Sections III-E and III-F. To date 3 of the 6 sessions have been completed

RDNA Renewal Form
Ben Fontes reported that a renewal form for rDNA experiments has been developed and will be used to track changes in personnel, room location and experimental procedures.

The meeting was adjourned at 10:15 AM. The next scheduled meeting is October 20, 2005.

Respectfully submitted,

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Yale University Biological Safety Committee
Recombinant DNA Meeting Minutes
December 15, 2005

The Yale Biological Safety Committee Biosafety meeting was held on December 15, 2005 in the Office of Environmental Health & Safety Conference Room, 135 College Street.

Attendance:
Members: Chairman Dean Rupp, Jon Clune, Abe Colon, Susan Compton, Louise Dembry, Ben Fontes, Elan Gandsman, Douglas Kankel, Karen Lamb (ex officio), Sara Rockwell, Mark Solomon, Dorothy van Rhijn, and Herbert Yu.
Guests: Fred Brown, Kevin Charbonneau, and Rob Klein.
Absent: Tina Agentis, Linda Buonocore-Buzzelli, Paul Kowalski, James Macy, Craig Roy, and George Zdru.

Chairman's Report:

The minutes of the September 15, 2005 rDNA meeting were distributed for review. Chairman Rupp asked members to submit comments on the minutes to Ben or Joy. The meeting was called to order at 9:20 AM.

PI Non-Compliance Pathway
The PI Non-Compliance Pathway (developed by the OEHS Safety Advisor Program for addressing health and safety issues) was distributed for review by Committee. To date the pathway has been endorsed by a Research Compliance Committee, the University Safety Committee, and the Radiation Safety Committee. The Biosafety Committee was asked to provide its endorsement. Chairman Rupp asked members to review and provide comments or suggestions. The Committee will vote to endorse at its next meeting. Dr. Rockwell requested that the policy be shared with the Institutional Animal Care and Use Committee (IACUC). Ben Fontes agreed to share the protocol with that group.

New Business

New Protocols:

Protocol #05-40: Dr. [redacted]
Title: "Use of Recombinant Vaccinia Virus."
Description: Dr. [redacted] will utilize recombinant Vaccinia virus to insert structural genes from Hepatitis C virus into mice.
Comments: Dr. [redacted] has prior research experience with BL2 pathogens, including Vesicular Stomatitis Virus (lab strains). Dr. [redacted] and his staff have completed all

required Biosafety Training for the work. Dr. [redacted] laboratory has been previously inspected and found in conformity with BL2 requirements. Since the protocol involves animals, he'll also need an IACUC registration and approval and a BL2 start up meeting with YARC, Biosafety and his staff prior to the initiation of the research. The Biosafety Office will schedule a lab inspection to verify the containment practices for the proposed experiments.

Dr. van Rhijn reported that one of the researchers has a contraindication for the immunization and would be at greater risk of infection if exposed. After discussion, the Committee determined that the risk could be significantly minimized for cell culture experiments through use of Biosafety Level 3 practices in a BL2 facility under negative pressure, through the elimination of all sharps, and by requiring full-face protection. The Committee did not believe that it could engineer out the hazard in animal experiments involving Vaccinia virus. The PI will be asked to have the contraindicated researcher avoid working with animals until after viral shedding has subsided. Ben Fontes reported that he would communicate this information to Dr. [redacted] during the upcoming laboratory inspection for the proposed work. The Committee will be provided with an update on this protocol at the next meeting.

Protocol #05-41: Dr. [redacted]
Title: "Retroviral Injection to Mark Cells of the SV2 (Subventricular Zone)."
Description: Dr. [redacted] will utilize a defective murine retroviral vector containing GFP to label cells in the lateral ventricle of mice.
Comments: The lead researcher has completed Biosafety Training and has also completed the Animal Biosafety start-up meeting to develop the BL2 animal procedures for the experiment. Dr. [redacted] laboratory has prior experience with the defective murine retroviral vectors. He also has an IACUC registration for the work and had a successful YARC start-up meeting.

Protocol #05-42: Dr. [redacted]
Title: "In Vivo and In Vitro Use of Retroviruses."
Description: Dr. [redacted] will use a defective murine retrovirus to express various human and mouse genes into cells in culture and in mice.
Comments: Dr. [redacted] staff has prior research experience with a wide array of defective BL2 vectors and numerous BL2 human pathogens. Dr. [redacted] lab has been inspected frequently for BL2 compliance and his previous inspection demonstrated that his lab is in compliance with BL2 work practices and his new facility in [redacted] is well in conformity with BL2 requirements.

Protocol #05-43: Dr. [redacted]
Title: "Analysis of SynCAM 1 Knockdown Effects in Hippocampal Neurons."
Description: Dr. [redacted] will utilize a defective lentivirus vector to study the role of SynCAM 1 in synapse formation in the brain.
Comments: Dr. [redacted] laboratory has prior experience with human cells and toxins. The lead researcher has completed Biosafety Training in preparation for this experiment. The OEHS Safety Advisor ahs met with Dr. [redacted] to review BL2 precautions for work

with human cells and for work with toxins. She has also conducted a special inspection to verify that Dr. [redacted] lab is in compliance with the additional BL2 practices needed for the safe handling of lentiviral vectors. Dr. [redacted] lab was found in conformity with these requirements.

Incident – Dr. [redacted] Laboratory

Ben Fontes and Chairman Rupp provided a brief summary on the initiation of a rDNA experiment in Dr. [redacted] laboratory prior to Committee registration. A post-doctoral researcher, who recently moved to [redacted] laboratory from Dr. [redacted] laboratory, continued his research involving lab strains of Vesicular Stomatitis Virus in the new location. The work was previously registered in Dr. [redacted] lab and the researcher had completed all required training. The work was conducted in conformity with BL2 requirements. There were no spills, breaches of containment, exposures or waste issues associated with the work. Upon discovery by the OEHS Safety Advisor for Dr. [redacted] lab, the work was immediately halted and Dr. [redacted] has submitted the appropriate registration forms for the research. Chairman Rupp and Ben Fontes contacted the NIH Office of Biotechnology Activities (OBA) and spoke to technical representative Mr. Allan Shipp. The discussion hinged on whether this incident represented a "significant" violation of the NIH Guidelines. Mr. Shipp reported that this incident did not represent a significant violation of the guidelines, especially in light of the circumstances presented above. Mr. Shipp was informed that the incident would be reviewed by the Committee and filed in the Committee minutes.

With the exception of Protocol #05-40, The Committee unanimously approved the Chair's proposal to approve the rDNA protocols #05-41, #05-42, and #05-43, as presented to the Committee. The meeting was adjourned at 9:51 AM. The next scheduled meeting is January 19, 2006.

