INSTITUTIONAL BIOSAFETY MANUAL

The purpose of this manual is to define the biological safety policies and procedures pertaining to research operations at Boston University (BU) and Boston Medical Center (BMC). The policies and procedures located within this document are designed to safeguard personnel and the environment from biologically hazardous materials and to comply with federal, state, and local regulatory requirements. All BU and BMC Principal Investigators (PIs) and laboratory workers must adhere to the biological safety policies and procedures in the conduct of their research and the management of their laboratories.

For information about specific biological safety programs for operations not covered in this manual, contact the Institutional Biosafety Committee (IBC) office or the Biological Safety Officer (BSO).

Chair, Institutional Biosafety Committee

Associate Vice President, Research Compliance

Version/Year of Review	Summary of changes	Effective Date
2.0/2022	Contact updates, formatting; regulatory updates to information on prion research, select agents, RAC review, references to BSL3 and 4, updates to roles and responsibilities, approval processes, biosafety procedures, PPE practices; updated appendixes.	12/13/2022

Table of Contents

Chapter 1
Biological Safety Program: Purpose, Scope, and Responsibilities

Purpose

The purpose of this Biosafety Manual is to define policies and procedures pertaining to use of biological materials in research at BU and BMC. The policies and procedures within this document are designed to safeguard personnel and the environment from biologically hazardous materials without unduly limiting academic research. This manual also offers guidelines to comply with federal and state regulatory requirements.

The work practices, procedures, and policies specified in this manual are based on current regulatory requirements and accepted best biosafety practices. Implementation of these measures will reduce the likelihood that an incident involving a biological agent will occur and will fulfill regulatory biosafety expectations. Laboratory microbiological work usually involves potential exposure to biological hazards, as well as to chemical and radiological hazards. Consequently, this manual should be used in conjunction with the BU Chemical Hygiene Plans and Radiation Safety Manual, respectively. This manual will be reviewed tri-annually by Environmental Health & Safety, in coordination with Research Compliance, and updated as needed in accordance with any change in local, state, or federal biosafety regulations.

For information about specific biological safety programs for operations not covered in this manual, contact the Institutional Biosafety Committee (IBC) office or the Biological Safety Officer (BSO).

Scope

This manual applies to all individuals engaged in research at or under the jurisdiction of BU.

Affiliated Institutions

This manual also applies to all individuals engaged in Research at or under the jurisdiction of Boston Medical Center (BMC).

Biological materials include:

- All infectious microorganisms (i.e., virus, bacteria, fungi, parasite, prion, rickettsia) and the toxins derived from such organisms (biological toxins) that can cause disease in humans or pose significant environmental or agricultural impact;
- Recombinant or synthetic nuclei acid molecules;
- Human or non-human primate materials including blood, plasma, serum, body fluids, unfixed tissues, organs, and cells;
- Field studies involving wild animals and vectors including samples that may be inherently infected or would be experimentally infected with Biosafety Level 2 (BSL2) or higher agents;
- Transgenic plants, animals, or vectors.

Biological Safety Program Goals

The goals of the Biological Safety Program, referenced in this manual as the Biosafety Program, are to protect laboratory workers, the public, and the environment from potentially hazardous biological agents. The IBC advocates the use of biosafety precautions that effectively reduce or eliminate the risk of

exposure to potentially hazardous agents used in research. In developing its guidelines, the IBC is ensuring that all policies and procedures are in accordance with both the regulatory frameworks governing the use of biological materials and the best practices adopted nationally.

Chapter 3 contains a listing and summary of the regulations and guidelines that govern the use of biological materials in research.

Roles and Responsibilities

The success of the Biosafety Program, like any other safety program, requires a team effort involving the IBC, Research Compliance staff, Principal Investigators, laboratory workers, the Research Occupational Health Program (ROHP), and Environmental Health and Safety (EHS). **Principal Investigators are responsible for ensuring compliance with this policy as it applies to laboratory areas they may occupy, oversee or share, and ensuring that laboratory personnel who work under their supervision and occupy their laboratory space are informed of this policy and follow it**. The BU administration, the IBC, and the EHS endorse this manual and encourage active participation in maintaining high standards.

Associate Vice President, Research Compliance (AVPRC)

The AVPRC has overall responsibility for:

- Oversight for the control of hazards in the research laboratories and for ensuring that comprehensive, enterprise-wide programs are in place for the safe handling of all hazardous (e.g., biological, chemical, radiological) materials;
- All non-financial research compliance at BU;
- Direct functional responsibility for the IBC, Biosafety Program, EHS, Laboratory Safety Committee, Laboratory animal use and care programs (Institutional Animal Care and Use Committees (IACUC), Institutional Review Board (IRB), BU animal care programs, and other research-related oversight committees;
- Acts as the Responsible Official (RO) for the City of Boston's Public Health Commission (BPHC) laboratory regulations;
- In consultation with provosts and deans at the Medical Campus and the Charles River campus, as well as the BMC leadership, appoints various committee members. The IBC, Research Compliance staff, the Research Safety Director, the BSO, ROHP, and EHS have been charged with planning and implementing the Biosafety Program, the purpose of which is to protect all personnel, the public, and the environment from biohazardous or infectious agents.

Institutional Biosafety Committee

The IBC is responsible for overall oversight of the Biosafety Program at BU. The IBC carries out these functions pursuant to requirements set forth by the National Institutes of Health (NIH), the Centers for Disease Control and Prevention (CDC), Occupational Safety and Health Administration (OSHA), the City of Boston Public Health Commission (BPHC), the Massachusetts Department of Public Health (DPH), and Boston University.

The IBC's responsibilities are located in the IBC charter.

IBC Program

The IBC Program staff (housed in Research Compliance) responsibilities include, but are not limited to:

- Initiates the review process of the Biosafety Manual in consultation with EHS, ROHP, the IBC,

and other BU stakeholders;
- Receipt and review of BUAs via RIMS submission process;
- Monitoring and communication in consultation with EHS, BSO, ROHP, and other offices as needed;
- Providing ancillary review of IACUC and IRB protocols using biohazardous materials;
- Advising PIs on BUA submissions in the RIMS system and in completing their BUAs;
- Assigning review of BUAs for scheduled IBC meetings;
- Documenting IBC meeting discussion and votes;
- Submitting annual IBC registration updates to NIH.

Biological Safety Officer (BSO)
The BSO is responsible for providing guidance on the safe handling of biological agents and contributing to the overall management of the Biosafety Program. The BSO is a voting *ex-officio* member of the IBC.

The BSO's responsibilities include, but are not limited to:

- Provides technical advice to the IBC, PI and researchers on laboratory containment, security, and safety procedures;
- Works with EHS on oversight of periodic and unscheduled inspections to ensure that laboratory standards are rigorously maintained;
- Develop emergency plans for handling spills and personnel contamination;
- Develop guidelines and procedures for safe laboratory practices and oversee their implementation;
- Develop design specifications and criteria for laboratory containment facilities;
- Develop and implement training programs in consultation with the IBC;
- Prepare and provide reports on the Biosafety Program to the IBC. The BSO's report includes routine operational updates, any significant problems or regulatory violations and any research-related accidents or illnesses that have occurred;
- Work with the appropriate Institutional Official of BU, BMC, and BU tenant laboratories to prepare, renew, and submit the recombinant DNA permit application to BPHC;
- Prepare response to BPHC on inquiries concerning laboratory related incidents reported by ROHP;
- Act as a liaison and work with regulatory agencies during visits and inspections of laboratories;
- Oversee follow-up investigation and response to laboratory incidents involving biological, and rDNA materials.

Research Safety Director
The Research Safety Director (RSD) works with the different safety committees to ensure that laboratory research is conducted in appropriate facilities, using safety equipment, and implementing safety processes.

The RSD's responsibilities include, but are not limited to:

- Oversee Research Safety activities and response during regulatory inspections and visits of laboratories;
- Provide update as necessary to leadership;
- Works with the AVPRC, Research Compliance, IBC, and other institutional officials to coordinate responses to any regulatory findings;
- Reviews new and proposed regulations and other requirements and summarizes impact to the

institution;
- Determine programs and processes necessary for an effectively safe process to conduct laboratory research.

Environmental Health and Safety
The various programs within EHS work closely with the BSO to ensure that operations for which EHS has responsibility are conducted in accordance with the criteria and guidelines established by the BSO. These include, but are not limited to:

- Storage and disposal of biological and medical waste;
- Selection of appropriate Personal Protective Equipment (PPE) for individuals working with hazards, including biohazardous materials;
- Development and implementation of emergency response and preparedness plans;
- As necessary, assess and monitor work areas, including the presence of allergens.

