

## C-4. Biological 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, select agents and large-scale work. 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 and contractor 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), the NCI-Frederick Institutional Biosafety Committee (IBC Charter, and the Biosafety in Microbiological and Biomedical Laboratories (BMBL)), 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 Occupational Safety and Health Agency (OSHA) Bloodborne Pathogen (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 NCI-Frederick.

**Biosafety Level 1 (BSL-1):** This level is suitable for work involving well-characterized agents that present minimal potential hazard to laboratory personnel and the environment and are not known to consistently cause disease in immunocompetent adult humans. BSL-1 laboratories are not necessarily separated from the general traffic patterns in the building. Work is typically conducted on open bench tops using standard microbiological practices. Special containment equipment or facility design is not required, but may be used as determined by appropriate risk assessment. Laboratory personnel must have specific training in the procedures conducted in the laboratory and must be supervised by a scientist with training in microbiology or a related science.

**Biosafety Level 2 (BSL-2):** This level builds upon BSL-1. BSL-2 is suitable for work involving agents that pose moderate hazards to personnel and the environment. This level differs from BSL-1 in that; 1) laboratory personnel have specific training in handling pathogenic agents and are supervised by scientists competent in handling infectious agents and associated procedures; 2) access to the laboratory is restricted when work is being conducted; and 3) all procedures in which infectious aerosols or splashes may be created are conducted in biological safety cabinets (BSCs) or other physical containment equipment.

**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.

**Guideline Classification** - The method of categorizing rDNA experiments as defined in the NIH Guidelines.

**IBC Number** - 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 appointed by the Operations Technical Support Project Officer (per the IBC Charter).

**NIH rDNA Guidelines** – The purpose of the NIH Guidelines is to specify practices for constructing and handling: (i) recombinant deoxyribonucleic acid (DNA) molecules, and (ii) organisms and viruses containing recombinant DNA molecules.

**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.

**Occupational Health Services (OHS)** – OHS provides comprehensive health services, emergency medical response and treatment for accidental injury or illness affecting NCI-Frederick employees.

**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) from a human or non-human primate (living or dead), or other animal treated with a vector; 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.
4. Any pathogenic microorganism.
5. Human cell lines.

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 biological materials.

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 immediately upon notification of the incident, when required.

##### B. The NCI-Frederick is responsible for:

1. Assuring that research is conducted in full conformity with the provisions of the NIH Guidelines and NCI-Frederick IBC Charter.
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 assuring compliance of the NIH Guidelines by the PIs conducting research at the Institution.
6. Assuring 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 OHS and EHS.
  8. Establishing and maintaining health surveillance programs for personnel by OHS.
- C. The IBC is responsible for:
1. Reviewing all research conducted at or sponsored by the NCI-Frederick for compliance with the NIH Guidelines per the IBC Charter. The review will include:
    - a. Assessment of containment levels, independent of those designated by the PI.
    - b. Evaluation 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.
  7. In the event of a containment breach, biological spill, or other situation with the potential for biological contamination, a meeting of the NCI-IBC may be convened, if appropriate, to discuss the plan for containment and elimination of the hazard, and to obtain the advice of consultants as needed.

- D. EHS is responsible for:
1. Maintaining a current registry to include SOPs, inspection reports, and approved registration forms for work with potentially hazardous biological materials.
  2. Assuring the implementation of the Bloodborne Pathogen Exposure Control Plan and maintaining training records in accordance with the OSHA Bloodborne Pathogen Standard.
  3. Assigning a biosafety/biocontainment level for all registered laboratories per BMBL (current edition) guidance.
  4. Identifying all personnel on a registered program for enrollment in appropriate medical surveillance program(s).
  5. Working with OHS on all accident investigations involving potential exposure(s) to biological hazards.
  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 according to the NIH Guidelines and BMBL, current edition.
  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 guidance regarding laboratory security requirements.
  11. Keep copies of SOPs signed by each employee in the IBC file.
  12. Maintain records of additional initial training provided by supervisors.