Respectfully submitted,

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Yale University Biological Safety Committee
Recombinant DNA Meeting Minutes
January 19, 2006

The Yale Biological Safety Committee Biosafety meeting was held on January 19, 2006 in the Office of Environmental Health & Safety Conference Room, 135 College Street.

Attendance:
Members: Chairman Dean Rupp, Tina Agentis, Susan Compton, Louise Dembry, Ben Fontes, Elan Gandsman, Robert Heimer, Douglas Kankel, Paul Kowalski, Sara Rockwell, Mark Solomon, and Dorothy van Rhijn.
Guests: Fred Browne, Maryjo Lanzillotta, and Linda Mouning.
Absent: Jonathan Clune, Karen Lamb, James Macy, Craig Roy, and George Zdru.

Chairman's Report:

The minutes of the December 15, 2005 rDNA meeting were distributed for review. Chairman Rupp asked members to submit comments on the minutes to Ben Fontes or Linda Mouning. The meeting was called to order at 8:41 AM.

Old Business
Dr. [redacted] Protocol (#05-40)
The Biosafety Officer and the OEHS Safety Advisor assigned to the laboratory met with Dr. [redacted] and his lead researcher to evaluate the proposed protocol involving Vaccinia virus in cell culture and in rodents. The Committee concerns from the December 2005 rDNA meeting were also shared with Dr. [redacted] Dr. [redacted] reported that the virus will be prepared by a laboratory at the NIH and as such, there will be very little in vitro work with Vaccinia in his laboratory. He also identified a reference article that identified the length of viral shedding in mice. With this information, he has adjusted his protocol to postpone sampling of the mice until 3 weeks post inoculation, when viral shedding as subsided. Thus, no high risk procedures will be performed by a researcher who is contraindicated for immunization against Vaccinia. OEHS has also helped draft biosafety precautions for the proposed research and will also assist with the development of a standard operating procedure for work with animals once approved.

New Business

<u>New Protocols:</u>

<u>Protocol #05-44</u>: Dr. [redacted]
<u>Title</u>: "Use of Lentiviral Vector to Express Recombinant Proteins in Neurons."

Description: Dr. [redacted] will use replication defective lentiviruses to express recombinant proteins in mouse cortical/ hippocampal neurons. The vector contains VSV-G protein, which expands the host range.
Comments: Dr. [redacted] and his lab staff have prior BL2 research experience with human material, retroviral and adenoviral vectors at BL2 containment. Researchers have completed required Biosafety Training. Dr. [redacted] Safety Advisor has met with Dr. [redacted] to review BL2 requirements and additional precautions for handling defective lentiviral vectors and found his lab and proposed practices to be in conformity with NIH and Yale requirements for BL2 containment. Sharps (needles/glass Pasteur pipettes) have also been eliminated from the protocol.

Protocol #06-01: Dr. [redacted]
Title: "Use of RNA Technology to Inhibit Expression of Virulence Genes of Biowarfare Agents."
Description: Dr. [redacted] will clone individual genes from BL3 and BL2 bacterial pathogens in E. coli to prepare External Oligonucleotide Sequences.
Comments: Dr. [redacted] staff has prior BL2 research experience with human pathogens, cell lines, and defective vectors and has completed relevant Biosafety Training classes. Dr. [redacted] will use existing approved BL2 laboratory research space for the proposed experiments. The [redacted] Safety Advisor has found Dr. [redacted] lab consistently in conformity with BL2 requirements. A BL2 SOP was prepared by the lab for the proposed experiments and is attached to the rDNA protocol for Committee review.

The Committee requested that a letter be provided by the Armed Forces Institute of Pathology indicating how the materials were prepared and verifying that the materials do not contain any pathogenic or toxic sequences. Ben Fontes will communicate this requirement to Dr. [redacted]

Protocol #06-02: Dr. [redacted]
Title: "Phophotidyl Inositol Signaling in the Prefrontal Cortex."
Description: Dr. [redacted] will use a defective Adeno-Associated Viral Vector to over express Protein Kinase C in vivo in the rat brain as part of an experiment studying bipolar disorder.
Comments: Dr. [redacted] staff has prior BL2 research experience with human and non-human primate cells and with non-human primates. The research group has completed OSHA Bloodborne Pathogens training and will attend the January 2006 Biosafety training session. OEHS will also meet with the lab to review BL2 transport requirements. Dr. [redacted] research facility was found in conformity with BL2 requirements by the Safety Office and the State of CT. Dept. of Human Health. Animal experiments must be approved by the Yale IACUC. In addition, a start-up training and orientation with YARC and Biosafety representatives must occur prior to the initiation of this work in animals.

Protocol #06-03: Dr. [redacted]
Title: "Neurogenetic Processes in the Brain."
Description: Dr. [redacted] has submitted a protocol utilizing defective retroviral vectors containing GFP to label newly divided cells in the brains of non-human primates.

Comments: Dr. [redacted] lab has prior research experience with defective BL2 vectors and extensive experience with non-human primates. The protocol will require Yale IACUC registration and a YARC start-up meeting to develop the Animal BL2 requirements for experiments with non-human primates. This would represent the 1st use of BL2 materials implanted in NHP's in > 10 years at Yale. Ben Fontes will schedule a preliminary meeting with YARC staff and the lead researchers to start outlining the standard operating procedures for the experiment.

Incidents:

The Chair's proposal to approve Protocol #05-44 as presented by the Biosafety Officer was unanimously approved by the Committee. Protocol #06-01 and #06-02 may be administratively approved by the Biosafety Office once all outstanding items have been completed. Protocol #06-03 was not considered as a joint safety meeting with Yale Animal Resources Center Personnel to discuss Animal BL2 containment for non-human primates. The meeting was adjourned at 9:00 AM. The next scheduled meeting is February 16, 2006.

Respectfully submitted,

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Yale University Biological Safety Committee
Recombinant DNA Meeting Minutes
February 16, 2006

The Yale Biological Safety Committee rDNA meeting was held on February 16, 2006 in the Office of Environmental Health & Safety Conference Room, 135 College Street.

Attendance:
Members: Chairman Dean Rupp, Tina Agentis, Jonathan Clune, Susan Compton, Frederick Browne (for Louise Dembry), Ben Fontes, Robert Heimer, Douglas Kankel, James Macy, Sara Rockwell, Mark Solomon, and Dorothy van Rhijn.
Guests: Robert Klein, Maryjo Lanzillotta, and Linda Mouning.
Absent: Abraham Colon, Elan Gandsman, Paul Kowalski, Karen Lamb, Craig Roy, and George Zdru.

