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## **I. GUIDELINES FOR STUDIES INVOLVING RECOMBINANT DNA MOLECULES**

### **A. POLICIES AND PROCEDURES:**

The Guidelines for Research Involving Recombinant DNA Molecules issued by the Department of Health and Human Services (DHHS), National Institutes of Health (NIH) May 7, 1986 have been adopted as the standard for such studies at the Medical University of South Carolina (MUSC). The MUSC Policies and Procedures and the NIH Guidelines apply to all studies involving recombinant DNA molecules which are conducted by or under the direction of a MUSC investigator using University facilities, or involving University funds (including extramural funds administered by the University) and regardless of location of the work site. Approval and/or notification of the IBC is required prior to initiation of all research programs involving recombinant DNA molecules, except those experiments exempted by the NIH.

In the context of these Guidelines, recombinant DNA molecules are defined as either:

- (i) 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-
- (ii) DNA molecules that result from the replication of those described in (i) above.

### **B. APPLICATION FOR APPROVAL OR REGISTRATION:**

All research programs at MUSC involving recombinant DNA molecules, except those categories of research specifically exempted by the NIH Guidelines, require either approval by or registration with the Institutional Biosafety Committee (IBC). Approval or registration is required regardless of whether the research program is funded by an agency requiring such certification or not. All new, continuation, or renewal applications involving non-exempt recombinant DNA molecules submitted to the Office of Research and Sponsored Programs should be accompanied by the approval from the IBC. Approval from or notification of the IBC is also required whenever investigators initiate or significantly change research involving recombinant DNA molecules under existing grants or contracts.

To comply with institutional policies for studies involving recombinant DNA molecules, the Principal Investigator must submit to the Biosafety Committee a Recombinant DNA Registration Document (Appendix I) addressing the following points:

- source(s) of DNA;
- nature of inserted DNA sequences (including identification by name of the biological source);
- host(s) and vector(s) to be used;
- statement whether a deliberate attempt will be made to obtain expression of a foreign gene, and, if so, what protein will be produced;
- containment conditions as specified by the current NIH Guidelines;
- if applicable, information on medical surveillance; and,
- a signed statement that the Principal Investigator is familiar with the current NIH Guidelines and agrees to abide by their provisions, including a statement that the recombinant DNA molecules being used will not be transferred to other investigators or institutions unless their facilities and techniques have been assured to be adequate.

The Principal Investigator has the continuing responsibility to consider whether there is any reason that an increase in biocontainment practices or facilities may be appropriate in any ongoing program approved by the IBC. Should he/she perceive the need for any such increase, the investigator has the responsibility to notify the IBC and to institute the appropriate increases in the level of biocontainment. In contrast, the biocontainment practices and facilities approved by the IBC may not be decreased without prior approval by the IBC and by the funding agency and/or NIH/Office of Recombinant DNA Activities(ORDA) provided that such approval is required.

## C. ROLES AND RESPONSIBILITIES OF THE PRINCIPAL INVESTIGATOR

The following section is adapted from the approved NIH Guidelines for Research Involving Recombinant DNA Molecules. The principles stated here apply to all studies at MUSC regardless of the source or type of funding. On behalf of MUSC, the Principal Investigator is responsible for complying fully with the MUSC Policy in conducting any recombinant DNA research.

### 1. General

The Principal Investigator shall:

- a. Ensure that IBC approval is obtained before initiating or modifying any research procedures which are classified as Class A or B according to the NIH guidelines (see Appendix I for classification descriptions);
- b. Notify the IBC of the use of research procedures which are classified as Class C experiments according to the NIH guidelines (see Appendix I for classification description);
- c. Report within 30 days to the IBC and to NIH (ORDA) all significant problems with and violations of the Guidelines and all significant research-related accidents and illnesses;
- d. Report to the IBC and to NIH (ORDA) new information bearing on the Guidelines;
- e. Be adequately trained in appropriate microbiological techniques;
- f. Adhere to IBC-approved emergency plans for dealing with accidental spills and personnel contamination; and,
- g. Comply with shipping requirements for recombinant DNA molecules. (See Appendix H of the Federal Register, May 7, 1986 for packaging and shipping requirements and the Laboratory Safety Monograph for Technical recommendations. The requesting laboratory must be in compliance with the NIH Guidelines and under appropriate review by its Institutional Biosafety Committee and the sending investigator must maintain a record of all shipments of recombinant DNA materials not exempt from the Guidelines.)

