

## Section 1 – Introduction

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### A. PURPOSE OF MANUAL

This manual has been prepared for the purpose of providing students, staff, and faculty at the University of Washington (UW) with information that is necessary to protect them and the surrounding community from possible hazards associated with the use of biohazardous agents and recombinant or synthetic DNA/RNA (recDNA) molecules. Refer to the [UW Radiation Safety Manual](#) and the [UW Laboratory Safety Manual](#) for additional laboratory safety guidelines.

## B. DEFINITION OF BIOHAZARDOUS AGENTS

For the purpose of this manual, potentially hazardous biological agents and by-products are called **biohazardous agents**. The UW IBC's working definition of a biohazardous agent includes the following:

- 1) Pathogenic agents (bacteria, rickettsia, fungi, viruses, protozoa, parasites, prions, and [Select Agents](#))
- 2) Recombinant or synthetically derived nucleic acid, including those that are chemically or otherwise modified analogs of nucleotides (e.g., morpholinos) or both. The NIH defines synthetically derived nucleic acid molecules as follows:
  - a. Molecules that (a) are constructed by joining nucleic acid molecules and (b) can replicate in a living cell (i.e., recombinant nucleic acids);
  - b. Nucleic acid molecules that are chemically or otherwise modified but can pair with naturally occurring nucleic acid molecules (i.e., synthetic nucleic acids);
  - c. Molecules that result from the replication of those described in (a) or (b) above
- 3) Recombinant DNA molecules, organisms, vectors (e.g., plasmids, viral vectors), and viruses containing recombinant DNA molecules
- 4) Human and non-human primate blood, tissue, body fluid, and cell culture (primary and established cell lines)
- 5) Plants, animals, or derived waste which contains or may contain pathogenic hazards (including xenotransplantation tissue)

This manual also includes guidelines for containment of biohazards to control the spread of contamination. The control practices contained in this manual are meant to supplement conventional safety efforts, including accident and fire prevention.

## C. THE OCCURRENCE OF LABORATORY-ASSOCIATED INFECTIONS

Research and clinical laboratories are work environments that pose unique risks to persons working in or near them. Personnel have contracted infections in the laboratory throughout history.

The following information on the occurrence of Laboratory-Associated Infections (LAIs) in clinical (diagnostic) and research laboratories is taken from Section I of the Centers for Disease Control and Prevention (CDC)/National Institutes of Health (NIH) publication, [Biosafety in Microbiological and Biomedical Laboratories \(BMBL\)](#).

Published reports of LAIs first appeared around the start of the twentieth century. By 1978, four studies by Pike and Sulkin collectively identified 4,079 LAIs resulting in 168 deaths occurring between 1930 and 1978. These studies found that the ten most common causative agents of overt infections among workers were *Brucella* spp., *Coxiella burnetii*, hepatitis B virus (HBV), *Salmonella typhi*, *Francisella tularensis*, *Mycobacterium tuberculosis*, *Blastomyces dermatitidis*, Venezuelan equine encephalitis virus, *Chlamydia psittaci*, and *Coccidioides immitis*. The authors acknowledged that the 4,079 cases did not represent all LAIs that occurred during this period since many laboratories chose not to report overt cases or conduct surveillance programs to identify sub-clinical or asymptomatic infections.

In addition, reports of LAIs seldom provided data sufficient to determine incidence rates, complicating quantitative assessments of risk. Similarly, there were no distinguishable accidents or exposure events identified in more than 80% of the LAIs reported before 1978. Studies did show that in many cases the infected person worked with a microbiological agent or was in the vicinity of another person handling an agent.

During the 20 years following the Pike and Sulkin publications, a worldwide literature search by Harding and Byers revealed 1,267 overt infections with 22 deaths. Five deaths were of fetuses aborted as the consequence of a maternal LAI. *Mycobacterium tuberculosis*, *Coxiella burnetii*, hantavirus, arboviruses, HBV, *Brucella* spp., *Salmonella* spp., *Shigella* spp., hepatitis C virus (HCV), and *Cryptosporidium* spp. accounted for 1,074 of the 1,267 infections. The authors also identified an additional 663 cases that presented as sub-clinical infections. Like Pike and Sulkin, Harding and Byers reported that only a small number of the LAI involved a specific incident. The non-specific associations reported most often by these authors included working with a microbiological agent, being in or around the laboratory, or being around infected animals.