Chairman's Report:

The minutes of the January 19, 2006 rDNA meeting were distributed for review. Chairman Rupp asked members to submit comments on the minutes to Ben Fontes or Linda Mouning. Chairman Rupp also reported that Dr. Elan Gandsman, who was visiting family and not present at the meeting, had announced his retirement from the University and would be leaving at the end of February. The University is planning a retirement celebration for Dr. Gandsman and Committee members will be informed of the details. The meeting was called to order at 8:37 AM.

Old Business
Dr. [redacted] Protocol (#05-40)
Dr. [redacted] has scheduled his medical consult for vaccinia virus immunization with Employee Health and will schedule a start up meeting with the Yale Animal Resources Center (YARC) and Biosafety prior to the initiation of this work with animals. The biosafety elements of the protocol have been completed by Dr. [redacted] and the protocol is cleared for full approval.

Dr. [redacted] Protocol (#06-01)

Dr. [redacted] has received a letter from the Armed Forces Institute of Pathology identifying how the materials were prepared and verifying that the materials do not contain any pathogenic or toxic sequences. Dr. [redacted] is in the process of obtaining a USDA permit for the receipt of genetic material from select agents. Once Dr. [redacted] has obtained the

USDA permit for genetic material from USDA select agents, he will be eligible to obtain these items from the Armed Forces Institute of Pathology.

Dr. [redacted] Protocol (#06-02)
The start-up training and orientation with YARC, Biosafety representatives, and Dr. [redacted] staff has been completed. She has been assigned a dedicated animal BL2 room in the BCMM animal facility, and has established decontamination protocols for each of the animal test chambers that will be used in the experiment. The protocol is now cleared for full approval.

Dr. [redacted] Protocol (#06-03)
The protocol will require Yale IACUC registration and a YARC start-up meeting to develop the Animal BL2 requirements for experiments with non-human primates. Ben Fontes will schedule a preliminary meeting with YARC staff and the lead researchers to start outlining the standard operating procedures for the experiment.

New Business

New Protocols:

Protocol #06-04: Dr. [redacted]
Title: "Role of IK Channels in Rat Distal Colon and Ca2+-Activated Cl Secretion in Colon: an Alternate Mechanism of Cl Secretion."
Description: Dr. [redacted] will utilize a defective adenoviral vector (AdEasy System) to express various K channel isoforms in cell culture and in colon tissue in vivo to determine their role in fluid secretion.
Comments: Dr. [redacted] has extensive BL1 and BL2 experience in the laboratory of Dr. [redacted] Although he does not have direct experience with the AdEasy System, he will work with Dr. [redacted], who has previous approval for work with adenoviral vectors to conduct the initial experiments. Dr. [redacted] Safety Advisor has been working with him to set up his own lab area within Dr. [redacted] laboratory. Dr. [redacted] laboratory and Dr. [redacted] lab area are in full compliance with CDC/NIH and Yale BL2 requirements. Dr. [redacted] lab has also been frequently inspected and found in conformity with BL2 requirements.

For this experiment, the Safety Advisor will conduct a lab inspection to review BL2 procedures at the start of the experiment. OEHS will also be part of the start up meeting to develop an Animal BL2 safety protocol with YARC once Dr. [redacted] has obtained Yale IACUC approval for his animal research.

Protocol #06-05: Dr. [redacted]
Title: "Biocompatible DNA Delivery Systems."
Description: Dr. [redacted] will create biomaterials (controlled delivery polymers) that contain marker, immune enhancing, or therapeutic genes and determine their expression and activity in cell culture and in mice.

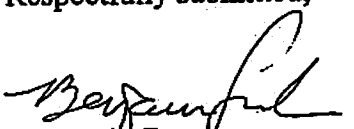
Comments: Dr. [redacted] and his staff have significant experience in biomedical engineering and the development of polymers for biological applications. Dr. [redacted] new lab space in the Malone Engineering Center was built to BL2 specifications and is well in conformity with the Biosafety Level 1 research materials utilized in this experiment. Although not listed in this protocol, any future work with human cells will require Biosafety Level 2 and Universal Precautions if utilized.

Request from Dr. [redacted] Regarding Protocol T-139
Dr. [redacted] informed the Biosafety Office that he has been requested to provide assurance that the recombinant DNA experiments described in a manuscript that he had submitted for publication were approved by the Committee. One of the reviewers had submitted this request over concerns that the experiments involved the introduction of genes coding for antibiotic resistance into Borrelia burgdorferi. Chairman Rupp provided a historical overview of experiments approved in Dr. [redacted] laboratory. Protocol #T-139, which was approved by the Committee in the early 1990's, involved the introduction of chloramphenicol in Borrelia burgdorferi. Chloramphenicol was selected as it was not a drug utilized for the treatment of the disease under study. Subsequently, Dr. [redacted] laboratory altered their delivery vector to utilize kanamycin in place of chloramphenicol. Kanamycin has proven to be more effective in gene knockout studies and it also not utilized for the treatment of Borrelia infection. The updated vector also contained the gene for ampicillin resistance. The reviewer was concerned that this gene, which is used for the treatment of Borrelia infections in children, would be introduced into the organism. Dr. [redacted] lab has engineered the vector so that ampicillin in not in the portion of the vector that integrates into the Borrelia genome.

Committee discussion ensued on this topic. Key points of consideration included the update of the vector, whether there was any potential for a single crossover event for ampicillin to integrate into Borrelia, and Dr. [redacted] response back to the editor. There was general sentiment that the switch to a vector utilizing kanamycin resistance instead of chloramphenicol was not a significant change in the protocol, but should have been updated by the principal investigator. Although not in the portion of the vector that integrates in the host, there was also sentiment that the vector could be reengineered to remove ampicillin from the plasmid. Additional discussion focused on the specific questions posed by the reviewer to Dr. [redacted] and a review of Dr. [redacted] detailed response back to the editor of the Journal. As full resolution of Dr. [redacted] request could not be completed during the meeting, a subset of Committee members agreed to continue to work with Dr. [redacted] on his request. The subgroup will review the molecular biology of the recombinant vector and will assist Dr. [redacted] with the review of his next response back to the editor.

The Chair's proposal to approve Protocols #05-40, #06-02, #06-04 and #06-05 as presented by the Biosafety Officer was unanimously approved by the Committee. Protocols #06-01 and #06-03 were not approved and will remain pending until the outstanding elements are completed. The meeting was adjourned at 9:24 AM. The next scheduled meeting is March 16, 2006.