### 2. Submissions to NIH.

The Principal Investigator shall:

- a. Submit information to NIH (ORDA) with a copy to the IBC in order to have new host-vector systems certified;
- b. Petition NIH, with approval from the IBC, for exemptions to the NIH Guidelines (for additional information on procedures contact the IBC); and
- c. Petition NIH, with concurrence of the IBC for approval to conduct experiments specified in Section III-A of the May 7, 1986

## Guidelines.

### 3. Submissions to the IBC

The Principal Investigator shall:

- a. Make the initial determination of the required levels of physical and biological containment in accordance with the NIH Guidelines;
- b. Select appropriate microbiological practices and laboratory techniques to be used in the research;
- c. Submit the initial research protocol (if the research procedures are classified as Class A, B, or C) and subsequent changes (e.g., changes in the source of DNA or host-vector system, which require a new or revised Registration Document) to the IBC for review and approval or disapproval;
- d. Remain in communication with the IBC throughout the conduct of the project; and,
- e. Provide to the IBC, upon request, a complete copy of the grant application or other pertinent material on which the Registration Document is based.

### 4. Prior to Initiating the Research the Principal Investigator is responsible for:

- a. Making available to the laboratory staff copies of the approved protocols that describe the potential biohazards and the precautions to be taken;
- b. Instructing and training staff in the practices and techniques required to ensure safety and in the procedures for dealing with accidents; and,
- c. Informing the staff of the reasons and provisions for any precautionary medical practices advised or requested, such as vaccinations or serum collection.

### 5. During the Conduct of Approved Research the Principal Investigator is responsible for:

- a. Supervising the safety performance of the staff to ensure that the required safety practices and techniques are employed;
- b. Investigating and reporting in writing to the Office of Recombinant DNA Activities, the MUSC Biological Safety Officer, and the IBC any significant problems pertaining to the operation and implementation of containment practices and procedures;
- c. Correcting work errors and conditions that may result in the release of recombinant DNA materials, or other related hazardous materials, into the environment;
- d. Ensuring the integrity of the physical containment (e.g., purity, and genotypic and phenotypic characteristics); and,
- e. Publications  
Principal Investigators are urged to include, in all publications

reporting on recombinant DNA research, a description of the physical and biological containment procedures employed.

## II. GUIDELINES FOR STUDIES INVOLVING INFECTIOUS AGENTS

### A. POLICIES AND PROCEDURES

The recommendations contained in the Centers for Disease Control (CDC) publication Biosafety In Microbiological and Biomedical Laboratories, May, 1988 (NIH 88-8395), have been adopted by MUSC as the standard for working with infectious agents. This publication provides a description of the appropriate laboratory practices and physical containment associated with different classes of infectious agents. Investigators who use infectious agents in research and teaching must be familiar with current policies and practices for safe handling of hazardous organisms. Appendix II includes a listing of agents, classified on the basis of hazard, which should be consulted in assessing the level of biosafety required in the use of a particular agent.

These policies and procedures are designed to provide protection to laboratory personnel from possible exposure to the biological hazards involved in work with a particular organism. It is required that the responsible investigator in each laboratory advise all personnel on the hazards that will or may be encountered and those practices and procedures designed to minimize or eliminate risks associated with those hazards.

