

Use of Recombinant DNA in Research and Teaching Laboratories

Policy 212

1 Introduction

1.1 Laboratories working with microorganisms and/or recombinant DNA technologies are special, often unique, work environments. The materials being used may pose risks to persons working in or near the laboratory or to the environment, should the material escape the laboratory. The University has therefore established an Institutional Biosafety Council (IBC) to promote the safe handling of recombinant DNA, appropriately assess potential risks, and reduce the chance of personnel exposure or accidental environmental release.

1.2 The Institutional Biosafety Council will review research involving the use of recombinant DNA molecules with the goal of ensuring that it is conducted safely and in compliance with guidelines established by the National Institutes of Health and the Centers for Disease Control. The IBC will work to protect the safety of the research for the university and general community by providing outreach, education and support for principle investigators and their staff.

2 Scope

2.1 This policy applies to all persons who perform research involving recombinant DNA molecules, as well as those whose job duties involve interactions with such persons in the course of their research.

3 Definitions

3.1 Recombinant DNA

Refers to novel “unnatural” DNA molecules that are constructed outside of living cells by joining natural or synthetic DNA segments to DNA molecules that can replicate in a living cell¹, or molecules that result from their replication. By definition recombinant DNA is chimeric, and the possibility for novel life forms of unknown toxicity or environmental hazard has been a concern since recombinant DNA technology was invented in 1973. Thus, recombinant DNA is considered a potential biohazard, and the National Institutes of Health (NIH) has mandated that institutions receiving NIH funds monitor and regulate its use.

3.2 Biohazardous Agents

In laboratory settings are organisms, or substances derived from organisms, that pose a threat to (primarily) human health, but also to certain animals and plants. Information on biosafety of biohazardous agents can be found in the Biosafety in Microbiological and Biomedical Laboratories (BMBL). In addition to some recombinant DNAs, biohazards, as broadly defined, include the following categories.

1. Infectious/pathogenic organisms, including certain bacterial, fungal, parasitic, viral, rickettsial or chlamydial agents, or other infectious/pathogenic agents having the potential for causing disease in healthy individuals, animals, or plants. (A list of infectious agents and their assigned biosafety level can be found in the CDC/NIH Guidelines).
2. Biological toxins including metabolites of living organisms and materials rendered toxic by the metabolic activities of microorganisms (living or dead).
3. Blood - Human blood, human blood components, and products made from human blood.
4. Other Potentially Infectious Materials - (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; and (2) Any unfixed tissue or organ (other than intact skin) from a human (living or dead).
5. Biological Select Agents and Toxins are highly controlled biological agents or toxins with potential as biowarfare agents, as listed by the Centers for Disease Control (CDC) and/or the USDA Animal Plant Health Inspection Service (APHIS). See <http://emergency.cdc.gov/agent/agentlist.asp> for more information

3.3 NIH Guidelines

Refers to the National Institutes of Health Guidelines for Research Involving Recombinant DNA Molecules.

4 Policy and Procedure Statements

4.1 Administration

4.1.1 The Institutional Biosafety Council (IBC)

4.1.1.1 The Institutional Biosafety Council (IBC) is responsible for reviewing and recommending policies and procedures with the goal of ensuring the safe use of recombinant DNA in research and teaching laboratories at Appalachian State University (ASU) and compliance with guidelines established by the National Institutes of Health (NIH) and the Centers for Disease Control.

4.1.1.2 In accordance with the NIH Guidelines, the IBC is responsible for the review, approval, and oversight of activities with recombinant DNA conducted at or sponsored by the University, regardless of the source of funding. The IBC works with the Office of Occupational Safety and Health and other applicable University departments and groups (e.g., Public Safety and Risk Management) with the goal of ensuring that activities with recombinant DNA are operating within the scope of University-wide safety and security initiatives.

4.1.1.3 The IBC shall consist of faculty, staff and community members with experience and expertise in recombinant DNA technology and biosafety and physical containment. In accordance with the NIH Guidelines, members should have knowledge of institutional policies, applicable laws, standards of professional conduct, community attitudes and environmental considerations. Members of the IBC and the Chair of the IBC shall be appointed by the Chancellor for two and three year terms. The composition of the membership of the IBC shall meet all membership requirements in the NIH Guidelines.

4.1.1.4 In order to conduct business, a quorum of the IBC must be present. A quorum of the IBC is defined as a simple majority of members present that have no conflicts of interest with the review of an activity.