Respectfully submitted,



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Yale University Biological Committee
Recombinant DNA Meeting Minutes
April 20, 2006

The Yale Biological Safety Committee rDNA meeting was held on April 20, 2006 in the Office of Environmental Health & Safety Conference Room, 135 College Street. The meeting was called to order at 8:35 AM.

Attendance:
Members: Chairman Dean Rupp, Abraham Colon, Louise Dembry, Robert Heimer, Douglas Kankel, Sara Rockwell, Craig Roy, Dorothy van Rhijn, George Zdru
Guests: Rob Klein, Richard Maffei, Salvatore Rubano, Maryjo Lanzillotta, Fred Brinne
Absent: Tina Agentis, Benjamin Fontes, Susan Compton, Jonathan Clune, Paul Kowalski, James Macy, Mark Solomon.

Chairman's Report:
The Minutes of the February 16, 2006 rDNA meeting were distributed for review. Chairman Rupp asked members to submit comments on the minutes to Ben Fontes or Linda Mouning. Chairman Rupp informed the Committee that Maryjo Lanzillotta, Associate Biosafety Officer, would assist with presentation of the protocols in the absence of Ben Fontes. Chairman Rupp had members of the committee introduce themselves to the newest members and guests before presentation of the agenda. Chairman Rupp also informed new members on how the committee meeting is conducted.

Old Business
Dr. [redacted] Protocol (# 06-01)
Maryjo Lanzillotta informed the committee members that Dr. [redacted] protocol is still pending, awaiting a USDA permit for receipt of genetic elements from regulated animal pathogens.

Dr. [redacted] Protocol (#06-03)
Dr. [redacted] protocol, which involves the introduction of a defective retroviral vector into the brains of non-human primates, was held over from the last Committee meeting. The Biosafety Office has received information from [redacted] IBC regarding their classification of defective retroviral vectors along with an email from the Biosafety Officer at [redacted] University to help support the risk assessment of the work here at Yale. [redacted] is also utilizing a containment level of Animal Biosafety Level 2 (ABSL-2), which is similar to what Yale has proposed. [redacted] will collect waste from the animals in this experiment for 3 days post inoculation as regulated biomedical waste.

Yale will employ ABSL-2 and will collect the waste from the non-human primates inoculated with the defective retroviral vector for one week following initiation of the experiment. The Committee approved the experiment at ABL2.

New Business

Dr. [redacted] Protocol (#06-06)
Title: Mitichondrial Ion Channels
Description: Dr. [redacted] will utilize a defective lentiviral vector to over express Bc1-2 Protein in rat hippocampal neurons to examine its effect on synaptic transmission. Bc1-2 proteins are involved in the response to apoptosis.
Comments: Dr. [redacted] will serve as lead researcher for this project. All personnel involved in the work have completed Biosafety Training. Dr. [redacted] has prior BL2 cell culture experience with non-human primate cell lines. Dr. [redacted] lab will also be working with the assistance of Dr. [redacted] of Dr. [redacted] lab that has prior experience with this vector. The Biosafety Officer has met with Dr. [redacted] and her staff to conduct a BL2 inspection and found the proposed cell culture lab, [redacted], to be well in conformity with BL2 requirements. Their proposed BL2 protocol has been modeled after Dr. [redacted] existing protocol for work with defective lentiviral and adenoviral vectors. The protocol is recommended for approval at BL2. Maryjo Lanzillotta informed the committee that an exposure to the defective lentiviral vector may generate a false positive reaction on an HIV antibody test. Dr. [redacted] indicated that this vector may not express HIV proteins that would lead to a false positive reaction. Dr. [redacted] will review the protocol and notify Maryjo Lanzillotta regarding final approval. Dr. Craig Roy does not see any risk with the vector. This protocol is pending and will be finalized upon review by Dr. Heimer. Dr. Heimer will notify the Biosafety Office of his decision.

Dr. [redacted] Protocol (#06-07)
Title: Effects of EC gene expression on adhesion, coagulation and longevity
Description: Dr. [redacted] will utilize defective retroviral and adenoviral vectors to study the effects of endothelial cell related genes on coagulation, adhesion and longevity with relation to cellular scaffolds.
Comments: Dr. [redacted] has performed these experiments previously at [redacted] University. She and her staff are in the process of completing the required Biosafety training classes at Yale. The [redacted] Safety Advisor has had multiple meetings with the Principal Investigator and her staff to help set up the laboratory and review proposed procedures. Once all of the proposed lab equipment is in place a final walk through inspection will be conducted. The existing cell culture facility in [redacted] is in full compliance with BL2 requirements. The Committee did not approve the protocol at this time.

Dr. [redacted] Protocol (#06-08)
Title: Determination of HPV Copy Number and Genotype Using Real-Time PCR and Molecular Beacon Reporter Probes.
Description: Use of purified plasmids that contain HPV DNA as a positive control for an HPV assay of biopsy samples

Comments: Dr. [redacted] has extensive BL2 experience with human pathogens, human cells, and human clinical materials. The lead researcher has completed required biosafety training classes. Dr. [redacted] research laboratory has been inspected previously by the [redacted] Safety Advisor and has been found in conformity with BL2 requirements. The protocol was approved by the Committee at BL2.

Dr. [redacted] Protocol (#06-09)
Title: Structural Biology of Janus Kinases
Description: Dr. [redacted] will use the baculovirus expression system to clone janus kinase genes for structural analysis
Comments: All researchers have prior experience with BL1 materials and have completed basic lab safety training required for these experiments. The OEHS Safety Advisor has conducted a BL1 inspection and has found the lab to be in compliance with level 1 requirements. The protocol was approved at BL1.

Dr. [redacted] Protocol (#06-10)
Title: Use of VSV-g cDNA
Description: Dr. [redacted] will use a lab strain of Vesicular Stomatitis Virus for recombinant DNA experiments that study the role of spectrin and ankyrin in the cellular secretory pathway.
Comments: The lab-adapted strains of VSV used in this protocol are not select agents. Also, since the strains of VSV will be obtained from within the University, a USDA permit is not needed. The lead researcher, [redacted] has previously worked with the VSV vector with Dr. [redacted]. He will bring this experience with him to Dr. [redacted] protocol. He has also completed biosafety training requirements and will train new personnel in the lab. Dr. [redacted] Safety Advisor has previously inspected the laboratory for BL2 compliance. The lead researcher has transferred the protocol used in Dr. [redacted] lab to Dr. [redacted] cell culture suite and is in compliance with BL2 requirements and the additional precautions prescribed by the Biosafety Office for work with VSV. There will not be any animal work with this vector by the lab.
The protocol was approved at BL2.