The findings of Harding and Byers indicated that clinical (diagnostic) and research laboratories accounted for 45% and 51%, respectively, of the total LAIs reported. This is a marked difference from the LAIs reported by Pike and Sulkin prior to 1979, which indicated that clinical and research laboratories accounted for 17% and 59%, respectively. The relative increase of LAIs in clinical laboratories may be due in part to improved employee health surveillance programs that are able to detect sub-clinical infections, or to the use of inadequate containment procedures during the early stages of culture identification.

Comparison of the more recent LAIs reported by Harding and Byers with those reported by Pike and Sulkin suggests that the number of LAIs is decreasing. Harding and Byers note that improvements in containment equipment, engineering controls, and greater emphasis on safety training may be contributing factors to the apparent reduction in LAIs over two decades. However, due to the lack of information on the actual numbers of infections and the population at risk, it is difficult to determine the true incidence of LAIs with any degree of certainty.

Publication of the occurrence of LAIs provides an invaluable resource for the microbiological and biomedical community. For example, one report of occupational exposures associated with *Brucella melitensis*, an organism capable of transmission by the aerosol route, described how a staff member in a clinical microbiology laboratory accidentally sub-cultured *B. melitensis* on the open bench. This error and a breach in containment practices resulted in eight LAIs with *B. melitensis* among 26 laboratory members, an attack rate of 31%. Reports of LAIs can serve as lessons in the importance of maintaining safe conditions in biological research.

## **D. RULES, REGULATIONS, AND GUIDELINES GOVERNING USE OF BIOHAZARDS AND recDNA MOLECULES**

The following is a brief summary of the regulatory authorities that either regulate or provide guidelines for the use of biohazards.

### **1. NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules**

In the early 1970s the NIH established a committee to provide advice on recDNA technology. The [NIH Guidelines](#), which were announced on June 23, 1976, and which continue to be updated, established carefully controlled conditions for conducting experiments involving recDNA molecules. These guidelines describe the roles and responsibilities of the Institution, the IBC, and the Principal Investigator (PI).

### **2. CDC/NIH Biosafety in Microbiological and Biomedical Laboratories**

In 1984, the CDC and NIH published [BMBL](#). The publication was last updated in 2009 and provides specific descriptions of combinations of microbiological practices, laboratory facilities,

safety equipment, and recommendations for use in the four biosafety levels of laboratory operation with selected human infectious agents.

### 3. The Select Agent Rule

The CDC is required to regulate the possession of biological agents and toxins that have the potential to pose a severe threat to public health and safety. CDC's [Select Agent Program](#) oversees these activities. The Select Agent Program currently requires registration of facilities including government agencies, universities, research institutions, and commercial entities.

### 4. Washington Industrial Safety and Health Act

Under provisions of the [Washington Industrial Safety and Health Act \(WISHA\)](#), occupational safety and health standards are promulgated by the Department of Labor and Industries as chapters of the Washington Administrative Code (WAC). It is the intent of the UW to comply fully with the standards and regulations developed by the Department of Labor and Industries.

### 5. Bloodborne Pathogens Standard

[WAC 296-823, Occupational Exposure to Bloodborne Pathogens](#) is an extension of the Bloodborne Pathogens Standard promulgated by the Federal Occupational Safety and Health Administration (OSHA). It applies to staff with reasonably anticipated exposure to blood or other potentially infectious materials (including human cell lines) during the course of their work.

### 6. Seattle Municipal Code Infectious Waste Management

In 1989, the City of Seattle and the [King County Board of Health](#) adopted [SMC 21.43](#) covering regulations on infectious waste management. These regulations include requirements for a waste management plan that includes a policy on storage and containment of infectious waste, infectious waste treatment, disposal (including special disposal requirements for needles and other sharps waste), and transportation of this type of waste. These regulations were updated in 1992, the major modification being the change in terminology from infectious waste to biomedical waste. The University's [Biohazardous Waste Management Plan](#) is written per the requirements in this rule.

### 7. Washington State Definition of Biomedical Waste

The Washington State legislature adopted a statewide definition of biomedical waste that preempts any definitions previously established by individual local health departments or governments. This definition is the minimum requirement for defining infectious (biomedical) waste in the State of Washington:

- a. "Animal waste" consists of animal carcasses, body parts, and the bedding from animals that are known to be infected with or that have been inoculated with human pathogenic microorganisms infectious to humans.
- b. "Cultures and stocks" consist of wastes infectious to humans and include specimen cultures, cultures and stocks of etiologic agents, wastes from production of biologicals and serums, discarded live and attenuated vaccines, and laboratory waste that has come in contact with cultures and stocks of etiologic agents or blood specimens. Such waste includes, but is not limited to, culture dishes, blood specimen tubes, and devices used to transfer, inoculate, and mix cultures.