4.1.2 The Office of Research Protections (ORP) and the IBC Administrator

4.1.2.1 The Office of Research Protections provides administrative support to the IBC, maintains the most current version of Appalachian's Policy on the Use of Recombinant DNA in Research and Teaching Laboratories, manages all IBC registration and reporting processes, maintains appropriate records, and serves as liaison with the NIH. The Director of Research Protections shall serve as the IBC Administrator. The IBC Administrator will work with the IBC to establish procedures to implement this policy.

4.1.3 Biosafety Officer

4.1.3.1 Most large research universities have a Biosafety Officer (BSO), whose duties typically involve facilitating the operation of the biosafety program, assuring that the use of biohazardous agents conforms to the University policy and applicable governmental regulations, conducting periodic inspections of biological laboratories, and providing biosafety training as needed. The responsibilities of this role are defined in the NIH Guidelines section IV-B-3a-c.

4.1.3.2 At its current level of biological research activity, ASU is not required by the NIH to appoint a Biosafety Officer (BSO). Various functions recognized as typical BSO responsibilities which cannot easily be met by the IBC are addressed by the Occupational Health and Safety Office. These include activities such as: assisting investigators in developing lab safety plans, conducting lab safety inspections, advising on personal protection equipment and assisting with incident response for exposures or spills/environmental release.

4.1.4 Principal Investigator or Laboratory Director

4.1.4.1 The Principal Investigator (PI) or Laboratory Director (for both teaching and research laboratories) working with recombinant DNA has the following responsibilities:

1. Registering recombinant DNA experiments with the IBC. The registration must be approved by the IBC or determined to be exempt before any work with recombinant DNA can be initiated. Researchers or lab directors who plan to use recombinant DNA are responsible for knowledge of the University's procedures.
2. Adhering to determinations of the IBC with respect to all work with recombinant DNA;
3. Assuming primary responsibility for the proper use, response to exposure or release incidents, handling and disposal of all biohazardous agents and recombinant DNA molecules associated with their research. ASU principal investigators and teaching/research personnel must comply with applicable Federal, State, local regulatory standards, and university safety and health policies and procedures as well as any administrative requirements established by ASU.
4. Instructing and training laboratory staff in the practices and techniques required to enhance safety and in the procedures for dealing with accidents;
5. Making available to all laboratory staff the protocols that describe the potential biohazards and the precautions to be taken;
6. Providing instruction regarding specific techniques for recombinant DNA research and dangers of materials to be handled;
7. Familiarizing his/her staff with the symptoms of exposure and other pertinent information about the biohazardous agent used in the experiment before allowing lab personnel to work with the agent;
8. Supervising the laboratory staff's safety performance with the goal of ensuring that the required safety practices and

- techniques are employed;
9. Informing the staff of the reasons and provisions for any precautionary medical practices advised or requested, such as immunization or serum collection;
 10. Providing personal protective equipment to all laboratory staff members based on the experimental procedures used in the lab and documenting this as required by OSHA and the ASU Office of Occupational Health and Safety Office;
 11. Maintaining written documentation of all training activities, which includes instruction in laboratory safety procedures, for all laboratory staff personnel;
 12. Investigating and reporting in writing to the IBC and the Office of Occupational Safety and Health any significant problems or incidents pertaining to the operation and implementation of containment practices and procedures;
 13. Correcting conditions that may potentially result in the release of biohazardous agents;
 14. Complying with shipping requirements for recombinant DNA molecules; (See Appendix H of the NIH Guide.)
 15. Having biosafety cabinets certified by an approved contractor on an annual basis, or when moved; and
 16. Implementing appropriate measures with the goal of ensuring compliance with other procedures established by the IBC and other university entities governing the use of biohazardous agents.
 17. Complying with annual reporting requirements and report within 30 days any problems related to containment practices to the Chairperson of the Institutional Biosafety Council;

4.1.4.2 In addition:

1. Investigators shall not possess nor permit the University to possess on their behalf any biological agents, toxins, or delivery systems that are inconsistent with the mission of the university.
2. BL3 and BL4 agents are not approved for use at ASU. Furthermore, the procurement and use of any agent designated by the Federal Government as a Select Agent is currently prohibited at ASU. Any ASU investigator desiring to initiate work with BL3 or Select Agents must contact the IBC and the Occupational Health and Safety Office for guidance.

4.2 The Review Process

4.2.1 Review of Activities with Recombinant DNA

4.2.1.1 The IBC will establish review procedures consistent with this policy and the NIH Guidelines. In some cases, the IBC may choose to establish a review procedure that is more stringent than that required by the NIH Guidelines. For example, the IBC may require review of research that is exempt from the NIH Guidelines.