Dr. [redacted] Protocol (#06-11)
Title: VSV and Adenovirus Vaccination against CMV
Description: Dr. [redacted] has submitted an update to his existing approved recombinant VSV Cytomegalovirus vaccine protocol to add a booster immunization with a defective adenovirus vector.
Comments: Dr. [redacted] and his colleagues from Comparative Medicine have extensive experience with human and rodent pathogens, animals, and recombinant vectors. All biosafety training was completed previously for earlier BL2 experiments. Dr. [redacted] laboratory space and work practices have been previously inspected and approved by the Biosafety Office. He has also recently completed a comprehensive start up meeting with Biosafety and the Yale Animal Resources Center to outline the BL2 and BL2+ requirements for work with recombinant VSV in rodents. The protocol was approved at BL2.

Dr. [redacted] Protocol (#06-12)
Title: ER to Golgi Transport Assay
Description: Dr. [redacted] will use a recombinant Vaccinia virus and a standard cloning vector expressing VSV-G protein to study the transport of protein in the endoplasmic reticulum.
Comments: The post-doctoral associate who will be conducting the work has obtained roughly 2 weeks of initial hands on training for work with the virus at his former institution. He is currently getting additional training in the laboratory of Dr. [redacted] He has also completed Yale biosafety training. Biosafety and the OEHS Safety Advisor has met with the Principal Investigator to outline the facility and procedural requirements for BL2 work with recombinant vectors and also for human pathogens. Dr. [redacted] is in the process of addressing the facility and equipment recommendations outlined by OEHS. Once the lab is prepared and Dr. [redacted] has signed off on the post-doctoral associates training, the protocol will be ready for full approval. The lead researcher will also have to complete a medical evaluation with the Employee Health Office prior to initiation of the work. The protocol is on hold until the additional requirements have been satisfied.

Dr. [redacted] Protocol (#06-13)
Title: Deleting Genes in B. burgdorferi and Complementing the Mutants
Description: Dr. [redacted] proposal is an update and clarification of previously approved experiments involving the knockout/deletion of single genes in Borrelia burgdorferi using several antibiotic resistance markers. He will also introduce the deleted genes back into mutant Borrelia to confirm its function.
Comments: Dr. [redacted] and his staff have extensive experience and prior approvals for recombinant work with Borrelia and for work with BL2 and BL3 human pathogens. All researchers have completed required Biosafety training. The existing BL2 laboratory and containment work practices are inspected annually and have been found in conformity with BL2 requirements. A pBluescript-based vector will be used to introduce either Kanamycin, Streptomycin or Spectinomycin, or Erythromycin resistance markers to replace single genes in Borrelia. One additional antibiotic, Erythromycin, generated discussion as consideration of NIH rDNA Guidelines section III-A-1 (transfer of a drug resistant trait to an organism not known to acquire it naturally is not appropriate if such acquisition could compromise the use of the drug to control disease) must be ruled out by the Committee. Chairman Rupp indicated that Dr. [redacted] is currently out of the country and communication has been delayed. Dr. Dembry noted that the use of erythromycin with the pathogen may have clinical implications. Rob Klein indicated that a call to the NIH Office of Biotechnology Activities is in order for the remaining questions on this protocol. A final decision on the protocol was tabled until additional information from NIH OBA on the use of antibiotic resistance genes can be obtained.

Dr. [redacted] Protocol (#06-14)
Titles: A. Tick Gene Expression in the Context of Lyme Disease. B. Lentivirus Mediated Delivery of WNV siRNA Therapeutics
Description: Dr. [redacted] has presented 2 rDNA protocols in this registration. Part A involves the introduction of a defective lentivirus vector into the salivary glands of ticks

to assess the level of expression of this system. He will also investigate the role of tick genes in the survival of Borrelia burgdorferi in the host. Part B of the protocol will test if this vector with an RNA interference cassette has any ability to block WNV infection in cells and in mice.
Comments: Dr. [redacted] laboratory has previously been certified by the State of CT Dept. of Public Health and the Yale Biological Safety Committee for work with human pathogens at BL2 and BL3. He has also successfully passed federal inspections for work with West Nile Virus at BL3 and at Animal BL3. All personnel involved in the proposed protocol have prior work experience and have completed BL2 or BL3 training. Dr. [redacted] has 2 BL2 cell culture rooms in the [redacted] building that have been inspected annually by an OEHS Safety Advisor and found in conformity with BL2 requirements. His BL3 laboratory and his work practices have also passed Yale, State, and Federal biosafety inspections and were authorized for work with West Nile Virus. The last inspection was in January 2006. Comment on BL3 Work: This rDNA experiment involves the introduction of a BL2 vector into BL2 cells in the in vitro BL3 lab, with subsequent inoculation of cells with a BL3 agent (WNV). Also involves the introduction of the same BL2 vector into clean mice in the in vivo BL3 lab, with follow up challenge of the existing/approved BL3 agent (WNV). This should not change the existing biosafety level for the BL3 lab (all work will remain at BL3 containment for both proposed experiments). The protocol was approved as presented by the Committee (BL2 for lentiviral work and BL3 for work with WNV).

Dr. [redacted] Protocol (#06-15)
Title: Stem Cell Regulation and Neuronal Patterning in the Forebrain
Description: Use of replication defective retroviral vectors to deliver genes involved in brain development into mouse neural cells in vitro and in vivo
Comments: Dr. [redacted] has conducted experiments with these vectors previously in the laboratory of Dr. [redacted] He is completing independent registrations, as he has become a Principal Investigator. Dr. [redacted] laboratory has been previously audited and found in conformity for BL2 work by OEHS. A start up meeting to outline animal biosafety practices is required between the researchers, Biosafety and the Yale Animal Resources Center. The protocol was approved by the Committee at Animal BL2 with the contingency of a start-up meeting with Animal Care and Biosafety prior to initiation of the experiment.

Dr. [redacted] Protocol (#06-16)
Title: Analysis and study of RNA based regulatory elements in Pseudomonas syringae
Description: Dr. [redacted] will use the broad host range plasmid RK2 to transfer drug resistance (tetracycline and ampicillin) to Pseudomonas syringae, a saprophytic organism. He will also clone genes from Pseudomonas syringae to examine their role in the regulation of metabolism
Comments: Although the protocol involves the transfer of antibiotic resistance, the transfer is transitory. P. syringae is not a human or animal pathogen, and has a protective role in plants. Dr. [redacted] has extensive experience with the BL1 materials described in the protocol. The OEHS Safety Advisor has inspected Dr. [redacted] laboratory annually for compliance with BL1 requirements and has found his facility and work practices in

full conformity with BL1 requirements. No work with live plants will be conducted. Researchers will promptly inactivate waste before disposal from the laboratory as regulated medical waste. The protocol was submitted to Dr. [redacted] from the Biology Department for review as plants are involved. Dr. [redacted] serves as one of two technical experts to the Committee for rDNA experiments involving plants. Dr. Craig Roy reflected that the researchers have taken precautions to avoid transfer of resistance and believed that the protocol was safe to pursue. Dr. Kankel felt that Dr. [redacted], who has substantial experience with plant pathogens, should be contacted to review the protocol. Maryjo Lanzillotta agreed to submit the protocol to Dr. [redacted] The protocol was not approved by the Committee at this time.

