SELECT AGENT RESEARCH

All [redacted] training program participants who will be working with select agents will be working under an approved IBC protocol. Upon approval of funding, grant project and IBC approval information will be provided at request. For [redacted] training program trainees and their program mentors whose research will involve recombinant DNA, the institutional policy is described below.

The Biological Safety Program at the [University] strives to adhere to the highest ethical standards in the protection of personnel and the environment. The safe use of recombinant DNA (rDNA), pathogenic microorganisms, and other infectious agents and toxins in research and teaching activities is ensured through compliance with federal regulations.

All research conducted by the training program participants and their mentors involving biohazardous agents, including infectious agents, select agents and toxins, must receive authorization by the Biohazard Committee (BHC) or Biosafety Manager prior to receiving the material or beginning work. Authorization by the BHC indicates compliance with Federal Regulation 42 CFR 73 related to Select Biological Agencies and Toxins as implemented by the Center for Diseases, Control and Prevention of the US Department of Health and Human Services. Information to be provided to the [University] BHC includes but is not limited to:

- Select Agent(s) to be used in the proposed research,
- Registration status of all entities where Select Agent(s) will be used,
- Procedures that will be used to monitor possession use and transfer of Select Agent(s), and
- Plans for appropriate biosafety, biocontainment, and security of the Select Agent(s).

Policy on Research Involving Recombinant DNA

All research involving Recombinant DNA (rDNA) must be approved by the Institutional Biosafety Committee (IBC). The IBC is responsible for reviewing this research to insure compliance with the NIH Guidelines for Research Involving Recombinant DNA Molecules and University policy.

Definition of Recombinant DNA Molecules
As defined in the Guidelines, recombinant DNA molecules are either (1) molecules which are constructed outside living cells by joining natural or synthetic DNA segments to DNA molecules that can replicate in a living cell, or (2) DNA molecules that result from the replication of those described in (1) above.

Containment Levels
As outlined in the Biosafety in Microbiological and Biomedical Laboratories manual, containment is described as the use of safe methods for managing infectious agents in the laboratory environment where they are being handled or maintained. The three elements of containment include laboratory practice and technique, safety equipment, and facility design.

There are four different levels of physical containment designated as Biosafety levels (BL) 1 through 4, which consist of combinations of laboratory practices and techniques, safety equipment, and laboratory facilities appropriate for the operations performed and the hazard posed by the infectious agents and for the laboratory function or activity. These levels are fully described in the NIH Guidelines.

Instructions and Forms for Research Submissions
Research applications are submitted to the Institutional Biosafety Committee (IBC) for review and approval of those research projects that it finds are in conformity with the Guidelines. The convened IBC meets monthly to review new full Committee submissions. Exempt registrations and transgenic/knockout rodent submissions are not reviewed by the convened IBC; rather, they are forwarded to members of the IBC for review and approval on an ongoing basis. This review includes: a) an independent assessment of the containment levels; b) an assessment of the facilities, procedures, practices, and of the training of

personnel working with recombinant DNA. Principal investigators are notified in writing of the results of these reviews.

Committee Actions
The Committee may take one of the following actions regarding proposed research:

a) Final Approval - For applications which fall under Section III-E of the NIH Guidelines, the PI may initiate the research simultaneous to submission of the IBC application. For all other research, the PI may commence the research only after receiving written approval indicated by a signed copy of the last page of the research application with a cover letter outlining the additional responsibilities for conducting research at the university. Note that animal resource center will not allow investigators to order or house transgenic or knockout rodents without prior IBC approval.

b) Provisional Approval - The PI must respond to provisions requested by the Committee and receive final approval prior to initiating the research.

c) Tabled - Deferred for consideration at a subsequent meeting after the PI has responded to significant modifications requested by the Committee.

d) Disapproved - The PI will be notified in writing of reasons for disapproval.

Upon completion of the review, the investigator will receive a formal response from the IBC. Any questions raised by the Committee must be responded to within sixty (60) days (provisionally approved or tabled studies). No work may be initiated until final approval is received from the IBC, unless the research falls under Section III-E of the NIH Guidelines, and may be initiated simultaneous with IBC submission.

Responsibilities of the Investigator

Compliance
The PI is responsible for complying fully with the NIH Guidelines and [University] policy in conducting any recombinant DNA research.