- c. "Human blood and blood products" are discarded human blood and blood components and materials containing free-flowing blood and blood products.
- d. "Pathological waste" consists of human source biopsy materials, tissues, and anatomical parts that emanate from surgery, obstetrical procedures, and autopsy. Pathological waste does not include teeth, human corpses, remains, or anatomical parts that are intended for interment or cremation.
- e. "Sharps waste" - The term "sharps" is a regulatory waste classification associated with those instruments used to puncture, cut, or scrape body parts and that, in a waste container, can cause punctures or cuts to solid waste handlers or the public. This means that all sharps waste must be placed in appropriate sharps containers and decontaminated prior to disposal.

Sharps include the following:

- a. Needles, including syringes with needles and IV tubing with needles attached
- b. Syringes without needles when removed from their original sterile containers (part of Oregon's definition of sharps)
- c. Lancets
- d. Scalpel blades
- e. Other sharps items not defined above only if contaminated with biohazardous material including recDNA (e.g., broken glass; razor blades; fragile glass tubes, vials, or ampoules including glass Pasteur pipettes; glass slides and cover slips)

## 8. Department of Transportation

[Department of Transportation Title 49](#) regulations apply to all untreated biohazardous waste that is shipped off-site for treatment and disposal by a UW waste contractor. Employees who prepare biohazardous waste for collection by a waste contractor must complete mandatory training before offering shipments.

## 9. United States Government Policy for Institutional Oversight of Life Sciences DURC (Dual Use Research of Concern)

The Dual Use Research of Concern (DURC) policy aims to preserve the benefits of life sciences research, while minimizing the risk of misuse of the knowledge, information, products, or technologies provided by the research. The [United States Government Policy](#) applies to research involving high consequence pathogens and toxins. If research with botulinum neurotoxins or a subset of select agents is anticipated to create categories of experimental concern, it is considered to be DURC. The UW Environmental Health & Safety and the Institutional Biosafety Committee (IBC), with assistance from the Office of Research, are responsible for developing and implementing [the University's DURC policy](#).

## E. UNIVERSITY POLICY

The UW has an established policy on health and safety programs in [UW Presidential Order 55](#), including:

*The University of Washington is committed to providing a healthy and safe environment for faculty, staff, students, visitors, and volunteers in all sites owned, operated, or controlled by the*



*University. This commitment includes supporting a culture of health and safety across the University. . . .*

*The University President has the ultimate responsibility for health and safety programs for the University. Under the authority delegated by the President, the Provost, the vice presidents and vice provosts, chancellors, deans, directors, chairs and unit supervisors, including faculty supervising academic activities, are responsible for:*

- *Reinforcing the importance of health and safety and creating a culture of health and safety in their units;*
- *Providing oversight of facilities, equipment, and practices to support a safe work and academic environment;*
- *Ensuring individuals under their supervision have sufficient authority and support to properly implement health and safety regulations, policies, and procedures;*
- *Being aware of and following safety plans for all University workplaces, classrooms, laboratories, field work locations, and student life areas;*
- *Assuring compliance with mandatory health and safety training in their units;*
- *Acting in support of the Department of Environmental Health and Safety (EH&S) and units with related responsibilities (see Sections [5](#) and [6](#) below) to monitor adherence to applicable health and safety regulations, policies, and procedures; and*
- *Establishing priorities and committing resources for correction of health and safety deficiencies.*

## **F. ROLES AND RESPONSIBILITIES FOR CONTROL OF BIOHAZARDOUS RESEARCH**

The responsibility for the control of biohazards and the safety of employees and the public rests with:

### **1. Principal Investigator**

At the UW, the primary responsibility for establishing, following, and enforcing rules, procedures, and methods for the proper control of biohazardous agents, including the use of recDNA, rests with the PI.

The PI is responsible for ensuring all research with biohazardous agents, including recDNA, is reviewed and approved by the IBC and/or the EH&S Research and Occupational Safety (ROS). The PI must complete the EH&S Biosafety Training every three years if their research includes the use of biohazardous agents.

The PI must be adequately trained on the *NIH Guidelines* and laboratory specific procedures involving use of recDNA. The PI must be adequately trained in good microbiological techniques and is responsible for seeing that laboratory staff are adequately trained in safety practices. The PI is responsible for correcting work errors, identifying defective working conditions that could result in personal injury, and developing a positive attitude among laboratory staff toward accident prevention. The PI is responsible for informing the laboratory staff of the reasons and provisions for any precautionary medical practices advised or requested (e.g., vaccinations or serum collection).