Protocols #06-07, #06-12, #06-13, and #06-16 were not approved by the Committee at the meeting. All other rDNA protocols were unanimously approved by the Committee as presented. The rDNA meeting was adjourned at 9:24 AM. The next scheduled meeting will be held on June 15, 2006.

Respectfully submitted,

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Yale University Biological Committee
Recombinant DNA Meeting Minutes
June 15, 2006

The Yale Biological Safety Committee rDNA meeting was held on June 15, 2006 in the Office of Environmental Health & Safety Conference Room, 135 College Street. The meeting was called to order at 8:34 AM.

Attendance:
Members: Chairman Dean Rupp, Jon Clune, Susan Compton, Louise Dembry, Benjamin Fontes, Robert Heimer, Douglas Kankel, James Macy, Sara Rockwell, Craig Roy, Mark Solomon, Dorothy van Rhijn.
Guests: Salvatore Rubano, MaryJo Lanzillotta
Absent: Tina Agentis, Abraham Colon, Paul Kowalski, George Zdru.

Chairman's Report:
The Minutes of the April 20, 2006 rDNA meeting were distributed for review. Chairman Rupp asked members to submit comments on the minutes to Ben Fontes or Linda Mouning.

Old Business
Dr. [redacted] Protocol (# 06-07)
Dr. [redacted] has completed the set up of her laboratory and she and her staff have completed required OEHS trainings. She has also had successful lab inspections by OEHS and the State of Connecticut Department of Public Health. Her rDNA protocol, which was now eligible for authorization, was formally approved by the Committee at BL2 containment.

Dr. [redacted] Protocol (#06-12)
Dr. [redacted] also had a successful start up inspection for initiation of her BL2 rDNA experiments. Dr. [redacted], who agreed to provide hands-on training for the handling of Vaccinia virus for Dr. [redacted] lead researcher, has officially signed off on the successful completion of the training internship. With completion of this final requirement, the Committee also approved this experiment at BL2 containment.

Dr. Heimer noted that researchers such as Dr. [redacted] have provided an invaluable service to those investigators who lack sufficient research experience by offering these training opportunities. The University and the Committee also benefit substantially from this training as the procedures and hands on biosafety precautions are provided by a lab experienced with biocontainment practices. Researchers providing this service should be formally thanked by the Committee for their efforts. Ben Fontes agreed to draft a letter and will forward to a subset of Committee members for comment.

Dr. [redacted] Protocol (#06-13)
Dr. [redacted] update of his rDNA experiments involving the transfer of antibiotic resistance markers to knock-out various genes in Borrelia burgdorferi was tabled pending further review. Ben Fontes will contact the NIH Office of Biotechnology to get background information on their assessment of suicide vectors, alternate antibiotic therapies, the transfer of antibiotic resistance markers not used for therapy, and vectors that contain therapeutic antibiotic resistance markers but not on the portion of the vector involved in gene transfer or ablation.

Dr. [redacted] Protocol (#06-16)
Dr. [redacted] has agreed to provide a risk assessment for this recombinant DNA protocol involving the transient transfer of an antibiotic resistance marker to Pseudomonas syringae. Dr. [redacted] will also need a permit from the USDA for experiments with Pseudomonas syringae. The protocol was not considered for approval by the Committee at this meeting.

New Business

Dr. [redacted] Protocol (#06-17)
Title: "Analysis and Study of RNA Based Regulatory Elements in Bacillus cereus"
Description: Dr. [redacted] research involves the study of RNA regulatory elements from Bacillus cereus that are involved in metabolism.
Comments: Dr. [redacted] staff has attended all required Biosafety training courses. The Biosafety Office is currently in the process of assisting the laboratory in the set up and start-up of their BL2 research experiments. The bulk of the work in this protocol is Biosafety Level 1 (cloning individual genes from B. cereus in E. coli). Live B. cereus will be inactivated to extract genomic material for their research. The Biosafety Office and Dr. [redacted] OEHS Safety Advisor are assisting the lab with the registration of human pathogen work with the State of CT. The protocol was not approved at the meeting, but the Biosafety Office was provided with clearance to approve the protocol once the State of Connecticut Department of Public Health has given the lab authorization for experiments with B. cereus.

Dr. [redacted] Protocol (#06-18)
Title: "Analysis and Study of RNA Based Regulatory Elements in Staphylococcus aureus."
Description: Dr. [redacted] research involves the study of RNA regulatory elements from Staphylococcus aureus that are involved in metabolism.
Comments: Dr. [redacted] staff has attended all required Biosafety training courses. The Biosafety Office will assist the laboratory in the set up and start up of their BL2 research. The bulk of the work in this protocol is Biosafety Level 1 (cloning individual genes from S aureus in E. coli). Live S. aureus will be inactivated to extract genomic material for their research. The Biosafety Office and Dr. [redacted] OEHS Safety Advisor are

assisting the lab with both the set up of their BL2 work areas and the registration of human pathogen work with the State of CT. As noted above in #06-17, the protocol was not approved but awaits conformation official authorization from the State prior to initiating work with an infectious agent.

Dr. [redacted] Protocol (#06-19)
Title: "Leishmania – Expression and Vaccines"
Description: Dr. [redacted] protocol is an update of her existing experiments utilizing a recombinant Vaccinia virus expressing genes from Leishmania to develop a vaccination for cutaneous and visceral Leishmania disease.
Comments: Dr. [redacted] research group has prior BL2 experience with both biohazards involved in this protocol (Vaccinia and Leishmania). All researchers have completed applicable biosafety training. Researchers working with Vaccinia must complete a medical consult for immunization with Employee Health. Dr. [redacted] lab is already registered with the State of CT Dept. of Public Health for research with Leishmania and Vaccinia. Her laboratory and work practices have been successfully inspected for BL2 compliance by Yale OEHS and the State of CT. Animal work will require a start-up meeting with Biosafety and Animal Care personnel. The update, which does not deviate significantly from the existing protocol, was recommended for approval at BL2 containment.