Principal Investigators (PIs)

Principal Investigators (PIs) or Laboratory Directors are responsible for ensuring compliance with this manual as it applies to laboratory areas they may occupy or oversee; and ensuring all laboratory personnel who work under their supervision and occupy their laboratory space are aware of this manual and understand how it applies to their areas. The PI responsibilities should include, but are not limited to, the following:

- Ensures that specific laboratory hazards are effectively communicated to laboratory personnel; personnel have received appropriate training and are competent to conduct procedures performed in the laboratory, and that appropriate controls are in place to minimize risks associated with these hazards;
- Ensures that specific laboratory hazards are effectively communicated to laboratory visitors prior to entering the laboratory, including posting of signs at the entrance to the laboratory to inform individuals of laboratory hazards; and that visitors have met the specific requirements prior to entering or exiting the laboratory;
- Develops standard operating procedures (SOPs), when warranted, to address the hazards so that work can be performed safely.
- Ensures that engineering controls are available, in good working order, and are used appropriately to prevent or minimize exposure to biohazardous materials;
- Ensures that appropriate PPE are available and used by laboratory personnel.
- Ensures that all laboratory personnel receive appropriate training including biosafety training that is conducted as part of the Biosafety Program, as well as specific training on the hazards, procedures, and practices relevant to the laboratory in which they are working. Documents and maintains all training records;
- Ensure that research personnel have completed their required medical clearance from ROHP before starting work on an approved IBC protocol.
- Notifies the IBC and obtains IBC approval prior to starting work with recombinant or synthetic nucleic acid molecules and/or biohazardous material, and conforms to all terms and conditions of the IBC approval;
- Ensures that laboratory workers are provided access to immunizations and medical surveillance prior to, and in the event of, exposure to biohazardous agents as appropriate (based on current CDC and IBC recommendations). Immunizations are provided through BU's ROHP;
- Notifies the BUMC Control Center at (617) 358-4144or EHS emergency telephone, (617) 414-

4075 at the Charles River Campus, of any spills or incidents involving biological agents. The Control Center notifies the BSO;
- Ensures that all biological wastes including biological agents are disposed of according to regulations, as outlined in this manual;
- Ensures that biohazardous materials to be transported are packaged, transferred, or shipped in accordance with regulations and BU policies;
- Ensures that periodic self-inspections of the laboratory are conducted by the PI or designee.

Laboratory Safety Coordinators
The Laboratory Safety Coordinator's responsibilities include, but are not limited to:

- Supports the PI and ensures that safety practices are implemented and followed in the lab's daily operations;
- Represents the PI in matters related to the implementation of laboratory and worker safety.
- Serves as the primary laboratory contact with EHS for issues related to safety (e.g., biological, chemical, fire, general safety, controlled substances, etc.);
- Takes positive actions to help reduce the potential for accidents and incidents associated with laboratory operations;
- Instructs all laboratory personnel and students in safe work methods;
- Informs laboratory personnel and/or students of the safety hazards associated with their work.
- Reports all accidents or safety concerns to the PI and EHS;
- Ensures that appropriate SOPs are established and that lab personnel and students are appropriately trained to follow them;
- Works with EHS to determine best safe practices and procedures;
- Works with EHS to ensure that lab personnel and students complete all required safety trainings in a timely manner;
- Ensures that all deficiencies identified by EHS or outside regulatory inspectors are addressed and corrected within the time required;
- Participates in the incident review process;
- Stop operations that are in clear violation of the safety requirements, approved SOPs, or may potentially result in injuries or potential exposures.

ROHP and Occupational Health Officer (OHO)

The OHO has overall responsibility for the ROHP and is responsible for reporting BU exposure incidents involving select agents (see Chapter 10 CDC/USDC Select Agents). ROHP is responsible for establishing and performing appropriate medical surveillance for all personnel performing or supporting research, such as animal care workers, facilities, EHS, Police and Public Safety. Medical surveillance is required at the time of hire, or transfer into the research environment, prior to beginning work on an IBC-approved protocol, and periodically depending on the work environment, occupational exposure, and risk for each position or job category.

The ROHP and Occupational Health Officer's responsibilities include, but are not limited to:

- Develops exposure treatment and management plans for laboratory exposures or incidents, including post-exposure management and monitoring;
- Reviews IBC protocols and determine additional medical surveillance requirements for PI's and other personnel included in protocols; creates and issues wallet-sized agent cards, agent; information sheets, and emergency medical response protocols to those personnel approved by

the IBC to work with biological agents with the potential to cause LAI (see Appendix G, List of Biological Agents with the Potential to Cause LAI in Use at Boston University);
- Participates in Laboratory Safety Committee, IBC, IACUC, Radiation Safety Committee and other committee meetings, as required, to ensure appropriate health and safety practices are followed;
- Assists PIs and EHS in the preparation and presentation of biosafety and agent specific training;
- Provides medical support coverage 24 hours a day, 7 days a week, for researchers and other personnel to call for triage, evaluation, and medical care referral based on severity, location and time of laboratory exposure or incident;
- Works with EHS to develop SOPs and appropriate health and safety practices;
- Performs return to work assessments in conjunction with BPHC for laboratory exposures involving "high risk" agents;
- Issues generic wallet-sized agent cards to personnel with potential to exposure with hazardous materials in research laboratories and animal care facilities.

Laboratory Workers

Laboratory workers are an important element in developing and maintaining a safe laboratory environment. An incident caused by one laboratory worker can have a widespread effect on others.

Laboratory workers responsibilities include, but are not limited to:

- Follows procedures and practices established by BU, the IBC, and the laboratory;
- Uses best biosafety laboratory practices to minimize exposures to biological agents and to avoid other incidents (such as personal injuries, chemical and radiation spills, laboratory fires, explosion, etc.);
- Completes the required Laboratory Safety Training and annual refresher training thereafter.
- Follow established procedures and report spills, accidents, and unsafe laboratory conditions to the PI, EHS, and other responsible parties;
- Utilizes control measures, such as biological safety cabinets and PPE, to prevent or minimize exposure to biological agents and contamination of personnel and facilities;
- Immediately contacts ROHP at (617) 358-ROHP (7647) in the event of an exposure or injury so that medical triage and evaluation, documentation and notification can be performed.

Dual Use Research of Concern Committee

Academic research institutions are expected to comply with the federal requirement for institutional Dual Use Research of Concern (DURC) oversight. The federal requirement applies to all institutions that receive federal funding to perform life science research that meets the DURC standard. BU's DURC committee is responsible for the oversight and implementation of the standards in the research community at BU.

The Dual Use Research of Concern's responsibilities include but are not limited to:

- Develop the policy that all research projects as specified in the US Governmental Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern are subject to review and approval prior to the initiation of the project;
- Identify and develop a process for reviewing the proposed research protocol and identify key stakeholders and their responsibilities;

- Review research protocols and determine if fully compliant with the standard; determine and identify the risk mitigation plan to be implemented with the PI;
- Review and as needed, revise or update approved risk mitigations plans annually;
- Provide a report of the final Committee review of protocols determined as DURC to the Office of Research Compliance. The report shall be submitted to the appropriate funding agency;
- Report lab noncompliance to the approved risk mitigation plan to the appropriate funding agency and impose sanctions as appropriate on the PI or the lab. Review appeals by the PI to the sanctions. Such sanctions may include but are not limited to restriction or suspension of research work;
- Identify the process for keeping of all documents and records for protocols that were reviewed as DURC including reports to funding agencies, risk mitigation plans, others.

Chapter 2
Approval of Research Projects

What Needs Approval

PIs planning to conduct research using recombinant or synthetic nucleic acid molecules and/or hazardous biological materials that pose a potential risk to the health of humans, animals, or plants, either directly through infection or indirectly through damage to the environment, must submit an IBC Application entitled "Biological Use Authorization" (BUA) to the IBC Program for review and approval by the IBC.

Researchers using any of the following must complete and submit a "Biological Use Authorization" (a.k.a. IBC protocol) for review and approval:

- Recombinant and synthetic nucleic acid molecules;
- Hazardous biological agents (e.g., virus, bacteria, fungi, parasite, prion, rickettsia etc.);
- Other potentially infectious materials (e.g., human or non-human primate blood, serum, plasma, body fluids, unfixed tissue, organ and cells);
- Inactivated Biological Samples derived from BSL3 or higher agents;
- Select agents and biological Toxins;
- Transgenic animals or plants;
- Human gene transfer;
- Sheep and any tissues derived from them (these tissues can transmit *Coxiella burnetii*, the causative agent of Q-fever); and
- Field studies with wild animals and vectors and their tissues potentially infected or would be experimentally infected with BSL2 or higher agents.

For work with potentially infectious agents on human subjects or experimental animals, IBC review is necessary in addition to review by the appropriate IRB or IACUC.