4.2.1.2 The IBC will review recombinant DNA activities conducted at or sponsored by ASU for compliance with the NIH Guidelines as specified in Section III, Experiments Covered by the NIH Guidelines, and approve those research projects that are found to conform with the NIH Guidelines. IBC review will include: a. independent assessment of the containment levels required by the NIH Guidelines for the proposed research; b. assessment of the facilities, procedures, practices, and training and expertise of personnel involved in recombinant DNA research; c. implementing appropriate measures with the goal of ensuring compliance with all surveillance, data reporting, and adverse event reporting requirements set forth in the NIH Guidelines; and d. implementing appropriate measures with the goal of ensuring that the research does not involve human subjects in gene transfer trials as the IBC will not approve this research at this time.

4.2.1.3 Activities involving recombinant DNA that are not exempt from the NIH Guidelines will be reviewed at a convened meeting of the IBC. Members with a personal or financial interest in the activity will be recused. In addition, members with expertise to review the proposed activities must be present for the IBC to approve activities. For example, a member with expertise in plant, plant pathogens or plant containment principles must be present to approve experiments described in Appendix P of the NIH Guidelines.

4.2.2 Continuing Review

4.2.2.1 The IBC can approve activities with recombinant DNA for a period of one year or less. After activities with recombinant DNA have been approved by the IBC, it is the investigator's responsibility to report to the Council any proposed changes in the research as well as unanticipated problems that arise involving risk.

4.2.2.2 The NIH Guidelines require that the IBC perform continuing review of all ongoing activities with recombinant DNA that have been approved by the IBC. It is the principal investigator's responsibility to initiate the request for continuation, which must include a summary of the protocol and a status report on the progress to date. The continuing review of activities with recombinant DNA will be conducted in the same manner as the initial review of the protocol.

4.2.3 Training

4.2.3.1 All individuals engaged in activities with recombinant DNA must be adequately trained in good microbiological techniques. Principal investigators are responsible for training laboratory staff and students in the practices and techniques required to maintain safety and in the procedures for handling accidents. The IBC may mandate additional training.

4.2.4 Non-Compliance

4.2.4.1 If the IBC becomes aware of serious or continuing noncompliance with the determinations of the IBC, including ongoing research with recombinant DNA without IBC approval, the IBC may request a meeting with the PI and/or suspend the research until the problem can be further evaluated. Under these circumstances, the Chief Research Officer will be made aware of the situation immediately and advised of any further sanctions recommended by the IBC. In these circumstances, the IBC may impose sanctions on an individual by suspending the individual's right to conduct or supervise research involving recombinant DNA, and recommending discipline of a faculty member of the University. These sanctions are provided as examples and are not intended to be exhaustive; individual situations may call for specific actions and remedies not specified here.

4.3 Risk Assessment and Selection of Appropriate Safeguards

4.3.1 In order to establish appropriate safeguards for activities with recombinant DNA, the investigator will make an initial risk assessment based on the Risk Group (RG) of an agent (see Appendix B, of the NIH Guidelines: Classification of Human Etiologic Agents on the Basis of Hazard). Agents are classified into four Risk Groups (RGs) according to their relative pathogenicity for healthy adult humans: Risk Group 1 (RG1) agents are not associated with disease in healthy adult humans. Risk Group 2 (RG2) agents are associated with human disease which is rarely serious and for which preventive or therapeutic interventions are often available. Risk Group 3 (RG3) agents are associated with serious or lethal human disease for which preventive or therapeutic interventions may be available. Risk Group 4 (RG4) agents are likely to cause serious or lethal human disease for which preventive or therapeutic interventions are not usually available.

4.3.2 Biosafety Levels (BL) are categories for biocontainment precautions, based on levels of hazard, Level 1 being minimum risk and Level 4 being extreme risk. Various organisms and biohazardous materials are referred to as "BL1-BL4 agents", or sometimes as Class 1 through Class 4 agents. These BL-based categories are not to be confused with the "Risk Group" classification used by the NIH.

1. Biosafety Level 1 (BL1): Work involving minimal or no known hazard to laboratory personnel and the environment. Standard microbiological procedures are adequate and a biosafety cabinet is not required for personal protection (but may be used to protect the biological sample from contamination).
2. Biosafety Level 2 (BL2): Work involving agents of moderate potential hazard to personnel and the environment, requiring a type II biosafety cabinet for containment. Also applies to standard recommendations for handling human blood or body fluid specimens, as covered in the OSHA Bloodborne Pathogen Program standard.
3. Biosafety Level 3 (BL3): Work involving indigenous or exotic agents which may cause serious or potentially lethal disease as a result of exposure by the inhalation route. Requires additional containment practices and protective equipment beyond that used for BL2.
4. Biosafety Level 4 (BL4): Exclusively applies to viruses that cause severe to fatal disease in humans, that are easily transmissible by aerosols or contact entry, and for which vaccines or other treatments are not available. Requires the highest level of containment, unlikely to be attained in an academic research environment.

