

C-4. Research Registration Program

I. Scope

The Research Registration Program is applicable to all Principal Investigators (PIs) at NCI-Frederick who conduct research involving human pathogens, oncogenes, biological toxins, blood, blood components, human cell lines, other potentially infectious material (OPIM), 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 shared services provided by the NCI-Frederick.

II. Purpose

The Research 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 Research Registration Program is designed to meet the requirements of the Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines current edition).

III. Definitions

Additional Initial Training - Training required for employees working in Hepatitis B Virus (HBV) and Human Immunodeficiency Virus (HIV) laboratories and production facilities without prior experience handling human pathogens, oncogenes, and toxins, per the OSHA BBP Standard.

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. There are no BSL-4 laboratories at National Cancer Institute-Frederick.

Biosafety Level 2* (BSL-2*) – Designates a laboratory that meets Biosafety Level 2 facility requirements (infrastructure building design) but is operated using BSL-3 practices, procedures, and/or equipment.

Blood - Human blood, human blood components, and products made from human blood.

Bloodborne Pathogens (BBP) - Microorganisms that are present in human blood and can cause disease in humans. These include, but are not limited to, HIV, HBV and HCV.

EHS – Environment, Health, and Safety Program.

Exposure Control Plan - A site-specific manual required by the OSHA Bloodborne Pathogen Standard (29CFR1910.1030) to describe institutional policies to prevent the transmission of bloodborne pathogens in the work setting.

Exposure Incident - A specific eye, mouth, other mucous membrane, non-intact skin, or parenteral contact with blood or other potentially infectious materials that results from the performance of an employee's duties.

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 - The method of categorizing rDNA experiments is defined in the NIH Guidelines.

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

Institution - Any facility using or creating rDNA molecules, rDNA techniques, transgenic animals, pathogens, toxins, or OPIM. 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 all protocols. 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.

Occupational Exposure - Reasonably anticipated skin, eye, mucous membrane, or parenteral contact with blood or other potentially infectious materials that may result from the performance of an employee's duties.

Office of Biotechnology Activities (OBA) - 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 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.

Other Potential Infectious Material (OPIM) - 1) The following human body fluids: semen, vaginal secretions, cerebrospinal fluid, synovial fluid, pleural fluid, pericardial fluid, peritoneal fluid, amniotic fluid, saliva in dental procedures, any body fluid that is visibly contaminated with blood, and all body fluids in situations where it is difficult or impossible to differentiate between body fluids; 2) Any unfixed human tissue or organ (other than intact skin); and 3) HIV-containing cell or tissue cultures, organ cultures, and HIV- or HBV-containing culture medium or other solutions; and blood, organs, or other tissues from experimental animals infected with HIV or HBV.

Principal Investigator (PI) - Any investigator who conducts or oversees the research 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.

Production Facility - Facility engaged in industrial-scale, large-volume (>10L), or high- concentration production of HIV or HBV.

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).

rDNA Experiments Involving Animals - Experiments involving viable rDNA-

modified microorganisms tested on whole animals.

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 research-related accident and/or illness will be reported in a timely manner according to the following schedule:

1. The employee will report to the PI.
2. The PI will report to the Biological Safety Officer (BSO).
3. The BSO will report to the IBC.
4. The IBC will report to the NCI-Frederick.
5. The NCI-Frederick will report to NIH/OBA within 30 days, or immediately upon notification of the incident, when required.

B. The NCI-Frederick is responsible for:

1. Ensuring that 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 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 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 all 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.
 - c. Verification and assignment of the classification of 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 periodic reviews of 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. EHS is responsible for:

1. Maintaining a current registry to include SOPs, inspection reports, and approved registration forms for work with human pathogens, blood, oncogenes, toxins, OPIM, and rDNA.
2. Maintaining training records in accordance with the OSHA Bloodborne Pathogen Standard.
3. Assigning a Biosafety Level for all registered laboratories, biocontainment level – replace all per SMBL guidance.
4. Identifying all personnel on a registered program for enrollment in appropriate medical surveillance program(s) in conjunction with OHS.
5. Working with OHS on all accident investigations involving potential biological hazard exposure incidents.
6. Providing initial and annual refresher bloodborne pathogen training.
7. Providing technical advice to PIs and the IBC on research safety.
8. Ensuring that annual inspections of laboratories are conducted to verify that laboratory standards are followed.
9. Providing guidance to the IBC and the PI in developing emergency plans for handling spills and personnel exposures and investigating laboratory accidents involving potentially hazardous research material.
10. Providing advice regarding laboratory security.

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

1. Ensuring that he or she will not initiate or modify any research without documented IBC approval.
2. Ensuring all laboratory employees are adequately trained per requirements of OSHA Bloodborne Pathogen Standard 29 CFR 1910.1030(g)(2)(ix) “Additional Initial Training for Employees in

HIV and HBV Laboratories and Production Facilities” and that these employees attend annual Bloodborne computer-based Pathogen Training required by EHS..