PIs whose research will involve the above mentioned category agents or infectious materials are required to complete a BUA and obtain IBC approval prior to receiving such materials or commencing such research. PIs are also required, where applicable, to maintain a medical surveillance program for laboratory employees (see Appendix P). Relevant federal, state, and local governmental regulations include the following (see Chapter 3 for more details):

- *NIH Guidelines for Research Involving Recombinant or synthetic nucleic acid molecules (NIH Guidelines);*
- BPHC regulations governing labs in the city of Boston:
  - Recombinant DNA Technology: Use Regulations
  - Biological Laboratory Regulation with accompanying Guidelines;
- Disease Surveillance and Reporting Regulation with accompanying Guidelines;
- OSHA Bloodborne Pathogens Standard;
- OSHA Tuberculosis Standard;
- OSHA Laboratory Standards;
- Massachusetts State Regulations:
  - Minimum Requirements for the Management of Medical or Biological Waste
  - Reportable Diseases, Surveillance, and Isolation and Quarantine Requirements;
- Biosafety in Microbiological and Biomedical Laboratories (BMBL) 6th edition;

- The Centers for Disease Control and Prevention (CDC) and United States Department of Agriculture (USDA) Select Agent regulations; and
- International, federal, and state transport regulations.

Note: *A PI performing this type of work without IBC approval is non-compliant with current NIH and local regulations and the IBC will take appropriate corrective actions and may impose sanctions*.

Types of IBC Protocols

New Applications

A new BUA must be submitted and reviewed by the IBC program for any research mentioned previously. PIs seeking IBC approval for the first time also need to submit a curriculum vitae (CV) or two-page NIH biosketch with their application. Applications need to be submitted via the Research Information Management System (RIMS).

The PI may designate others to assist in completing the application, however, only the PI may submit the application. The BU IBC requires that all PIs be members of the faculty. Projects from post-docs or other non-faculty members require a faculty PI sponsor.

All individuals listed on a new BUA must complete the following training and ROHP medical health clearance requirements before engaging in any approved protocol related activities:

- Laboratory Safety Training
- Health Questionnaire (must be filled out, submitted, reviewed, and cleared by ROHP); and
- Laboratory Specific Training.

All Principal Investigators (PIs) listed on a new BUA, and all individuals listed on a new BUA involving recombinant or synthetic nucleic acids, must complete the following training before engaging in any approved protocol related activities:

- IBC Policy /Recombinant DNA Training and Quiz.

Personnel will need a RIMS Training Profile in order to complete these requirements. Other training will be required based on the nature of project including, but not limited to: BSL3 annual training; shipping biologicals training; select agent training; and agent specific training for *Francisella tularensis*, *Mycobacterium tuberculosis*, and *Yersinia pestis*.

All applications must be received by the meeting date deadline to allow time for review by the committee members and a Biological Use Authorization Site Assessment by EHS. Meeting date deadlines can be found on the IBC Program website. Each application will be assigned to a primary and secondary reviewer. Reviewer comments will be discussed at a convened IBC meeting.

Renewals

A renewal of the original BUA approval must the completed in RIMS at the third year after initial approval of a protocol. Email notice of 3-Year Renewal will be sent to the PIs. Detailed instructions on completing the 3-Year Renewal in RIMS is found in the IBC website. The PI is asked to list all proposed modifications from the protocol as initially approved (or since the last renewal notice), including: changes in laboratory location or equipment, changes in laboratory staff working on the project, any project titles to be added, and any agent of experimental changes.

If there are significant modifications to the protocol, especially those that affect the biosafety containment level (e.g., new study on organisms, a new host-vector-donor system, or any other modifications that may affect the containment level), the IBC Program will send the protocol for committee review and approval. When a project is renewed, the PI and all staff listed on the protocol must complete the "Laboratory Safety Annual Refresher Training" and the annual ROHP clearance update (*contact ROHP at rohp@bu.edu* or at *(617) 358-7647*), and any other training requirements applicable to the project.

Amendments
Amendments must be submitted to the IBC Program for changes within an approved project. All changes should be detailed in RIMS and submitted to the IBC Program and the IBC must review and approve the amendment prior to implementing the changes. Detailed instructions on completing the amendment in RIMS are found in the IBC Amendment Instructions document. Title additions approval may be applied to several different granting agencies, but all grant titles must be registered with the IBC Program. Approval of lab space additions applies only to work performed in registered lab space.

For non-PI personnel changes, individuals must complete the "Initial Laboratory Safety Training" and "ROHP Clearance" requirements. Individuals on protocols involving recombinant or synthetic nucleic acids, must also complete the IBC Policy /Recombinant DNA Training and Quiz. Additions of titles, lab space, and personnel are reviewed administratively reviews and approvals, and do not to go the full IBC.

Some amendments may require full committee review and when extensive, may require the PI to submit a completely new application. A change in PI also requires submission of an amendment where CV (or NIH biosketch) of the new PI must be attached to the amendment, and this must be reviewed by the IBC Chair and the BSO.

The IBC Program will notify the PI when the Amendment has been processed and approved. IBC approval is required before any changes in the work can commence.

Protocol Review Outcomes

The IBC has the authority to decide to approve, conditionally approve, defer or withhold approval of the proposed research activity. These actions will be taken by a vote of a majority of the members present. At the conclusion of discussion during its scheduled meeting, the IBC determines the outcome of its review, which will be one of the following:

Approved
A protocol that receives full approval requires no (additional) changes or clarifications to comply with IBC policies. Work may commence immediately upon full approval of a protocol. Approval is valid for the study as described in the protocol form for a period of three years from the original approval date. PIs must complete a renewal form tri-annually (annually in the first year for BSL 3 and BSL4) after the first and second year following initial approval and must submit a new application to continue the work beyond the approved three-year time period.

Conditionally Approved
"Conditionally Approved" is a determination that the IBC makes when minor changes or clarifications are required to bring the protocol into compliance with IBC policies. The investigator must respond in writing to the IBC's notice of conditional approval.

Deferred

"Deferred" is used when numerous and/or major changes or clarifications are required to bring the protocol into compliance with IBC policies or there is insufficient time at the IBC meeting to conduct a thorough review.

Withhold Approval
The IBC may withhold approval of a protocol if it fails to meet one or more criteria used by the IBC for approval of research.

Use of Materials that Require Clarification for the IBC Approval

Biohazardous and Potentially Infectious Materials
Biohazardous agents and potentially infectious materials present a risk or potential risk to the health of humans or animals, either directly through infection or indirectly through damage to the environment. Infectious agents have the ability to replicate and give rise to potentially large populations in nature when small numbers are released from a controlled situation.

PIs should follow the instructions in the BUA carefully to ensure that all appropriate sections of the application are completed. It is important that the PI clarifies the intended use of the agents, how risks associated with its handling are mitigated, and the management of the wastes generated from such work. If a PI intends to use biological agents that are not listed in this section, he or she should contact the IBC Program or BSO for advice regarding proper completion of the BUA.

For the list of biological agents with the potential to cause Laboratory Acquired Infection (LAI) see the Appendix G. The ROHP has developed additional "Agent Information Sheets" that are available on the IBC website. Where applicable, agent specific vaccines will be offered at no charge to all persons who are approved by the IBC to work with or could potentially get exposed to these materials.

Recombinant or synthetic nucleic acid Materials
When a BUA protocol involves the use of recombinant or synthetic nucleic materials, most of those work require IBC approval before initiation of work. The NIH Guidelines for Recombinant and Synthetic Nucleic Acids provide specific guidelines on the facility containment and specific regulatory requirements depending on the exact detail of the proposed work. A PI must follow the defined containment directive. There may be experiments not covered by the guidelines that would require review and approval by outside agencies before initiation. If the experimental protocol is not covered by the NIH's guidelines, contact the BSO at (617) 358-7840 at BUMC and (617) 353-4094 at CRC to determine further review requirements.

Human Gene Transfer
All protocols involving human gene transfer must be submitted to both the IBC and the IRB for review. However, a public review and discussion by the NIH Recombinant DNA Advisory Committee (RAC) is no longer required as it has been decided that existing FDA guidelines and requirements for the review of gene therapy protocol is sufficient. The NIH Office of Science Policy will also not accept annual reports, safety reports, amendments or other documentation for any previously registered human gene transfer protocols under the NIH Guidelines. The roles and responsibilities of local IBCs will continue as described in the NIH Guidelines 2024 Section III-C. These studies remain subject to FDA and other clinical trial regulations, and only after FDA, IBC, and other relevant approvals are in place can these protocols proceed.

However, the deliberate transfer of recombinant or synthetic nucleic acids into one human research

participant, conducted under a Food and Drug Administration (FDA) regulated individual patient expanded access Investigational New Drug (IND) or protocol, including for emergency use, is not research subject to the *NIH Guidelines* and thus does not need to be submitted to an IBC for review and approval.

For more details about IBC approval of human gene therapy protocols, contact the IBC Office at (617) 358-7910 or ibc@bu.edu. For information about IRB submissions, contact the BUMC IRB at (617) 358-5372 or the CRC IRB at (617) 358-6115.

Use of Animals
All PIs planning to use recombinant or synthetic nucleic acid molecules and/or biohazardous materials in their laboratory or in research animals must receive IBC approval prior to commencing the work. The use of animals in research also requires compliance with the "Animal Welfare Act," administered by the USDA's Animal and Plant Health Inspection Service (APHIS); the "Public Health Service Policy on Humane Care and Use of Laboratory Animals," administered by NIH's Office of Laboratory Animal Welfare (OLAW); and all applicable state, local or University regulations covering the care and use of animals. All protocols involving the use of live animals must be reviewed and approved by the IACUC before their implementation.