Dr. [redacted] Protocol (#06-20)
Title: H Regulation in Rat Hippocampal Neurons with Silenced Bicarbonate Transporter."
Description: Dr. [redacted] will utilize a defective lentiviral vector to disable individual genes in neuronal cells. The vector will allow his lab to study the mechanism of a specific pH-regulatory transporter.
Comments: Dr. [redacted] staff has attended applicable Biosafety training classes. Dr. [redacted] group will receive hands on training from Dr. [redacted] in his Department, who has prior approval for research with lentiviruses. Dr. [redacted] will sign off on the training for Dr. [redacted] group after the hands-on training. The Biosafety Office and Dr. [redacted] OEHS Safety Advisor will conduct a BL2 cell culture lab inspection once Dr. [redacted] has completed the hands-on BL2 training for cell culture work with defective lentiviruses. The proposed cell culture suite is currently used by 3 groups in the Department of Pharmacology and has been previously found in conformity with BL2 requirements by the Biosafety Office. Dr. [redacted] protocol was recommended for approval at BL2 containment with the hands-on training described above.

Dr. [redacted] Protocol (#06-21)
Title: Endothelial Modification that Reduces T Cell Activation"
Description: Dr. [redacted] will utilize a defective adenoviral vector to deliver human genes to immunodeficient mice to study issues associated with transplantation.
Comments: Dr. [redacted] staff has extensive BL2 research experience in cell culture and in animals with defective vectors and human pathogens. His staff has completed required Biosafety training. Dr. [redacted] research facility, safety practices, and animal biosafety procedures have been previously inspected and found in compliance with applicable BL2

requirements. A start-up meeting with the Yale Animal Resources Center (YARC), Biosafety, and the research group will be required prior to initiation of the work. The protocol was recommended for approval at BL2 containment and the requirement of an Animal Biosafety start-up meeting with YARC.

Dr. [redacted] Protocol (#06-22)
Title: "Use of Adenoviral NFAT Reporter Gene in Primary Mouse Neuronal Cultures."
Description: Dr. [redacted] will use a defective adenoviral vector containing a copy of a neuronal transcription factor in rat neurons in cell culture.
Comments: Dr. [redacted] lab has completed required Biosafety training classes. However, the graduate student who will be performing the experiment has not had prior experience with this vector system. Dr. [redacted] has access to a BL2 cell culture facility, but does not have prior BL2 cell culture experience. The OEHS Safety Advisor assigned to Dr. [redacted] and the Biosafety Officer will meet with the lab and provide hands on training in BL2 lab practices in the field and assist with the set up of their laboratory. OEHS will also attempt to establish a BL2 field internship for the graduate student in Dr. [redacted] lab with another lab group working with defective adenovirus. The protocol was approved at BL2 containment contingent upon a successful training internship by Dr. [redacted] lead researcher to gain hands on experience with the vector system.

Protocols #06-13, #06-17, and #06-18 were not approved by the Committee at the meeting. All other rDNA protocols (#06-07, #06-12, #06-19, #06-20, #06-21, #06-22, and #06-23) were unanimously approved by the Committee as presented. The rDNA meeting was adjourned at 9:00 AM. The next scheduled meeting will be held on July 21, 2006.

Respectfully submitted,

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Yale University Biological Committee
Recombinant DNA Meeting Minutes
September 21, 2006

The Yale Biological Safety Committee rDNA meeting was held on September 21, 2006 in the Office of Environmental Health & Safety Conference Room, 135 College Street. The meeting was called to order at 8:52 AM.

Attendance:
Members: Chairman Dean Rupp, Tina Agentis, Robert Bienstock, Susan Compton, Louise Dembry, Benjamin Fontes, Robert Heimer, Douglas Kankel, James Macy, Sara Rockwell, Craig Roy, Mark Solomon, Dorothy van Rhijn.
Guests: Ann MacIntyre, MaryJo Lanzillotta, Bruce McCann.
Absent: Abraham Colon, Paul Kowalski, James Macy, Craig Roy, Cynthia Smith.

Chairman's Report:
The Minutes of the June 16, 2006 rDNA meeting were distributed for review. Chairman Rupp asked members to submit comments on the minutes to Ben Fontes or Linda Mouning.

To open the first Committee meeting of the new academic year, Chairman Rupp introduced himself along with his responsibilities as Chair and asked each member of the Committee and guests to introduce themselves to the group. Following the introductions, Chairman Rupp provided an overview of the Committee for the new members, reviewing the history, process and schedule for the upcoming academic year. A copy of the mandate of the Biological Safety Committee was distributed to Committee members. Chairman Rupp also spent a few moments highlighting the useful links from the NIH Office of Biotechnology Activities, (including the NIH rDNA Guidelines), to help transition new Committee members to their roles. Web links to pertinent sites at the Centers for Disease Control and Prevention, the United States Department of Agriculture, and Yale University's Office of Environmental Health & Safety were also provided. Additional handouts describing the review of rDNA registrations for Committee members and guidelines for addressing non-compliance and reporting were also provided.

Old Business
Dr. [redacted] Protocol (#06-01)
Dr. [redacted] protocol to clone non-toxic and non-pathogenic fragments from Select Agent bacteria was approved administratively by the Biosafety Committee once all of the stipulations required by the Committee during its previous review have been satisfied. Dr. [redacted] laboratory was inspected and found in full conformity with BL2 requirements. Dr. [redacted] has also received a permit from the USDA for the transfer of

non Select Agent regulated genetic fragments. The FAS Grants and Contracts Office (FAS) has also finalized the Material Transfer Agreement for Dr. [redacted] to clear his receipt of the fragments. The federal laboratory shipping the fragments will inactivate the organisms, test for viability, and then cut the DNA with a restriction endonuclease to break the genome up in to fragments prior to shipment to Dr. [redacted] laboratory.

Dr. [redacted] Protocol (#06-13)
Dr. [redacted] update of his rDNA experiments involving the transfer of antibiotic resistance markers to knock out various genes in Borrelia burgdorferi has been divided into two separate protocols. The transfer of non-clinically significant antibiotic resistance markers into Borrelia burgdorferi was assigned Yale Biological Safety Committee #06-13A. Yale Biological Safety Committee #06-13B has been assigned to the proposed rDNA experiment that involves the transfer of a gene coding for erythromycin resistance into Borrelia burgdorferi. Protocol #06-13A was approved by the Biosafety Office at BL2 containment as an extension of pre-existing approved work in Dr. [redacted] laboratory. Protocol #06-16B was submitted to the NIH Office of Biotechnology Activities for evaluation of whether the protocol had to be treated as a Major Action under Section III-A-1 of the NIH rDNA Guidelines. Chairman Rupp has submitted a letter to the NIH outlining the request for guidance. A copy of his letter was provided to the Committee. Erythromycin is listed as a 2nd line antibiotic for treatment of Lyme disease, for those who may be allergic to primary antibiotics. Dr. [redacted] has provided references that show that alternative treatment options are available for Lyme disease and also provided. He also provided the Committee with a reference that demonstrated that Borrelia could acquire resistance to erythromycin naturally. Despite these facts, the University believed that assistance from the NIH Office of Biotechnology Activities was needed in the review of this protocol. Chairman Rupp will update the Committee on his correspondence with the NIH at its next meeting.

