C-5. RECOMBINANT DNA REGISTRATION PROGRAM

I. SCOPE

The recombinant DNA (rDNA) Registration Program is applicable to all Principal Investigators (PIs) at NCI-Frederick who conduct research involving rDNA molecules and rDNA experiments involving whole animals or plants, including the generation/use of transgenic animals or genetically engineered plants. The program also applies to any off-site PI who conducts research at the NCI-Frederick or utilizes rDNA shared services provided by the NCI-Frederick.

II. PURPOSE

The rDNA Registration Program is intended to protect the health and safety of NCI-Frederick employees, visitors to the facility, and the public as well as to ensure the protection of the environment. The rDNA Registration Program is designed to meet the requirements of the Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines current edition).

III. DEFINITIONS

Biological Safety Level (BSL) - Designates a combination of laboratory practices and techniques, safety equipment, and laboratory facilities designed to minimize the potential for exposure to pathogens, rDNA, and/or other biohazards. There are four Biosafety Levels (BSLs) that are designated in ascending order by degree of protection provided to personnel, the environment, and the community. BSL-1 provides the least stringent containment conditions and BSL-4 provides the most stringent.

Genome - Represents the entire genetic complement of a prokaryote or virus or the haploid genetic complement of a eukaryotic species, including eukaryotic gametes.

Guideline Classification - Is the method of categorizing rDNA experiments based on level of approval required, as defined in the NIH Guidelines.

IBC Number (IBC#) - Is the chronological number given to each new rDNA protocol that is reviewed and approved by the NCI-Frederick Institutional Biosafety Committee (IBC).

Institution - Is any facility using or creating rDNA molecules, rDNA techniques, or transgenic animals. The NCI-Frederick is typically the institution for this program.

Institutional Biosafety Committee (IBC) - Is a committee established to meet the requirements specified in Section IV-B-2 of the NIH Guidelines. It reviews, approves, and maintains rDNA protocol registrations. Membership of the committee will consist of no fewer than five individuals with experience and expertise in rDNA technology and other biosafety issues. At least two members will not be affiliated with the NCI-Frederick and should represent the surrounding community with respect to public health and protection of the environment. At least one member will have expertise in animal containment principles and one member will be the Biological Safety Officer (BSO). The IBC will be chaired by a senior member of the NCI-Frederick management.

Office of Recombinant DNA Activities (ORDA) - Is the office located at the NIH that is responsible for reviewing and coordinating all activities related to the NIH Guidelines for Research Involving Recombinant DNA Molecules.

Off-site PI - Is any investigator located at an institution other than NCI-Frederick who utilizes rDNA shared services offered by the NCI-Frederick and/or who conducts research at the NCI-Frederick in support of research conducted at his or her institution.

Principal Investigator (PI) - Is any investigator who conducts or oversees research involving rDNA molecules and is ultimately responsible for all aspects of the research conducted, including personnel safety and full compliance with the appropriate NIH Guidelines in the conduct of this research.

rDNA Experiments Involving Animals - Are experiments involving viable rDNA-modified microorganisms tested on whole animals.

Recombinant DNA (rDNA) Molecules - Are molecules that are (1) constructed outside living cells by joining natural or synthetic DNA segments to DNA molecules that can replicate in living cells or (2) result from the replication of those molecules described in (1).

Transgenic Animals - Are animals whose genome has been altered by the stable introduction of rDNA or DNA derived from rDNA into the germline. This includes animals derived from embryonic stem (ES) cells, especially when modified by homologous recombination.

IV. RESPONSIBILITIES

A. General

All significant rDNA research-related problems, violations of the NIH Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines) and/or any significant rDNA research-related accident and/or illness will be reported in a timely manner according to the following schedule:

1. The NCI-Frederick will report to NIH/ORDA within 30 days.

2. The IBC will report to the NCI-Frederick.

3. The BSO will report to the IBC.

4. The PI will report to the Biological Safety Officer (BSO).

5. The employee will report to the PI.

B. The NCI-Frederick is responsible for:

1. Ensuring that rDNA research is conducted in full conformity with the provisions of the NIH Guidelines.

2. Establishing and implementing policies that provide for the safe conduct of rDNA research.

3. Establishing an IBC.

4. Appointing a Biological Safety Officer (BSO).

5. Assisting with and ensuring compliance of the NIH Guidelines by the PIs conducting research at the Institution.

6. Ensure that the IBC, BSO, PIs and laboratory personnel have appropriate training regarding laboratory safety and implementation of the NIH Guidelines.

7. Determining the eligibility of health surveillance programs for personnel involved in rDNA research projects. This is a joint function of Occupational Health Services (OHS) and the Environment, Health and Safety Program (EHS).