Transgenic Animals
PIs who create transgenic animals, either in the PI's lab or through the BU Transgenic Core facility, as well as PIs who use transgenic animals at ABSL2, or at ABSL1 if not considered exempt under the NIH Guidelines (Section III-E, Appendix C-VIII), must complete an IBC application and submit it to the IBC for approval prior to initiation of experimentation. In addition, the IACUC must approve the protocol. The IACUC can be reached at (617) 358-5586 (BUMC) or (617) 358-3867 (CRC).

Tissue Culture/Cell Lines
All tissue and cell cultures derived from humans are considered potentially infectious under the OSHA Bloodborne Pathogens Standard, Title 29 Code of Federal Regulations (CFR) Part 1910.1030 and must be handled in a laboratory using BSL2 principles, practices and facilities (the concept of "universal precautions"). Nonhuman primate tissues and cell cultures are also considered potentially infectious and must be handled in the BSL2 laboratory. Persons who are exposed to these materials in the laboratory are considered to have potential exposure to bloodborne pathogens, such as human immunodeficiency virus (HIV) and hepatitis B virus (HBV), and must be included in the Bloodborne Pathogens program. These persons must be offered the HBV vaccination and complete annual bloodborne pathogens training. When cell cultures are known to contain any Risk Group 3 and higher organism, the cell line will be classified at the same higher containment level. Consequently, they must be handled using BSL3 and higher containment criteria.

Select and Biological Toxins
Use of biological toxins including the select agent toxins generally needs approval by the IBC (see Appendix F "Guidelines for Work with Toxins of Biological Origin" for more details). Please check with IBC staff directly if you have questions for a particular biological toxin. Use of select agent toxins such as Abrin, Bacillus cereus Biovar anthracis, Botulinum neurotoxins, Botulinum neurotoxin producing species of Clostridium, Conotoxins (Short, paralytic alpha conotoxins containing the following amino acid sequence X1CCX2PACGX3X4X5X6CX7) Diacetoxyscirpenol (DAS), Ricin, Saxitoxin, Staphylococcal Enterotoxins (Subtypes A, B, C, D, and E), T-2 toxin, Tetrodotoxin requires IBC approval.

Testing and Certification of Containment Equipment Required

Handling infectious or potentially infectious materials could potentially generate infectious aerosols. Such work must be performed in the Biological Safety Cabinet (BSC) and wearing appropriate PPE. All BSCs are required to be tested and certified when they are first installed. They are also required to be tested and recertified annually. BU works with an outside vendor that is experienced and certified to test and repair this equipment. Laboratories must ensure that their BSCs certifications are current before initiation of protocols. EHS will verify their status during BUA follow up of protocols under review by the IBC.

Completion of Laboratory Safety Trainings
The PI and all laboratory personnel that are listed on the protocol must complete their required lab safety trainings. The trainings are available on BioRAFT and can be accessed online. These trainings must be completed prior to initiation of lab work and they need to be refreshed annually. EHS will verify that the PI and personnel that are listed on the protocol have completed the required training during BUA follow up of protocols under review by the IBC.

What does the IBC review?

When reviewing a research protocol the IBC is responsible for assessing:

- Recombinant or synthetic nucleic acid molecule research for compliance with the *NIH rDNA Guidelines;*
- Use of hazardous biological materials in the laboratory;
- Use of hazardous biological materials on animals;
- Potential risk to the lab personnel, environment and public health;
- Appropriate Risk Category and BSL/ABSL Containment levels per NIH Guidelines and CDC BMBL 6th edition;
- Adequacy of facilities, safety equipment. PPE, procedures, practices, training, transport and shipping of specimen samples, and experience and expertise of personnel;
- Adverse event report.

Risk Group Definition

The investigator must make an initial risk assessment based on the Risk Group (RG) of an agent. Agents are classified into four RGs according to their relative pathogenicity for healthy adult humans by the following criteria:

RG1	Agents that are not associated with disease in healthy adult humans
RG2	Agents that are associated with human disease which is rarely serious and for which preventive or therapeutic interventions are *often* available
RG3	Agents that are associated with serious or lethal human disease for which preventive or therapeutic interventions *may be* available (high individual risk but low community risk)
RG4	Agents that are likely to cause serious or lethal human disease for which preventive or therapeutic interventions are *not usually* available (high individual risk and high community risk)

As a general rule, a biosafety level should be used that matches the highest risk group classification of the agents involved (see chapter 4). More information can be found in Appendix B of NIH Guidelines, April

2024.

For information about the risk group of a specific pathogen, please check the resource below:

- Pathogen Safety Data Sheets and Risk Assessment (from Public Health Agency of Canada)
- Risk Group Classification for Infectious Agents (from American Biological Safety Association)
- Classification Of Human Etiologic Agents On The Basis Of Hazard (Appendix B of NIH Guidelines

Biohazardous Pathogen Examples

Tuberculosis
Since 1985, the incidence of tuberculosis in the United States has been increasing steadily, reversing a 30-year downward trend. Recently, drug-resistant strains of *Mycobacterium tuberculosis* have become a serious concern. Outbreaks of tuberculosis, including drug-resistant strains, have occurred in health-care environments.

In 2005 the CDC published *Guidelines for Preventing the Transmission of Mycobacterium tuberculosis in Health-care Settings.* MMWR 2005; 54 (No. rr-17, 1-141). (Errata published September 25, 2006.) The guidelines contain specific information on ventilation requirements, respiratory protection, medical surveillance, and training for those personnel who are considered at-risk for exposure to tuberculosis. For more information, contact the BSO.

PIs intending to work with *Mycobacterium tuberculosis* in the laboratory must obtain full approval from the IBC via the IBC application process before beginning work. Propagation and manipulation of *Mycobacterium tuberculosis* cultures must be performed at BSL3. PI's and all other persons approved to work with *Mycobacterium tuberculosis* are required to undergo semi-annual tuberculosis screenings.

Vaccinia Virus
PIs wishing to use vaccinia virus must obtain full approval from the IBC via the application process. BSL2 practices and procedures must be followed. All employees who directly handle cultures or animals contaminated or infected with vaccinia virus, recombinant or defective vaccinia viruses, or other orthopox viruses that infect humans shall be offered the smallpox vaccine. PI's and all other persons approved to work with the vaccinia virus shall be offered the vaccinia virus vaccine at no charge. Individuals that decline the vaccinia virus vaccine must sign a declination form which will be kept on file with ROHP.

Francisella tularensis Bacteria
Tularemia, or rabbit fever, is a bacterial disease associated with both animals and humans. According to the CDC, "Tularemia is a potentially serious illness that occurs naturally in the United States. It is caused by the bacterium *Francisella tularensis* found in animals (especially rodents, rabbits, and hares)." PI's and all other persons approved to work with *F. tularensis* shall be offered the tularemia vaccine at no charge. Individuals that decline the tularemia vaccine must sign a declination form that will be kept on file with ROHP.

The use of tularemia-causing bacteria is strictly regulated by the IBC and must be conducted in designated BSL3 facilities.

Herpes B virus
Cercopithecine herpesvirus 1 (*Herpesvirus simiae* or B-virus) is an endemic infection in Old World

primates of the genus *Macaca*, which is the species most commonly used in biomedical research. It is assumed that all existing animals in the United States are carriers.

Although herpes B virus is relatively benign in the macaque monkey, it can cause rapidly ascending encephalomyelitis in humans with a fatality rate of approximately 80%. The most common routes of transmission of the virus are through bites, scratches, splashes, or cuts.

All research involving non-human primates must be approved by both the IACUC and the IBC. Additional occupational health screening and PPE requirements are described in this manual.

For a detailed description of a specific pathogen that has the potential to cause a laboratory acquired infection (LAI), please check on ROHP website for "Agent Information Sheets".

Chapter 3
List of Regulations and Guidelines

The following is a summary of federal, state, and local agency regulations and guidelines that either regulate or provide guidelines covering the use of biological agents:

- Centers for Disease Controls and Prevention and the National Institutes of Health: *Biosafety in Microbiological and Biomedical Laboratories* (BMBL), 6th Edition, 2020. This document contains guidelines for microbiological practices, safety equipment, and facilities that constitute the four established biosafety levels. The BMBL is generally considered the standard for biosafety and is the basis for this manual.

- National Institutes of Health: *Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules* (NIH Guidelines). This document provides guidelines for constructing and handling recombinant or synthetic nucleic acid molecules and organisms containing those molecules. Although these guidelines are not subject to regulatory enforcement, institutions that receive any NIH funding for research involving recombinant or synthetic nucleic acid molecules are required to comply with these guidelines as a condition of funding. This document requires that each institution establish an IBC with the authority to approve proposed research involving recombinant or synthetic nucleic acid molecules using the NIH guidelines as the minimum standard.