### B. APPLICATION FOR APPROVAL OR REGISTRATION

All research programs at MUSC involving infectious agents, except those involving only Class 1 organisms, require either approval by or registration with the Institutional Biosafety Committee (IBC). Approval or registration is required regardless of whether the research program is funded by an agency requiring such certification or not. All new, continuation, or renewal applications involving microorganisms (other than Class 1) which are submitted to the Office of Research and Sponsored Programs should be accompanied by the approval from the IBC. Approval from or notification of the IBC is also required whenever investigators initiate or significantly change research involving infectious agents under existing grants or contracts.

To comply with institutional policies for studies involving infectious agents, the Principal Investigator must submit to the Biosafety Committee an Infectious Agent Registration Document addressing the following points:

- classification of the agent, biosafety level available in the laboratory;
- whether or not laboratory animals will be infected with the agent;
- if applicable, information on medical surveillance; and,
- a signed statement that the Principal Investigator is familiar with the current NIH Guidelines and agrees to abide by their provisions, including a statement that the agents being used will not be transferred to other investigators or institutions

unless their facilities and techniques have been assured to be adequate.

The Principal Investigator has the continuing responsibility to consider whether there is any reason that an increase in biocontainment practices or facilities may be appropriate in any ongoing program approved by the IBC. Should he/she perceive the need for any such increase, the investigator has the responsibility to notify the IBC and to institute the appropriate increases in the level of biocontainment. In contrast, the biocontainment practices and facilities approved by the IBC may not be decreased without prior approval by the IBC and by the funding agency provided that such approval is required.

### C. ROLES AND RESPONSIBILITIES OF THE PRINCIPAL INVESTIGATOR

The principles stated here apply to all studies at MUSC involving infectious agents regardless of the source or type of funding. On behalf of MUSC, the Principal Investigator is responsible for complying fully with the MUSC Policy in conducting any research involving infectious agents.

#### 1. General

The Principal Investigator shall assure that:

- a. No research involving infectious agents requiring registration with and/or approval by the IBC is initiated unless it has met all of the requirements contained in this document.
- b. Appendix A has been consulted for appropriate classification of the involved microorganism and has determined that the prescribed procedures for that class are being followed.
- c. He/she will report immediately to the IBC all significant violations of the policies and practices and all significant research-related accidents which result in overt or potential exposure to infectious materials.
- d. He/she is prepared to implement methods for dealing with accidental spills and personnel contamination.
- e. Appropriate permits required by the USDA and/or the USPHS for work with certain animal and plant pathogens are obtained.
- f. Appropriate importation and interstate shipment requirements for biological materials are followed. PIs must maintain accurate records (log-book type) of Class 3 microorganisms transferred to other research sites.
- g. All personnel have appropriate training and information relative to the agents used in the laboratory. Laboratories where Class 2 or 3 agents are being studied shall be directly supervised by the P.I. or his/her designee. Laboratory personnel working with Class 1 agents must have standard training in microbiological practices to insure proper handling of the agent. Personnel working with Class 2 & 3 agents must also have specific training in handling pathogenic microorganisms, and individuals who work with Class 3 agents

must have specific training in handling potentially lethal agents. Procedures for handling Class 4 agents on the MUSC campus will be developed on a case-by-case basis.

- h. Competent medical advice has been sought before any person who is immunocompromised due to systemic corticosteroid therapy, chemotherapy for malignancies, radiation therapy, and/or certain diseases (e.g. lymphomas, leukemia, and AIDS) participates in research involving hazardous microorganisms. In addition, the P.I. is responsible for assessing any special risks to pregnant women working in the laboratory.