4.3.3 In order to determine the appropriate containment for an experiment, the initial risk assessment from the NIH Guidelines Appendix B should be followed by a thorough consideration of the agent itself and how it is to be manipulated. Factors to be considered in determining the level of containment include agent factors such as: virulence, pathogenicity, infectious dose, environmental stability, route of spread, communicability, operations, quantity, availability of vaccine or treatment, and gene product effects such as toxicity, physiological activity, and allergenicity. Any strain that is known to be more hazardous than the parent (wild-type) strain should be considered for handling at a higher containment level. Certain attenuated strains or strains that have been demonstrated to have irreversibly lost known virulence factors may qualify for a reduction of the containment level compared to the Risk Group assigned to the parent strain.

4.3.4 Experiments involving recombinant DNA lend themselves to a third containment mechanism, namely, the application of highly specific biological barriers. Natural barriers exist that limit either: (i) the infectivity of a vector or vehicle (plasmid or virus) for specific hosts, or (ii) its dissemination and survival in the environment. Vectors, which provide the means for recombinant DNA and/or host cell replication, can be genetically designed to decrease, by many orders of magnitude, the probability of dissemination of recombinant DNA outside the laboratory.

4.3.5 Careful consideration should be given to the types of manipulation planned for some higher Risk Group agents. For example, the RG2 dengue viruses may be cultured under the Biosafety Level 2 containment (see NIH Guidelines Section II-B); however, when such agents are used for animal inoculation or transmission studies, a higher containment level is recommended.

4.3.6 There are no laboratories at Appalachian State University certified to conduct BL-3 or BL-4 research. Biosafety levels are currently limited to BL-1 and BL-2. At this time, the IBC is not established to review research involving human gene transfer trials.

4.4 Emergency Procedures

An emergency or accident involving recombinant DNA will require varying degrees of action depending on the type and severity of the emergency. The initial handling of such an event rests with either the person directly involved or the person first alerted to

the situation. Much of what follows is of general applicability in any emergency.

4.4.1 Prepare Before an Emergency Occurs

4.4.1.1 Any faculty or staff member using recombinant DNA must become familiar with ASU emergency plans and policies. Information is available at <http://emergency.appstate.edu>, or by contacting the Office of Emergency Plans and Operations at x8081.

4.4.2 Evaluate the Emergency and Call for Help

4.4.2.1 The first person to observe the emergency should try to quickly estimate the severity of the situation and evacuate personnel from the immediate area. For larger emergencies, the first person to observe the emergency should utilize the nearest fire alarm pull station to initiate an evacuation of the building. One person must notify the University Police Department and/or fire department upon their arrival of the nature of the incident. The IBC Administrator (262-2130 or compliance@appstate.edu) and the facility/laboratory supervisor should be notified as soon as possible. Report all emergencies that threaten life or property to on-campus police at x8000.

4.4.3 Confine the Hazard

4.4.3.1 If possible, secure the area and stand by to provide information and assistance. Reduce the spread of contamination by limiting travel from the area and by checking shoes for contamination if practicable.

4.4.4 Protect Personnel

4.4.4.1 Warn other persons in the immediate vicinity and assist any persons who may be contaminated or injured. NOTE: Emergency action personnel who have been notified will take over after this first phase of the emergency. They will prescribe additional action to be taken and begin restoration to normal operating conditions.

4.4.5 Reporting

4.4.5.1 It is the responsibility of the faculty or staff member holding the registration to complete and submit a report on the accident to the IBC Administrator.

4.4.6 Injuries

4.4.6.1 Any time an employee's injury or overexposure requires medical evaluation or attention, the Workers' Compensation guidelines at www.hrs.appstate.edu must be followed.

5 Additional References

[Occupational Safety and Health Policy Statements](#)

[Office of Emergency Plans and Operations Policies and Guidance](#)

6 Authority

Guidelines for Research Involving Recombinant DNA Molecules

[Center for Disease Control publication, Biosafety in Microbiological and Biomedical Laboratories](#)

7 Contact Information

8 Original Effective Date

August 24, 2011

9 Revision Dates