- Occupational Safety and Health Administration: *Bloodborne Pathogens*. This regulation covers occupational exposure to human blood and other potentially infectious materials, including human tissue and cells. OSHA specifies a combination of engineering controls, work practices, and training to reduce the risk of infection. Personnel potentially exposed to human blood and other potentially infectious material must be offered immunization against hepatitis B and receive annual training. Personnel who work with HIV or hepatitis B in a research laboratory must receive additional training and demonstrate proficiency in working with human pathogens.

- BPHC*: Biological Laboratory Regulation* (passed January 16, 2019) and Biological Laboratory *Regulations Implementation & Enforcement* Guidelines (passed October 15, 2019). These regulations require that all institutions in the City of Boston that work with recombinant DNA molecules or that operates BSL3 or BSL4 laboratories be licensed by BPHC. These regulations require strict adherence to the CDC/NIH guidelines, as well as other regulations that the BPHC's Board of Health and Hospitals may apply. *Disease Surveillance and Reporting Regulation* (passed in 2019) requires all institutions in the City of Boston that engage in research with select agents, Risk Group 4 agents, and other agents named by BPHC as high-risk agents to be registered and maintain disease surveillance and reporting programs in effect to minimize potential exposures to these high-risk agents.

- Commonwealth of Massachusetts Department of Public Health: The Center for Environmental Health regulates the storage and disposal of potentially infectious material, and includes requirements for labeling and recordkeeping.

Select Agent Rule

- Department of Health and Human Services (HHS) 42 CFR Part 73 and United States Department of Agriculture (USDA) 7 CFR Part 331 and 9 CFR Part 121 Possession, Use, and Transfer of

Select Agents and Toxins Final Rule, effective December 4, 2012.These regulations require institutions that possess, use, or transfer certain biological agents and toxins ("select agents") to be registered and approved by DHHS and/or APHIS. Specific requirements are described in Chapter 10. Additionally, a subset of select agents and toxins have been designated as Tier 1 because they pose the greatest risk of deliberate misuse with significant potential for mass casualties or devastating effect to the economy, public and the environment.

Other Regulatory Requirements

- U.S. Department of Transportation and the International Air Transportation Authority: These organizations have strict requirements governing the packaging, shipment and transportation of hazardous materials, including biological agents. Chapter 11 provides information on shipping regulations.

- Centers for Disease Control and Prevention: The CDC has established specific regulatory requirements for importation or transportation of etiologic agents, which include a permit application that must be submitted and approved *prior* to any such importations. The federal regulation governing the importation of etiologic agents is USPHS 42 CFR - Part 71 Foreign Quarantine. Part 71.54, Etiologic agents, hosts, and vectors.

- U.S. Department of Agriculture, Animal and Plant Health Inspection Service, and Veterinary Services: USDA, APHIS, and VS regulate the importation of animals and animal-derived materials to ensure that exotic animal and poultry diseases are not introduced into the United States. Generally, a USDA veterinary permit is needed for materials derived from animals or exposed to animal-source materials. Materials that require a permit include animal tissues, blood, cells or cell lines of livestock or poultry origin, RNA/DNA extracts, hormones, enzymes, monoclonal antibodies for *in vivo* use in non-human species, certain polyclonal antibodies, antisera, bulk shipments of test kit reagents, and microorganisms, including bacteria, viruses, protozoa, and fungi. Exceptions to this requirement are human and non-human primate tissues, serum, and blood.

- U.S. Department of Commerce, Bureau of Industry and Security: The DOC has specific regulatory requirements for exportation of biological materials. These regulations are both agent and country specific and must be followed strictly. Link here for a basic overview of U.S. Export Controls for Biological Materials.

- Massachusetts Department of Public Health (MADPH): The MADPH regulates the management of biological wastes in the state (105 CMR 480) and also inspects BSL3 laboratory spaces on a regular basis.

- United States Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern (DURC): The policy addresses institutional oversight of DURC, which includes policies, practices, and procedures to ensure DURC is identified and risk mitigation measures are implemented, where applicable. The fundamental aim of this oversight is to preserve the benefits of life sciences research while minimizing the risk of misuse of the knowledge, information, products, or technologies provided by such research.

- IBC: The IBC has promulgated a number of specific policies and procedures that are incorporated into this document as requirements or have been included as appendices.

Chapter 4
Biosafety Principles

The risk of exposure to biological agents in a research environment depends on a number of factors (e.g., the agent, its virulence, subject's susceptibility, route of transmission, etc.). In general, the biosafety procedures followed are designed to prevent such exposures by containing the agents being handled and using the appropriate types of PPE. To properly design the containment, it is important to recognize the potential routes of transmission for the given agent.

Routes of Transmission

Skin and Mucous Membrane Contact
Procedures, such as decanting of liquids, pipetting, opening of screw caps, vortexing, streaking agar plates, and inoculation of animals, can potentially result in the generation of splatters of infectious droplets, as well as direct contact with infectious material. Direct contact to the mucous membranes of the eyes, nose, and mouth is considered a route of exposure. Appropriate eye and face protection should be used when performing work that generate splashes.

Ingestion
Performing mouth pipetting is prohibited in the laboratory. It presents a risks of ingesting infectious material. Touching the face and mouth when working can cause an oral exposure to the infectious material being handled. Storage of food or drinks and their consumption, and wearing of contact lenses in the laboratory is prohibited.

Laboratory personnel should refrain from the use of personal electronic mobile devices such as cell phones, headphones, and earbuds when working in the laboratory. They can cause distractions and could potentially become contaminated.

Percutaneous Inoculation
Use of syringes and needles presents the greatest risk of exposure through inoculation. Accidental inoculation can also occur as a result of cuts and scratches from contaminated items including syringes used for animal inoculations, as well as animal bites.

Inhalation
Certain procedures have the potential for generation of respirable aerosols, including sonication, centrifugation, "blowing out" of pipettes, heating inoculating loops, and changing bedding from the cages of infected animals. Aerosol refers to a droplet of 5 microns or less in diameter that can potentially be suspended in air for some amount of time. Aerosols may contain infectious particles.

Containment
The term "containment" is used to describe safe methods for handling infectious agents in the laboratory environment. The purpose of containment is to reduce or eliminate exposure of laboratory workers, other people, and the outside environment to potentially hazardous agents. The four elements of containment include administrative controls, work practices, personal protective equipment, and facility design.

Primary Containment
The protection of personnel and the immediate laboratory environment from exposure to infectious agents is provided by good microbiological techniques, use of appropriate PPE, and the use of appropriate safety equipment, such as the Biological Safety Cabinets (BSC).

Secondary Containment
Protecting the laboratory's external environment from exposure to infectious materials is accomplished by a combination of the facility design and safe operational practices. The risk evaluation of the work to be done with a specific agent will determine the appropriate combination of these elements

Safety Equipment

Safety equipment includes biological safety equipment, sealed containers, safety centrifuge cups, down-draft tables, and other engineered controls designed to minimize exposure to biological agents. Biological safety cabinets are among the most important safety equipment for protection of personnel and the laboratory environment, and most also provide product protection. Safety equipment is most effective at minimizing exposure when workers are trained in the proper use of such equipment and the equipment is regularly inspected and maintained.

Biological Safety Cabinets (BSC)
Proper use of a BSC provides a high level of containment that protects the operator from exposure while providing some protection from contamination of the material being handled within the work environment.

Because of its importance in providing containment and safety protections in the laboratory, a BSC is considered one of the most critical piece of safety equipment in the biological laboratories. When used appropriately, BSCs are designed to capture aerosols that may be generated during work with biological materials. The BSC is equipped with a high efficiency particulate air (HEPA) filtration that filters the air in BSC before being recirculated or exhausted. There are three types of BSCs (Class I, II, and III) used in laboratories. Open-fronted Class I and Class II BSCs are containment devices that provide a primary barrier offering significant levels of protection to laboratory personnel and to the environment when used in combination with good laboratory technique.

The Class I BSC is suitable for work involving low-to-moderate risk agents where there is a need for containment, but not for product protection. It provides protection to personnel and the environment from contaminants within the cabinet but does not protect the work within the cabinet from "dirty" room air.

The Class II BSC protects the material being manipulated inside the cabinet (e.g., cell cultures, microbiological stocks) from external contamination. It meets requirements to protect personnel, the environment, and the product. The two basic types of Class II BSCs are Type A and Type B. The primary difference between the two types may be found in the ratio of air that is exhausted or recirculated and the manner in which exhaust air is removed from the work area.

The Class III BSC is typically used to work with highly infectious microbiological agents including those classified as RISK Group IV or agents requiring a BSL4 laboratory. It provides the maximum protection to personnel, the environment, and the product. Another type of device that is typically referred to as a "laminar flow" or a "clean bench" can sometimes be seen used in the lab. It is important to note that this device *must not* be utilized for work with biohazardous or chemically hazardous agents. These units provide *product protection* by ensuring the product is exposed only to clean HEPA-filtered air. They do not provide protection to personnel working or the environment.