3. 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.
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. Developing and providing to EHS a standard operating procedure (SOP) for all work conducted at BSL-2, BSL-3, or BSL-2*.
7. Complying with NCI-Frederick, DOT and IATA shipping regulations.
8. Making initial determination of Biosafety Level (BSL) and NIH Guideline classification.
9. Selecting appropriate microbiological practices and laboratory techniques.
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. Maintaining written records to document safety and laboratory technique training of personnel.
13. Informing laboratory personnel of rationale and provisions of any health surveillance programs.
14. Supervising the performance of laboratory personnel to ensure that

safety practices and techniques are followed.

15. Correcting work errors and conditions that may result in the release of or accidental exposure to rDNA material.
16. Ensuring the integrity of the physical (e.g., biological safety cabinets) and biological (e.g., purity and genotype) containment.
17. Contacting Manager, OHS to arrange for any vaccinations or medical surveillance programs.

F. Supervisors are responsible for:

1. Reporting to the PI , OHS, and EHS all biological spills and potential exposure incidents.
2. Assisting EHS and OHS in the investigation of potential exposure incidents.
3. Reviewing lab SOPs and IBC registration forms with laboratory employees and ensuring employees understand them.
4. Conducting weekly ventilation checks for airflow direction.
5. Ensuring that all employees with occupational exposure to BBP are enrolled in the BBP program within 10 days of beginning work or initial work assignment.

G. Each employee is responsible for:

1. Complying with all safety procedures and practices as established within the laboratory and by EHS and the IBC.
2. Reporting all unsafe work practices or conditions to his or her supervisor as established within the laboratory and by EHS and the IBC.
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.

5. Attending annual Bloodborne Pathogen Training and other safety training programs.

V. Procedures

A. Registration

2. The PI will obtain a research Registration Form from Environment, Health and Safety Program (EHS), complete the form, and return it to the IBC Administrator. This can be found at <http://web.ncifcrf.gov/ehs/ibc>
3. The PI will provide the NCI-Frederick IBC with a copy of laboratory safety SOPs specific to their laboratory and signatures of employees to document training in safe work practices.
4. EHS, via the IBC Administrator, assigns each registration a number and reviews the registration for completeness prior to sending out to the IBC for review.
5. Once the IBC registration has been approved, appropriate medical surveillance will be assigned and each person checked for the corresponding training. After training is confirmed, the individual is added to the appropriate medical surveillance program.
6. EHS, via the IBC Administrator, will send a memo and a copy of the approved registration to the PI acknowledging IBC approval. The PI is to use the approved IBC# assigned to his or her protocol when requesting any shared service offered by the NCI-Frederick.
6. A PI who is responsible for BSL-2*/BSL-3 facilities shall:
 - a. Provide program-specific additional initial training for each BL-2*/BSL-3 employee within 6 months after their start date. OSHA's bloodborne pathogen standard requires that proficiency in handling human pathogens or tissue culture be demonstrated to the employee's supervisor. This is especially critical for individuals that have limited or no experience in handling human pathogens. The Program will document this training. Additional Initial Training forms

available from EHS or equivalent departmental forms may be used. The forms should document:

- i. That the PI has given the employee additional instruction regarding standard microbiological practices and handling human pathogens, or
- ii. That an exemption is requested because of previous education and/or on-the-job training.

B. Renewal and amendment of research protocols

1. Each protocol is given an active IBC# for 3 years. The PI is required to complete a new Research Registration Form to renew the registration. The renewal form is issued a new number upon review/approval by the NCI-Frederick IBC, and the original IBC # is de-activated.
2. For purposes of amending the protocol, the PI will inform the NCI-Frederick IBC, through the BSO or IBC Administrator, of any change in the status of the protocol. The amendment request must be made in writing.

C. Documentation

1. Proposed research protocols are kept in a "pending" file maintained by the IBC Administrator.
2. Upon approval, the original protocol and electronic files are maintained in the Biological Safety Office, EHS. A copy of the approved protocol is sent to the PI.
3. Employee training records (i.e., employee signatures from protocols) are maintained in the EHS, OHM system, noting IBC # in comments column, according to IBC#.

D. Bloodborne Pathogen Training

1. Initial Bloodborne Pathogen Training is provided by EHS upon the supervisor's request for all new employees covered by the NCI-Frederick Exposure Control Plan. Work with human pathogens

such as, HIV & HBV, or agents requiring BSL-2*/BSL-3 containment or practices is prohibited until this training has been completed.

2. Annual Bloodborne Pathogen Training in compliance with federal mandates is scheduled and provided by EHS. Completion of annual refresher training is required by any employee with occupational exposure to bloodborne pathogens or OPIM.

E. Accident Reporting

1. All potential exposure incidents shall be reported to OHS and the employee's supervisor immediately.
2. Refer to Sections B-2 Accident Reporting and C-6 Medical Surveillance.

VI. References

29 CFR 1910.1030 - OSHA Bloodborne Pathogen Standard.
Biological Safety in Microbiological and Biomedical Laboratories, current version.
Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines) current edition.
NCI-Frederick Bloodborne Pathogen Exposure Control Plan, current version.