- 2. Prior to Initiating the Research the Principal Investigator shall:
  - a. Register all Class 2 agents with the IBC at the time a new project is begun (see Registration Document).
  - b. Obtain IBC approval for projects involving Class 3 or 4 agents.
  - c. Determine in consultation with the IBC and the MUSC Employee Health Physician the usefulness of serological screening, requirements for medical surveillance, and the availability at vaccination for certain Class 2 and 3 agents. Inform laboratory staff of the reasons and provisions for any precautionary medical practices advised or requested, such as vaccination or serum collection. MUSC has specific policies which apply to laboratories where procedures involve the concentration of HIV.
  - d. Communicate to the IBC protocol changes which substantially modify the research procedure upon which approval was originally based.
  - e. Provide the IBC, upon request, with a complete copy of the grant application or other pertinent material on which the IBC approval may be based.
  - f. Assure that personnel working with infectious agents or biohazardous materials are appropriately trained so that they are aware of the hazards and are proficient in the practices and techniques required for safe handling of such materials.
- 3. During the Conduct of the Research the Principal Investigator shall:
  - a. Supervise the performance of the staff to ensure that the required safety practices and techniques are employed.
  - b. Investigate and report in writing to the IBC any significant biosafety problems pertaining to the pursuit of the research goals. The P.I. is responsible for correcting any conditions that might release biohazardous materials into the environment.
  - c. Implement the procedures prescribed for dealing with laboratory accidents.
  - d. Assess regularly the biological characteristics of the

microorganisms used in experiments. Such assessment should include the purity and phenotype of the strain. Special restrictive characteristics such as attenuation require regular surveillance.

- e. Assure that biological safety cabinets, and other equipment used to prevent exposure to hazardous microorganisms, are properly serviced and functioning appropriately.

### III. THE INSTITUTIONAL BIOSAFETY COMMITTEE

#### A. COMPOSITION

1. The IBC shall comprise no fewer than five members so selected that they collectively have experience and expertise in: recombinant DNA and infectious agents technology ; the capability to assess the safety of the research experiments; and , the capability to assess any potential risk to public health or the environment. The committee shall include two individuals whose only affiliation with MUSC is membership on the IBC and who shall represent the interest of the surrounding community with respect to health and the protection of the environment. The Biological Safety Officer shall be a member of the Committee.
2. Members are to be appointed by the designated university official for a term of three years. Members may succeed themselves.
3. A quorum is 51% of the Committee membership.
4. No member of the IBC may be involved except to provide information requested by the IBC in the review or approval of a project in which he/she has been, is, or expects to be engaged or in which he/she has a financial interest.

#### B. IBC FUNCTION

The Chairperson or his/her designee may use his/her expertise in assigning the review of the Registration Document to a subcommittee selected from the duly-appointed IBC. If the study is reviewed by the subcommittee without reservations, the Chairperson may sign the Approval Notice. In addition, should the study be approved unanimously by the subcommittee, the Chairperson has the prerogative to subject this study to review by the full committee. If the subcommittee has comments which require changes, these requested changes are transmitted to the Principal Investigator or the Principal Investigator is invited to appear before the full Committee at their regular meeting to justify his/her position. In case of a potential disagreement between the Committee and the Principal Investigator, the Chair has the prerogative to consult an independent (ad hoc) advisory source of peers. Additionally, in the case of potential conflicts of interest, an independent (ad hoc) advisory members may be appointed, as deemed necessary by the Chair to provide expertise in the subcommittee review.

The IBC review shall include but not be limited to:

1. Assessment of the containment levels for the proposed project;
2. Assessment of the facilities, procedures, and practices, and the training and expertise of the personnel performing the research;
3. Notification of the Principal Investigator of the results of the review;
4. Determination of appropriate containment as specified by the Guidelines, or as deemed necessary;
5. Annual review of the research being conducted;
6. Adopt emergency plans covering accidental spills and personnel contamination resulting from such research; and
7. Report within a reasonable time frame to the appropriate institutional official and to the NIH Office of Recombinant DNA Activities (RAG) (if applicable) any significant problems with or violations of the Guidelines, and any significant research related accidents or illnesses, unless it has been determined that the Principal Investigator has done so.