New Business

Dr. [redacted] Protocol (#06-23)
Title: "Inhibition of Autotaxin, a Prometastatic Enzyme Up regulated in Ovarian Cancer."
Description: Dr. [redacted] will use a Baculovirus vector to clone the gene Autotaxin as part of an examination of its role in ovarian cancer.
Comments: Dr. [redacted] lab staff have attended applicable OEHS training classes and have prior research experience involving BL1 containment and work with human cells at BL2. The OEHS Safety Advisor has inspected Dr. [redacted] laboratory and has found it in conformity with BL1 and BL2 requirements.

Dr. [redacted] Protocol (#06- 24)
Title: "Routine Transformation of Arabidopsis thaliana."
Description: Dr. [redacted] has submitted an update of his existing rDNA experiments involving the generation of transgenic plants (Agrobacterium tumefaciens to transform Arabidopsis thaliana).

Comments: Dr. [redacted] and his staff are in compliance with safety training requirements and the lab has a long history of experience with the generation of transgenic plants. The containment level required is Plant Biosafety Level 1. Dr. [redacted] was previously found in compliance with Plant BL1 requirements (i.e. the control of undesirable species in the greenhouse chambers) on previous OEHS lab inspections.

Dr. [redacted] Protocol (#06-25)
Title: "Generation of Adenovirus for Knockdown and Over Expression of p115."
Description: Dr. [redacted] will utilize a defective adenoviral vector to over express and knockout the gene for p115, a protein related to Macrophage Migration Inhibitory Factor 1 secretion.
Comments: Dr. [redacted] lab has prior work experience with retroviral vectors at BL2 containment. Dr. [redacted] laboratory has not utilized an adenoviral vector previously. The lead researcher will be provided with hands on training by an experienced colleague in an approved laboratory. The OEHS Safety Advisor has conducted the start up inspection to initiate the hands on training with the trainer and the lead researcher. Once both parties are comfortable with the training, the Safety Advisor will complete a follow-up inspection and observation of work practices for the lead researcher. Dr. [redacted] laboratory has previously been identified in compliance with BL2 requirements.

Dr. [redacted] Protocol (#06-27)
Title: "Role of Aging in Acute Vascular Injury"
Description: Dr. [redacted] has updated his experiments involving cell aging and vascular disease to add a defective adenoviral vector.
Comments: Dr. [redacted] and his staff have prior BL2 and BL3 authorization for biohazard research experiments and are in compliance with applicable OEHS training requirements. Dr. [redacted] cell culture laboratory has been inspected and found in conformity with BL2 requirements. The Safety Advisor has met with the lab group to review BL2 tissue culture requirements. All work in animals must also be approved by the Yale Institutional Animal Care and Use Committee (IACUC). A start up meeting with Biosafety, the Yale Animal Resources Center, and the lab staff is required prior to the initiation of any animal work.

Dr. [redacted] Protocol (#06-28)
Title: "Neurobiological Mechanisms of Cognitive Dysfunction in Psychiatric Disorders."
Description: Dr. [redacted] has amended her existing rDNA protocol utilizing HSV vectors to add the use of Adeno-Associated Virus vectors for both cell culture and animal experiments.
Comments: Dr. [redacted] has an established BL2 cell culture and animal biosafety protocol for these experiments through her prior research protocols with HSV. Researchers in her laboratory have prior experience handling BL2 agents at this containment level. As the new vector is being added, the Biosafety Office will schedule a meeting with the lab to review BL2 cell culture safety precautions. All work in animals must be approved by the Yale IACUC. A start up meeting with Biosafety, the Yale Animal Resources Center, and the lab staff is required prior to the initiation of any animal work.

Dr. [redacted] Protocol (#06-29)
Title: "Regulation of Gene Expression by a Novel Riboswitch in Rhizobium etli."
Description: Dr. [redacted] has submitted an update to his ongoing rDNA experiments. This project involves exempt cloning of genes from Rhizobium etli in E. coli as part of a study of vitamin synthesis.
Comments: Dr. [redacted] and his lab have prior BL1 containment experience and have completed applicable OEHS safety training classes. Dr. [redacted] laboratory and his work practices were previously found in conformity with BL1 requirements.

Dr. [redacted] Protocol (#06-30)
Title: "Effects of KRIT1 Expression in Retina."
Description: Dr. [redacted] will utilize a defective retroviral vector to deliver genes to the mouse retina to examine their role in angiogenesis and cell death.
Comments: Dr [redacted] and his lab staff have prior BL2 containment research experience and have completed required biosafety training. Dr. [redacted] cell culture lab has been inspected and found in compliance with BL2 requirements. The Biosafety Office will review BL2 cell culture precautions with the lead researcher prior to the initiation of the experiments. All work involving research animals must be approved by the Yale IACUC. A start up meeting with Biosafety, the Yale Animal Resources Center, and the lab staff is required prior to the initiation of any animal work.

Dr. [redacted] Protocol (#06-31)
Title: "Role of AdVEGF in Models of Angiogenesis."
Description: Dr. [redacted] has submitted an update to his existing approved protocol involving defective adenoviral vectors to add research with animals.
Comments: Dr. [redacted] and his staff have prior research experience with the vector system at BL2 containment and have completed relevant safety training courses. His group previously collaborated with Dr. [redacted] on these experiments with animals. The cell culture lab and work practices have been found in conformity with BL2 requirements. All work involving research animals must be approved by the Yale IACUC prior to initiation. A start up meeting with Biosafety, the Yale Animal Resources Center, and the lab staff is required prior to the initiation of any animal work.

The rDNA Protocols listed under new business on the 9/21/06 agenda were unanimously approved by the Committee as presented. Protocol #06-28 may be administratively approved by the Biosafety Office following a successful lab inspection. The rDNA meeting was adjourned at 9:42 AM. The next scheduled meeting will be held on October 19, 2006.

Respectfully submitted,

Benjamin Fontes
Biosafety Officer