PIs are responsible for ensuring the proper maintenance of lab equipment. BSCs used as primary barriers must be certified annually by a qualified vendor. Contact the Biosafety Officer or the EHS for

information about testing and certification vendors or other BSC-related information.

Proper operation and maintenance of a BSC requires knowledge of how the system operates, as well as training and experience in effective techniques for working within the cabinet volume without compromising its functions. Additional details concerning the design and use of BSCs are provided in Appendix C.

Two specialized forms of quality control are strongly recommended for all BSCs and are required for cabinets used to contain Risk Group 2 or higher agents:

- At least daily, or each time the BSC is operated, the operator or user should observe the magnahelic gauge and note its relative position. Magnahelic gauges measure the pressure drop across the outlet HEPA filter and are important indicators of filter integrity and loading. The gauge will typically indicate the same measurement over a long period of time. A significant change in the reading over a short period of time may indicate an issue including clogging or a leaking HEPA filter. In such cases, the BSC should not be used until the problem is identified and resolved. ***If the BSC located within a laboratory does not have a magnahelic gauge, users must understand the operation of the airflow monitor, controls, and alarm settings.***

- The BSC must be tested and recertified annually or after it is moved to a different location. Testing and recertification is performed by a contractor certified to test the BSC. EHS can provide information on qualified vendors. The certification ensures that the BSC is meeting its operating specifications and providing maximum protection. In addition, certifiers provide service and preventive maintenance for BSC and can often forecast expensive requirements like HEPA filter replacements, allowing PIs to budget for the event.

- If BSC recertification is required, the recertification must be completed before the current certification expires. If the certification lapses, the BSC may not be used for BSL2 or higher procedures until it is recertified. The lab will report the lapsed recertification to EHS immediately. EHS will inform the PI and lab workers not to use the BSC and affix an "OUT OF SERVICE" notice and assist the lab to get the BSC recertified. Unless a good reason exists for more frequent certification, a one-year certificate life is appropriate. The certificate will generally expire on the last day of the month in which the certification was performed, one year later (for example, a certificate issued on June 2, 2007 will expire on June 30, 2008).

Personal Protective Equipment (PPE)
PPE is designed to protect the wearer against chemical, biological, radiological, or mechanical irritants. Different types and levels of PPE may be required for individuals, depending upon each person's role within a laboratory, the materials handled, and the work being performed.

In order to ensure that all laboratory faculty, staff, students, affiliates and visitors are sufficiently protected from the hazards present in the workplace, the Personal Protection Equipment in Laboratories Policy has established the minimum PPE requirements, based on best laboratory practices.

Facility Design

The design of a facility is important in providing a barrier to protect people working inside and outside the laboratory, as well as to protect people or animals in the community from infectious agents that may be accidentally released from the laboratory. Facility design must be commensurate with the laboratory's

function and the recommended biosafety level for the agent being used or stored.

The recommended secondary barrier(s) will depend on the risk of transmission of specific agents. For example, the exposure risks for most laboratory work in BSL1 and BSL2 facilities will be direct contact with the agents or inadvertent contact exposures through contaminated work environments. Secondary barriers in these laboratories may include separation of the laboratory work area from public access; availability of decontamination equipment (e.g., autoclave*); and handwashing facilities. In BSL3 facilities, additional safeguards, such as directional airflow airlock-controlled entry and exiting, a shower used for personnel to shower out may be required.

As the risk for aerosol transmission increases, higher levels of primary containment and multiple secondary barriers may become necessary to prevent infectious agents from escaping into the environment. Such design features could include specialized ventilation systems to ensure directional airflow; air treatment systems to decontaminate or remove agents from exhaust air; controlled access zones; an airlock at the laboratory entrance; or separate buildings or modules for physical isolation of the laboratory building itself.

***Note:** *It is IBC policy that autoclaves used to sterilize biohazardous materials be validated quarterly using a sporulation test and that validation records be kept (see Appendix D). Unless sterilization of the waste is otherwise specified by the IBC, solid biohazardous waste should be directly disposed into red bags as medical waste without autoclaving.*

Biosafety Levels

Four biosafety levels (BSLs) represent combinations of laboratory practices and techniques, safety equipment, and laboratory facilities. Each combination is specifically appropriate for the operations performed and the documented or suspected routes of transmission of the infectious agents, as well as for the laboratory function or activity. The recommended biosafety level for an organism represents the conditions under which the agent can be ordinarily handled safely.

NIH's *Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules* classifies "human etiologic agents" on the basis of their relative pathogenicity. Agents are categorized into four risk groups (RG).

As a general rule for selecting the appropriate laboratory containment, the biosafety safety level (BSL) selected should correspond with the highest risk group (RG) category of the organisms involved. For example, work with vaccinia virus which is a Risk Group 2 (RG2) agent, should be conducted at BSL2 or higher and *Mycobacterium tuberculosis* which is a Risk Group 3 (RG3) should be conducted at BSL3.

Descriptions of biosafety levels, as well as assigned biosafety levels for specific organisms, are contained in the CDC/NIH document, *Biosafety in Microbiological and Biomedical Laboratories* (BMBL) 6th edition. The BMBL outlines four biosafety levels, summarized below:

Biosafety Level (BSL)	**Agents**	**Practices**	**Primary Barriers and Safety Equipment**	**Facilities (Secondary Barriers)**
1	Not known to cause disease in healthy adults; RG1	Standard microbiological practices	No primary barriers required. PPE: laboratory coats and gloves; eye, face protection, as needed	Open bench top, sink required
2	Associated with human disease, which is rarely serious and for which preventive or therapeutic interventions are *often* available; RG2	BSL1 practice plus: Limited access Biohazard warning signs Sharps precautions Biosafety manual BMBL BSL2 practices and procedures	*Primary barriers:* BSCs or other physical containment devices used for manipulations of agents that cause splashes or aerosols of infectious materials. *PPE:* lab coats; gloves; eye/face protection as needed.	BSL1 plus: Autoclave available BMBL BSL2 facility design
3	Associated with human disease for which preventive or therapeutic interventions *may be* available; RG3	BSL2 practice plus: Controlled access Decontamination of all waste Decontamination of lab clothing before laundering Baseline serum as recommended by Occupational Health BSL3 Biosafety Manual BSL3 SOPs BSL3 Emergency Response Plans	*Primary barriers:* BSCs or other physical containment devices used for all open manipulations of agents. *PPE:* protective lab clothing; gloves; face, eye and respiratory protection as needed.	BSL2 plus: Physical separation from access corridors Self-closing, double-door access Exhausted air not recirculated Negative airflow into laboratory BMBL facility design and verification

		(ERPs) BMBL BSL3 practices and procedures		
4	Agents are likely to cause serious or lethal human diseases for which preventive or therapeutic interventions *are not usually* available; RG4	BSL3 practices plus: BMBL BSL4 practices and procedures BSL4 Biosafety Manual BSL4 CDC/BPHC Plans BSL4 SOPs BSL4 ERPs	*Primary barriers:* All procedures conducted in the BSC in combination with full-body, air-supplied, positive-pressure personnel suit.	BSL3 plus: BMBL BSL4 facility design

Note: *Consult the BMBL 6th edition for a more complete description of the four biosafety levels, as well as recommended biosafety levels for specific organisms.*

In addition to the four biosafety levels described above, there are also four biosafety levels for work with infectious agents in vertebrate animals, referred to as the Animal Biosafety Level (ABSL).

ABSL	Agents	Practices	Primary Barriers and Safety Equipment	Facilities (Secondary Barriers)
1	Not known to consistently cause disease in healthy human adults; RG1	Standard animal care, use, and management practices, including appropriate medical surveillance programs.	As required under the Program of Veterinary Care and Use of Animals at BU for normal care, use, and handling of each species. *PPE*: laboratory coats and gloves; eye, face protection, as needed	Standard animal facility, remote housing facility, or laboratory No recirculation of exhaust air Directional air flow recommended Hand washing sink recommended
2	• Agents associated with human disease; • Hazard: percutaneous injury, ingestion, mucous membrane exposure RG2	• ABSL1 practices plus: • Limited access Biohazard warning signs • Sharps precautions Biosafety manual • Decontamination of all infectious wastes and of animal cages prior to washing	• ABSL1 equipment plus primary barriers: • Containment equipment appropriate for animal species. • *PPE*: laboratory coats, gloves, face, eye and respiratory protection as needed.	• ABSL1 facility plus: • Autoclave available • Hand washing sink available in the animal room. • Mechanical cage washer recommended. • Negative airflow into animal and procedure rooms recommended
3	Indigenous or exotic agents that may cause serious or potentially lethal disease through the inhalation route of exposure; RG3	ABSL2 practices plus: Controlled access Decontamination of clothing before laundering Cages decontaminated before bedding removed Disinfectant foot bath as needed	ABSL2 equipment plus: Containment equipment for housing animals and cage dumping activities Class I, II or III BSCs available for manipulative procedures (inoculation, necropsy) that may create infectious aerosols. *PPE*: appropriate respiratory protection	ABSL2 facility plus: Physical separation from access corridors Self-closing, double-door access Sealed penetrations Sealed windows Autoclave available in facility Entry through ante-room or airlock Negative airflow into animal and procedure rooms Hand washing sink near exit of animal or procedure room