The PI is responsible for adhering to IBC approved emergency plans for handling accidental spills and personnel contamination. The PI is also responsible for complying with [shipping requirements for recDNA or other biohazardous materials](#).

While conducting research, the PI is responsible for supervising the safety performance of the laboratory staff to ensure that the required safety practices and techniques are employed. The PI is responsible for investigating and reporting any significant problems pertaining to containment practices and procedures to EH&S and correcting any work errors and conditions that could result in the release of biohazardous agents, including recDNA.

UW-affiliated clinical investigators doing research with [recDNA in human research participants](#) have the responsibility to be familiar with the *NIH Guidelines* and ensure all aspects pertaining to NIH and local IBC review and reporting obligations are appropriately addressed. UW-affiliated clinical investigators must have [Institutional Review Board \(IRB\)](#) and [IBC approval](#) before enrolling subjects, regardless of the funding source or the molecular nature of the gene transfer reagent (plasmid or viral vector, vaccines).

## 2. Department of Environmental Health and Safety

This department is responsible for evaluating existing and potential biohazardous conditions at the UW, establishing safety standards, and providing staff support to the IBC (UW Administrative Policy Statements [12.3](#) and [10.1](#)).

### a. EH&S Biosafety Officers

The EH&S BSOs have expertise in developing and supporting the Biosafety Program (including BSL-1, BSL-2, BSL-3 laboratories, and select agents). They develop and implement policies, procedures, and processes required for an effective, compliant, and efficient biosafety program. They play a lead role in providing technical support to the UW IBC. They review research proposals, laboratory operations, and laboratory facilities for all aspects of biosafety to assure appropriate safety controls, containment, and compliance with federal, state, and local regulatory agencies as well as seeing that UW requirements are met. They work closely with research staff, faculty, students, university units, and institutional committees to promote safe laboratory practices, procedures, and proper use of containment equipment and facilities. They conduct compliance audits, identify corrective actions, and prepare written status and compliance reports. They develop and provide educational materials and training. They also respond to, investigate, and follow up with biological safety incidents.

### b. Employee Health Services

The Occupational Health Nurses (OHN) at EH&S screen written protocols and the Biological Use Authorization (BUA) application form for research-related risks, including those associated with animals. Specific requirements for personal and laboratory-based protections are determined by the potential for exposure to chemical, biological, or physical hazards. When necessary, referrals for immunizations and/or other clinically-based medical services are made to the appropriate Campus Health Service's Employee Health Center (EHC), located at Hall Health Center, the University of Washington Medical Center (UWMC) and/or Harborview Medical Center (HMC) (UW Administrative Policy Statement 12.3).

## 3. Institutional Biosafety Committee (IBC)

IBCs were originally established under the [NIH Guidelines](#) local institutional oversight for nearly all forms of research utilizing recDNA. Over time, however, the role of the IBCs has



been expanded to include review and oversight of a variety of experimentation that involves biological materials (e.g., infectious agents) and other potentially hazardous agents (e.g., carcinogens).

The [IBC](#) is composed of an IBC Chair; Biosafety Officer; public members not affiliated with UW who represent the interest of the surrounding community with respect to health and protection of the environment; research faculty with adequate expertise and training in human gene transfer protocol reviews, in plant, plant pathogen or plant pest containment principles, and in animal containment principles in accordance with the *NIH Guidelines*. This committee is responsible for advising the Executive Director for the Health Sciences Administration (HSA) and the Director of EH&S, in establishing standards, providing consultant services, reviewing research proposals for compliance with standards, approving or denying these proposals, and recommending training and education methods for laboratory personnel (UW Administrative Policy Statements 12.3). The IBC also reviews research protocols involving [recDNA in human research participants](#). This review compliments the IRB review ([UW Human Subject Division](#)) as both are necessary prior to subject enrollment.

#### **4. Deans, Directors, Chairpersons, and Organizational Supervisors**

These supervisors are responsible for all employees, students, faculty, and visitors in their areas of control. They must be aware of the hazards of research and approve control methods used by the PI (UW Administrative Policy Statements 12.3 and 10.3).

#### **5. Department of Comparative Medicine**

The Department of Comparative Medicine is responsible for the operation and maintenance of centralized animal vivarium facilities including centralized Animal Biosafety Level 1 (ABSL-1), Animal Biosafety Level 2 (ABSL-2) and Animal Biosafety Level 3 (ABSL-3) facilities, excluding the Washington National Primate Center (WaNPRC).

#### **6. Washington National Primate Research Center**

The WaNPRC is responsible for the operation and maintenance of all non-human primate (NHP) facilities