8. Establishing and maintaining health surveillance programs for personnel by OHS.

C. The Institutional Biosafety Committee (IBC) is responsible for:

1. Reviewing rDNA research conducted at or sponsored by the NCI-Frederick for compliance with the NIH Guidelines. The review will include:

   a. Assessment of containment levels, independent of those designated by the PI.

   b. Assessment of the facilities, procedures, practices, training, and expertise of the personnel involved in research with rDNA molecules.

   c. Verification and assignment of the classification of rDNA research in accordance with the NIH Guidelines.

2. Notifying the PI of the results of the IBC review.

3. Providing for the adjustment of containment levels for experiments as specified in the NIH Guidelines.

4. Conducting annual reviews of rDNA research conducted at the NCI-Frederick for compliance with the NIH Guidelines.

5. Reviewing and approving emergency plans covering spills and personnel contamination for containment laboratories.

6. Providing an open forum for the discussion of biosafety concerns and assisting in the resolution of any biosafety issues brought before the Committee.

D. The Biological Safety Officer (BSO) is responsible for:

1. Ensuring that periodic (at least annual) inspections of laboratories are conducted to verify that laboratory standards are rigorously followed.

2. Providing guidance to the IBC and the PI in developing emergency plans for handling spills and personnel exposures and investigating laboratory accidents involving rDNA molecules.

3. Providing advice regarding laboratory security.

4. Providing technical advice to PIs and the IBC on research safety.

E. The Principal Investigator (PI) is responsible for:

1. Ensuring that he or she will not initiate or modify any rDNA research without documented IBC approval.

2. Ensuring appropriate follow-up of any significant problems with or violations of the NIH Guidelines or any significant research-related accidents or illnesses that were reported to the BSO.

3. Reporting any new information bearing on the NIH Guidelines to the BSO.

4. Providing laboratory personnel with adequate training in good laboratory technique.

5. Developing laboratory-specific emergency plans for handling accidental spills and personnel exposure. (Reference Section B-1 “Emergency Response Procedures”, paragraph VIII.A “Spill Cleanup Procedures”.)

6. Complying with NCI-Frederick, State of Maryland and Federal shipping regulations.

7. Making initial determination of Biosafety Level (BSL) and NIH Guideline classification.

8. Selecting appropriate microbiological practices and laboratory techniques.

9. Submitting proposed research protocols and subsequent changes to the IBC for review and approval.

10. Providing relevant information (e.g., change of NIH Guideline classification or biohazard containment level) to the IBC throughout the duration of the protocol.

11. Making available to all laboratory personnel the standard operating procedures (SOPs) that describe the potential biohazards and precautions to be taken.

12. Instructing and training laboratory personnel in the practices and techniques required to ensure safety, including procedures for handling accidents and spills.

13. Maintaining written records to document safety and laboratory technique training of personnel.

14. Informing laboratory personnel of rationale and provisions of any health surveillance programs.

15. Supervising the performance of laboratory personnel to ensure that safety practices and techniques are followed.

16. Correcting work errors and conditions that may result in the release of or accidental exposure to rDNA material.

17. Ensuring the integrity of the physical (e.g., biological safety cabinets) and biological (e.g., purity and genotype) containment.

18. Complying with all data reporting requirements of the rDNA registration program (e.g., personnel updates and renewals).

F. Each employee is responsible for:

1. Complying with all established laboratory safety procedures and practices.

2. Reporting all unsafe work practices or conditions to his or her supervisor.

3. Reporting every accident or potential exposure to his or her supervisor, OHS, and EHS.

4. Wearing the appropriate personal protective equipment as established by his or her supervisor and established safety procedure.

V. PROCEDURES

A. Registration

1. The PI will obtain a rDNA Registration Form from Environment, Health and Safety Program (EHS), complete the form, and return it to the Executive Secretary of the NCI-Frederick IBC.

2. The PI will provide the NCI-Frederick IBC with a copy of laboratory safety SOPs and signatures of employees to document training in safe work practices.

3. Upon approval by the NCI-Frederick IBC, the PI is to use the approved IBC# assigned to his or her protocol when requesting any shared service offered by the NCI-Frederick.

B. Renewal and amendment of rDNA protocols

1. Each rDNA protocol is given an active IBC# for 3 years. A protocol is deactivated after 3 years and the PI is required to complete a new rDNA Registration Form to renew the registration. The renewal form is renumbered and reviewed/approved by the NCI-Frederick IBC.

2. For purposes of amending the protocol, the PI will inform the NCI-Frederick IBC, through its secretary, in writing, of any change in the status of the protocol.

C. Documentation

1. Proposed rDNA protocols are kept in a “pending” file maintained by the Biological Safety Office.

2. Upon approval, the original rDNA protocol is kept on file in the Biological Safety Office. A copy of the approved rDNA protocol is sent to the PI.

3. Employee training records (i.e., employee signatures from rDNA protocols) are maintained in the Biological Safety Office according to IBC#.

VI. **REFERENCES**

Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines) April 2002 or most current edition.