### C. FACILITY INSPECTIONS

The BioSafety Officer or his/her designee will conduct initial inspections in order to assist Principal Investigators and their coworkers to maintain and use safe conditions and procedures in recombinant DNA research. Additional persons not from the IBC may be included in the inspection as advisors as necessary.

The results of the inspection shall be brought to the immediate attention of the Principal Investigator and reported to the Chair of the IBC, and deficiencies must be corrected as specified by the BSO. In addition, the BSO will arrange any further unscheduled facility inspections he/she deems necessary to determine compliance with the MUSC regulations. If the deficiencies are not corrected by subsequent inspections, the matter shall be brought to the attention of the IBC for further action.

Serious infractions which result in a reduced level of containment or present a serious hazard require immediate suspension of the experiments in progress and a report to the IBC. Experiments may continue only after the discrepancy has been corrected by the Principal Investigator, a written report to that effect has been received by the Chair of the IBC, and a follow-up inspection of the facility has taken place to assure that correction of the identified infraction(s) has been made. Furthermore, a statement of assurance must be included in the written report by the Principal Investigator on how to prevent the infraction from recurring. Any continuation of the experiments at non-permissible levels of containment will be reported concurrently to the Department Chair and

the designated Institutional Official for further action.

Reinspections will be conducted every two years by Occupational Safety and Health.

#### **IV. BIOSAFETY OFFICER RESPONSIBILITIES**

The Institution shall appoint a BSO who shall be a member of the MUSC Biosafety Committee, and whose duties shall include, but need not be limited to:

1. Ensuring through periodic inspections that laboratory standards are rigorously followed;
2. Reporting to the IBC and the Institutional Official or his/her designee all significant problems with and violations of the Guidelines and all significant research-related accidents and illnesses of which the BSO becomes aware unless the BSO determines that the Principal Investigator has done so;
3. Ensuring that each laboratory has emergency plans for dealing with accidental spills and personnel contamination, and investigating research laboratory accidents.
4. Providing advice on laboratory security;
5. Providing technical advice to the Principal Investigator and the IBC on research safety procedures.

#### **V. INSTITUTIONAL RESPONSIBILITIES**

Since, in all cases, grants/awards (gifts/endowments) are made to institutions rather than to individuals, all the responsibilities of the Principal Investigator listed above are also the responsibilities of the institution, fulfilled on its behalf by the Principal Investigator. In addition, the institution is responsible for establishing an Institutional Biosafety Committee and meeting the requirements as stated in the NIH Guidelines.

- A. DEANS, DEPARTMENTAL CHAIRPERSONS and ADMINISTRATIVE OFFICIALS shall provide the support to researchers which insures that appropriate facilities are available to control biological hazards, and to enable investigators to comply with pertinent campus policies.
- .B. The DIVISION OF LABORATORY ANIMAL RESOURCES at the request of the IBC shall assist in:
  1. Periodically inspecting areas where infectious agents are used in animal experiments.
  2. Training and instructing animal caretakers in recognizing the potential risks and utilizing special precautions when animals are infected with pathogenic organisms.
  3. Clearly posting and labeling all such animal rooms.

4. Overseeing contamination control with regard to excreta, animal carcasses and tissues, contaminated cages, cage bedding, and any other equipment or object which has come in contact with animals or their products.
- C. The MUSC EMPLOYEE HEALTH PHYSICIAN shall recommend appropriate medical surveillance and preventive programs for personnel using hazardous infectious agents when deemed necessary. These programs may involve:
1. Drawing of blood for serum testing and storage.
  2. Conducting clinical tests for diagnosis and therapy in the event of a laboratory acquired infection.
  3. Reporting immediately to the IBC the results of medical examinations performed as a result of a laboratory acquired infection or accidental exposure.
  4. Advising the IBC on an annual basis regarding new developments in relevant medical surveillance programs.
  5. Providing recommendations about immunization practices and the availability of vaccines.