13. Conduct training programs to educate and implement methods for the safe handling of infectious agents and other biological materials.
  14. Assist investigators in laboratory design and selection of laboratory practices and engineering controls that assure a safe working environment.
- E. The PI/Supervisor is responsible for:
1. Register all work with human pathogens, human blood, or other potentially infectious materials, including human cell lines, recombinant DNA, and genetically modified animals with the IBC.
  2. Renew registrations every three years (modifications to previously approved registrations must be submitted to and approved by the IBC prior to commencement of modified activities or conditions.
  3. Assuring that he or she will not initiate or modify any research with potentially hazardous biological materials without documented IBC approval.
  4. Assuring 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 complete annual Bloodborne Pathogen computer-based training required by EHS. Assuring that all employees with occupational exposure to BBP are enrolled in the BBP program within 10 days of beginning work or initial work assignment.
  5. Assuring 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.
  6. Providing laboratory personnel with adequate training in good laboratory technique. Inform supervised employees listed on the PI's registration forms of the potential hazards associated with the use of infectious agents in the laboratory and how those hazards are mitigated using safe practices and procedures. Supervising the

performance of laboratory personnel to ensure that safety practices and techniques are followed. Maintaining written records to document safety and laboratory technique training of personnel. Notify the Biological Safety Office of any procedural or personnel changes in laboratories working with material covered under this policy. Instruct employees in safe laboratory practices and the use of engineering controls and personal protective equipment, and in the procedures for dealing with accidents involving infectious agents,

7. Developing laboratory-specific emergency plans for handling accidental spills and personnel exposure. Reporting to the PI, OHS, and EHS all biological spills and potential exposure incidents.
8. Developing and providing to EHS a standard operating procedure (SOP) for all work conducted with potentially hazardous biological materials. Making available to all laboratory personnel the standard operating procedures (SOPs) that describe the potential biohazards and precautions to be taken. Reviewing lab SOPs and IBC registration forms with laboratory employees and ensuring employees understand them. Provide the IBC with signed copies of the approved SOP for all personnel and the safe work practices and procedures for all employees in their labs; inform EHS of any changes in personnel status and/or protocols; and notify EHS of employee eligibility for medical surveillance.
9. Complying with NCI-Frederick, DOT and IATA shipping regulations.
10. Making initial determination of Biosafety Level (BSL) and NIH Guideline classification.
11. Selecting and implementing appropriate microbiological practices and laboratory techniques.
12. Providing relevant information (e.g., change of NIH Guideline classification or biohazard containment level) to the IBC throughout the duration of the registration via amendment requests. Notify the Biological Safety Office of any procedural or personnel changes in laboratories working with material covered under this policy.
13. Informing laboratory personnel of rationale and provisions of any health surveillance programs. Contacting Manager, OHS to

arrange for any vaccinations or occupational health medical surveillance programs.

14. Correcting work errors and conditions that may result in the release of or accidental exposure to rDNA material.
15. Assuring the integrity and operation of the physical (e.g., biological safety cabinets) and biological (e.g., purity and genotype) containment.
16. Assisting EHS and OHS in the investigation of potential exposure incidents.
17. Wearing the appropriate personal protective equipment as established by his or her supervisor and established safety procedure.
18. Attend required training as needed (EHS and IBC can facilitate in assessing the requirements).
19. Acquire the information needed to recognize and control infectious agents in the laboratory. Verify that all regulatory requirements for material acquisition, transfer, and use are completed and approved by the appropriate regulating entity.

F. 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 and/or PI 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. Completing annual Bloodborne Pathogen Training and other required safety training programs.

G. OHS is responsible for:

1. Implement medical surveillance programs.
2. Manage any potential laboratory exposures (in conjunction with EHS); and
3. Train affected individuals and groups on specific medical monitoring programs (in conjunction with EHS).

V. Procedures

A. Registration

1. 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.
2. 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 lab specific safe work practices.
3. 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.
4. 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.
5. 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 registration when requesting any shared service offered by the NCI-Frederick.
6. A PI who is responsible for production activities subject to the OSHA BBP standard 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. Amendment and Renewal of research protocols
1. 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.
  2. Each registration is given an active IBC number 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 number is inactivated.
- C. Documentation
1. Proposed research registrations are kept in a "pending" file maintained by the IBC Administrator.
  2. Upon approval, the original registration 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 are maintained in the EHS Occupational Health Manager (OHM) system, noting IBC number in comments column, according to IBC number.

#### 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 for 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. Near misses and all other health and safety concerns should be immediately reported to EHS at 301-846-1451.

#### 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.  
Frederick National Laboratory for Cancer Research Bloodborne Pathogen Exposure Control Plan, current version.