4	Dangerous/exotic agents which post high risk of aerosol transmitted laboratory infections that are frequently fatal, for which there are no vaccines or treatment. Agent with a close or identical antigenic relationship to an agent requiring BSL4 until data are available to redesignate the level. Related agents with unknown risk of transmission life-threatening disease; RG4	ABSL3 practices plus: Entrance through change room where personal clothing is removed and laboratory clothing is put on; shower upon exiting All wastes are decontaminated before removal from the facility	ABSL3 equipment plus: Maximum containment equipment (e.g., Class III BSC or partial containment equipment in combination with full body, air-supplied, positive-pressure personnel suit) used for all procedures and activities	ABSL3 facility plus: Separate building or isolated zone Dedicated supply and exhaust, vacuum, and decontamination systems Other requirements outlined in the text

Note: *Consult the BMBL 6th edition for a more complete description of the four Animal biosafety levels, as well as recommended containment requirements for biosafety specific type of animals.*

Chapter 5
Laboratory Biosafety Practices

The foundations of protective practices in a laboratory lie in an individual's laboratory experience, technical knowledge, personal work habits, and attitude toward laboratory safety. Unlike administrative controls, which are behaviors dictated by regulation or laboratory policy, the term "protective behavior" is used to define an innate part of each individual worker's personal approach to the laboratory environment. As such, "protective behaviors" form the first and most important line of defense against injury or exposure in the biomedical workplace.

Basic Laboratory Practices

Prudent practices and good techniques are of primary importance in laboratory safety. Both are based on sound technical knowledge, experience, common sense, and an attitude of courtesy and consideration for others.

Techniques and practices are spelled out in detail as "Standard Microbiological Practices" in the CDC/NIH's *Biosafety in Microbiological and Biomedical Laboratories,* 6th edition and the NIH's *Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*, as well as in the National Research Council's *Biosafety in the Laboratory - Prudent Practices for the Handling and Disposal of Infectious Materials* (National Academy Press, Washington, D.C., 1989). Many laboratory safety text and reference books also contain good information.

At a minimum, the seven basic rules of biosafety, based on the National Research Council's *Prudent Practices* document, should be the basis of any personal laboratory work ethic. They are noted in Table 1.

Table 1: Biosafety practices and blocked routes exposure

Biosafety Practice	Routes of Exposure Blocked
1.Do not mouth pipette.	Inhalation, ingestion, skin, and mucous membrane contact
2. Manipulate infectious fluids carefully to avoid spills and the production of aerosols.	Inhalation, skin, and mucous membrane contact
3. Restrict use of needles, syringes, and other sharps to those procedures for which there are no alternatives; dispose of sharps in leak- and puncture-proof containers.	Percutaneous, inhalation
4. Use lab coats, gloves, safety eyewear, and other personal protective equipment.	Skin and mucous membrane contact
5. Wash hands after all laboratory activities, following the removal of gloves, and immediately following contact with infectious agents.	Skin and mucous membrane contact
6. Decontaminate work surfaces before and after	Skin and mucous membrane contact

use, and immediately after spills.	
7. Do not eat, drink, store food, or smoke in the laboratory.	Ingestion, skin, and mucous membrane contact

Laboratory Practice and Technique

The most important element of containment is the strict adherence to standard microbiological practices and techniques.

Persons working with infectious agents or infected materials must be aware of potential hazards and be trained and proficient in the practices and techniques required for handling such material safely. The PI is responsible for ensuring that laboratory personnel are properly trained; the PI may delegate the provision of training to the laboratory supervisor or a designee, but the responsibility remains with the PI.

Each laboratory should adopt this Biosafety Manual and develop written procedures if there are lab-specific hazards not addressed in the Manual or those needing specific additional details that will or may be encountered. Personnel should be advised of special hazards and should be required to read and to follow the required practices and procedures. A scientist trained and knowledgeable in appropriate laboratory techniques, safety procedures, and hazards associated with the handling of infectious agents must direct laboratory activities.

When standard laboratory practices are not sufficient to control the hazard associated with a particular agent or laboratory procedure, additional measures may be needed. The PI is responsible for selecting additional safety practices, which must be in keeping with the hazard associated with the agent or procedure. The BSO or EHS may be consulted for more information.

Laboratory personnel safety practices and techniques must be supplemented by appropriate facility design and engineering features, safety equipment, and management practices.

Each laboratory will designate a person as the Laboratory Safety Coordinator (LSC).

Note: *Although each individual is responsible for his or her own safety, the PI has ultimate responsibility for ensuring that persons working in the laboratory are adequately trained, follow the prescribed safety measures and wear appropriate PPE*

Laboratory Housekeeping and Personal Hygiene
Personal safety is greatly enhanced by keeping work space areas neat, clean, and orderly. Injuries and exposures are more likely to occur in poorly maintained, disorderly areas.

If work space is shared, the importance of maintaining a neat, clean area increases significantly. Persons that share work spaces must understand their responsibilities to keep the work area and equipment clean and properly maintained. Coworkers must rely on one another to maximize efficiency and safety. Personal materials should be properly labeled, waste discarded, and the shared space disinfected or cleaned prior to leaving it for the next user.

The following guidelines should be observed in the laboratory:

- Routine housekeeping ensures work areas are free of sources of contamination and hazards;

- Establish and follow housekeeping procedures in order to maintain a clutter free and well organized work environment. Laboratory personnel are responsible for the routine cleaning of laboratory benches, equipment, and areas that are used during research work;
- Access to exits, sinks, eyewashes, emergency showers, and fire extinguishers must not be blocked;
- The workplace should be free of physical hazards;
- Follow electrical safety. Use of extension cords are temporary measures and placement must avoid heavily traffic areas. Equipment should be properly grounded. Overloaded electrical circuits and the creation of electrical hazards in wet areas are to be avoided;
- Work benches should be free of infrequently used chemicals, glassware, and equipment;
- Do not store unnecessary items on floors, under benches, or in corners;
- All compressed gas cylinders should be properly secured.

Personal hygiene, including proper handwashing techniques, is also a means by which to enhance personal protection in the laboratory. Scrubbing immediately after de-gloving ensures that contamination of the hand by glove micropuncture or prior exposure is cleaned.

The laboratory is also an inappropriate place to perform personal cosmetic tasks, such as applying makeup, cleaning or trimming fingernails, or brushing hair including wearing or removal of contact lenses. These activities provide new opportunities for exposure and contribute to retrograde contamination of the laboratory environment.

Universal Precautions

Prudent practices often overlap with a set of practices known as "universal precautions." The overarching universal precaution espoused by the Bloodborne Pathogens (BBP) Standard (see Appendix K for a list and more detailed discussion of universal precautions) should be adopted by all laboratory personnel.

Universal precautions require that all human blood and tissues be handled as though they are infectious. Adopting and applying universal precautions to all laboratory reagents clearly creates a heightened awareness of potential risk and adds another level of caution to activities involving reagents.

Administrative Controls

Administrative controls are policies and procedures designed to assist with the safe handling of potentially hazardous biological materials. They include training, medical surveillance, vaccinations, access control, etc.

Biological Hazard Information

Laboratory workers must be knowledgeable about the hazards associated with the biological agents present in the laboratory and have hazard information available to them. The following are sources of hazard information for biological agents.

Microbial Agents
The CDC/NIH's *Biosafety in Microbiological and Biomedical Laboratories* (BMBL) 6th edition has descriptions of biosafety levels and recommended biosafety practices for specific biological agents. The Canadian Laboratory Centre for Disease Control maintains Material Safety Data Sheets for microbial

agents.

Toxins
Isolated biological toxins are chemical hazards, although many such toxins produce adverse effects at doses significantly below that of "traditional" laboratory chemicals. Laboratory use of isolated toxins falls under the BU Lab Safety Manual and Chemical Hygiene Plans, and Safety Data Sheets (SDSs) must be maintained and available. SDSs for a specific toxin should be obtained from the vendor upon receipt of the toxin. Toxicology textbooks, such as *Casarett & Doull's Toxicology,* are also good sources of hazard information for toxins. Biological toxins that are listed under the select agent category and are over the permitted quantities are regulated by CDC/APHIS. The IBC also requires laboratories to register these toxins with their office regardless of the amount.

Each laboratory should adopt this Biosafety Manual, the CDC/NIH publications *Biosafety in Microbiological and Biomedical Laboratories, 6th edition,* and *Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules,* However, because these cover relatively general topics, individual laboratories should develop written procedures if there are lab-specific hazards not addressed in the Manual or CDC/NIH documents that cover the biosafety concerns and laboratory procedures for that particular laboratory.