Laboratory Safety Procedures
A description of laboratory procedures is required; however, the procedures are incorporated into the various IBC forms to facilitate the application process. BL1 and BL2 safety procedures information sheets are available on the RCA website. Investigators are required to report any significant problems or violations of the NIH Guidelines and any significant research-related accidents or illnesses to the Biosafety Officer, IBC, and the NIH Office of Biotechnology Activities (OBA) within 30 days.

Amendments and Continuing Reviews
Any change in an approved protocol must be submitted in writing by the principal investigator and receive written approval by the IBC prior to the initiation of the change. If the proposed change is in support of a different set of outcomes or objectives than those previously approved by the IBC, a new research submission should be prepared for review.

Changes considered minor (no increase in risk or Biosafety Level) will be reviewed on an expedited basis by an IBC reviewer. In this case, the IBC/BHC Amendment form and any necessary supporting documentation are to be submitted for review.

Changes considered major (increased risk or Biosafety Level) will be reviewed by the full Committee in a convened meeting. In this case, the IBC/BHC Amendment form, an updated IBC Protocol Submission form, and any necessary supporting documentation are to be submitted for review.

Note that any amendment may be brought for full Committee review upon recommendation from the IBC reviewer. A status report must be filed with the IBC on an annual basis for all non-exempt research

projects. RCA will generate these Continuing Review reports for completion. This form must be completed even if the study was never initiated or was terminated for any reason. Exempt and transgenic/knockout rodent experiments must be reviewed at the time of competitive grant renewal.

5-Year Resubmission Policy

To ensure the IBC has the most current information when reviewing studies, and to remain in line with NIH resubmission requirements, the IBC has established a 5-year re-review policy for ongoing studies that have been approved at BL1 or higher. This policy requires PIs to submit a new application to the IBC after 5 years of approval. Studies currently in progress that have reached or exceeded the 5-year duration will be granted approval for only 6 months at the time of continuing review. The investigator must subsequently file a new application with the IBC within this 6-month time frame. When a new application is received by the IBC, it will be assigned a new study number and reviewed by the full Committee. It is strongly recommended that the new application be submitted to the IBC within 60 days of the study's review date. By submitting the study in this time frame, delays will likely be avoided so that the project's approval does not lapse or expire. If no new application is received by the IBC within the 6-month period, the study's approval will indeed expire, and thus, the study will be terminated.

File Maintenance

It is important for the investigator to keep a copy of every document related to the research study which is submitted the Committee. These documents must be kept for at least three (3) years after terminating the study. RCA will NOT be responsible for duplicating any information submitted to the Committee.

Research Conducted at Other Campuses or Institutions

Proposal Routing and Protocol Review Procedures

Research studies are normally reviewed on a campus specific basis, except for the [redacted]. All [redacted] protocols, including the Regional Centers for Medical Education, will be reviewed by the [University] IBC. Campus specific is defined as the campus where the faculty applicant is located. Other variables may require that a decision to modify their normal procedure be made by the campus research administration offices representing the campuses involved.

Research Conducted at Other Institutions

If it is anticipated that the research may be conducted at another site or that another institution may be involved in the research, it is the investigator's responsibility to obtain permission to involve other sites by providing the appropriate individuals or campus IBC with the local IBC approval, as well as a copy of the research submission which outlines the proposed research activities.

Human Gene Therapy

Investigators are required to submit research applications to both the IBC and the Institutional Review Board (IRB) for experiments which involve gene therapy with human subjects. In addition, the Food and Drug Administration (FDA) must also review and approve experiments involving drug and biological products for use in gene therapy for human subjects, regardless of whether the project is federally funded. A research proposal for NIH will be considered by the NIH Recombinant DNA Advisory Committee (RAC) only after the protocol has been approved by the university IBC in accordance with DHHS Regulations for the Protection of Human Subjects (45 Code of Federal Regulations, Part 46). IRB review may occur before or after RAC review.

If the proposal involves children, special attention should be given to the regulations noted above. The IRB and IBC may, at their discretion, condition their approval on further specific deliberation by the RAC. Serious Adverse Event reports occurring during the conduct of the study must be submitted to the Biosafety Committee as well as the OBA.