For example, laboratory-specific SOPs should address safe manipulation of specific organisms, specific exposure control methods, and specific decontamination and waste-handling requirements. Appendix U provides a recommended standard format for SOPs, and laboratories are encouraged to use this format to effectively convey the biosafety information (including use of pictures and illustrations). The laboratory-specific SOPs do not need to duplicate the more general SOPs contained in this manual or the CDC/NIH documents, but should serve as supplements.

Security and Inventory of Biological Agents

Each PI must develop site-specific criteria that safeguard all biological materials, regardless of their risk group, from unauthorized removal. It is the PI's responsibility to ensure that his or her laboratory implements sufficient security measures and procedures to prevent unauthorized access to biological agents.

Select agents (see Chapter 10) and other higher-risk microorganisms and toxins must be stored in a locked container, and a detailed inventory must be maintained per CDC requirements. In many instances, during the application review process, the IBC will review the proposed acceptable safeguards and either approve or recommend enhancements to the proposed plans.

Prevention of Aerosols and Droplets

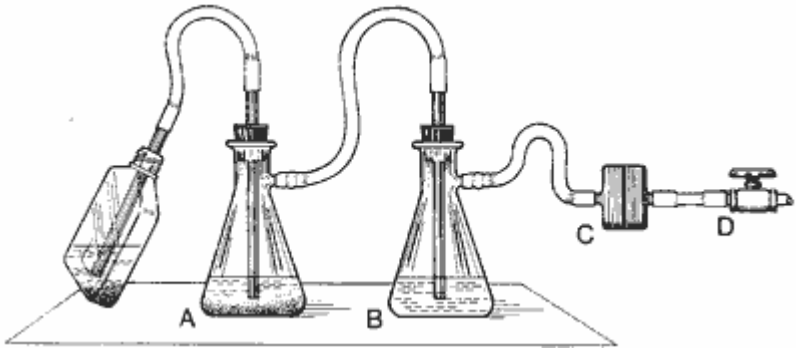
Handling of liquids or dry powders may generate aerosols or droplets. In practice, high-energy procedures, such as centrifuging, vortexing and mixing, tend to produce respirable aerosols that stay airborne for extended periods and are small enough to be inhaled, while low-energy procedures, including opening containers and streaking plates, produce droplets that settle quickly on surfaces, skin, and mucous membranes.

Utilization of Biological Safety Cabinets
In general, the following guidelines are recommended when using biological safety cabinets (BSCs):

- The BSC should be certified when it is initially installed and recertified after it is moved and installed into its new place, and annually thereafter (for information on cabinet certification, call (617) 358-7840 at BUMC and (617) 353-4094 at CRC.
- The magnahelic gauge should be checked each time before the BSC is used. This gauge will normally run at a relatively fixed value. When it deviates significantly, the cabinet should not be used until the cause of the deviation has been identified and fixed.
- Personnel should know how the BSC works.
- Personnel should be familiar with the safe and effective use of any UV lamps inside the BSC (if equipped) and use appropriate precautions to avoid any UV exposure.

  Note*: EHS has discouraged the use of UV lamps because they have a short half-life and are difficult to maintain.*
- The BSC's protective airflow pattern should not be disrupted. The user should avoid rapid arm movement, and heavy foot-traffic in front of the BSC while in use. Also avoid opening and closing nearby laboratory doors, as those activity may disrupt the airflow pattern and reduce the cabinet's effectiveness.
- Preplanning of the work and organization of necessary materials needed minimize the need to exit and reenter the BSC work space.
- Avoid the accumulation of materials inside the BSC and keep only the materials needed to conduct the work to reduce the disruption of airflow.
- The BSC should be left running whenever the cabinet is in use.
- Use of only appropriate disinfectants to avoid damaging the cabinet's interior.
- Work surface should disinfected with an appropriate chemical disinfectant. If 10% bleach solution is used, it must be followed by 70% ethanol to prevent surface damage from the bleach solution. Each item needed for the planned procedures should be wiped off with 70% ethanol and placed in the cabinet.
- After the work volume is set up, the BSC should run for at least 5 minutes to allow for stabilization of air flow before starting any procedure.
- If an equipment such as a centrifuge or blender could create air turbulence in the BSC, it should be placed in the back one-third of the cabinet. All other work should be stopped while this equipment is operating.
- Open flames should be avoided because they create air flow turbulence that may compromise sterility. In addition, the heat buildup may damage the HEPA filters. If a flame is necessary, a burner with a pilot light should be used. Electric devices, such as loop sterilizers, are often satisfactory alternatives to open flames.
- A pan with disinfectant and/or a sharps container should be placed inside the BSC for pipette/sharps disposal. Vertical pipette discard canisters on the floor outside the cabinet should be avoided.
- Contaminated and clean items should be segregated, and personnel should work from "clean to dirty." The biohazardous waste collection bag should be in a rigid container. Do not block air flow into the front and rear exhaust grilles.
- Move arms slowly when removing items from or introducing items into the cabinet work volume.
- Protect the facility vacuum system from biohazards by using dual aspirator flasks in series (A and B) and placing an in-line hydrophobic HEPA filter (C) between the vacuum trap and the source valve (D) in the cabinet:

  Note*: EHS requires that the flasks are placed in a secondary container, such as a Nalgene tub*.



- All spills in the cabinet should be cleaned immediately. Upon clean up, the BSC should be allowed to filter and purge its air and work should not resume for 10 minutes.
- When work is complete, all materials should be removed from the BSC and all interior surfaces should be wiped with an appropriate disinfectant.
- Gloves must be removed before exiting the BSC, and after touching or handling contaminated materials. Discuss the appropriateness of other alternatives, such as use of double gloves, with the Biosafety Officer before deploying as part of the protocol.
- Laboratory coats must be removed and hands thoroughly washed before leaving the laboratory.

Utilization of Pipettes

Pipettes are used for volumetric measurements and the transfer of fluids that may contain infectious, toxic, corrosive, or radioactive agents. Laboratory-associated infections have occurred from oral aspiration of infectious materials, mouth transfer via a contaminated finger, touching face (eyes, nose, etc.) and inhalation of aerosols. Exposure to aerosols may occur when liquid from a pipette is dropped onto the work surface; when cultures are mixed by pipetting; or when the last drop of an inoculum is blown out.

The following outlines safe pipetting techniques to minimize the potential for exposure to hazardous materials:

- Do not mouth pipette. Always use a pipetting aid.
- If working with biohazardous or toxic fluid, confine pipetting operations to a biological safety cabinet.
- Always use cotton-plugged pipettes when pipetting biohazardous or toxic materials, even when safety pipetting aids are used.
- Do not prepare biohazardous materials by bubbling expiratory air through a liquid with a pipette.
- Do not forcibly expel biohazardous material out of a pipette.
- Never mix biohazardous or toxic material by suction and expulsion through a pipette.
- When pipetting, avoid accidental release of infectious droplets.
- Use “to deliver” pipettes rather than “to contain” pipettes, which require “blowout.” Be careful not to dislodge the residual liquid.
- Do not discharge material from a pipette at a height. Whenever possible, allow the discharge to run down the container wall.
- Place contaminated, reusable pipettes horizontally in a pan containing enough liquid disinfectant to completely cover them. Autoclave the pan and pipettes as a unit before processing them for reuse.

- Discard contaminated, broken, or intact Pasteur pipettes and broken glass in a sharps container. Dispose of the container properly when it is, at most, three-fourths full.
- Pans or sharps containers for contaminated pipettes should be placed inside the BSC, if possible.
- Proper procedures for disposal of plastic pipettes are presented in Chapter 9**.**

Utilization of Centrifugation
Hazards associated with centrifuging include mechanical failure and the creation of aerosols. To minimize the risk of mechanical failure, centrifuges must be maintained and used according to the manufacturer's instructions. Users should be properly trained and operating instructions that include safety precautions should be prominently posted on or near the unit.

Aerosols are created by activities such as filling centrifuge tubes, removing plugs or caps from tubes after centrifugation, removing supernatant, and re-suspending sediment pellets. A significant aerosol hazard can be created if a tube breaks during centrifugation.

To minimize the generation of aerosols when centrifuging biohazardous material, the following procedures are recommended:

- Use sealed tubes and safety buckets that seal with O-rings. Before use, inspect tubes, O-rings, and buckets for cracks, chips, erosions, bits of broken glass, etc. Do not use aluminum foil to cap centrifuge tubes because it may detach or rupture during centrifugation.
- Only use appropriate centrifuge tubes. Open and fill the centrifuge tubes, rotors, and accessories in a biological safety cabinet. Avoid overfilling centrifuge tubes to prevent closures from becoming wet. After tubes are filled and sealed, wipe them down with disinfectant.
- In the event of a tube breakage during centrifugation or an abnormal stoppage that could result into a spill in the centrifuge bucket, the bucket should be brought into the BSC and opened for inspection of potential breakage or spills. The bucket containing the spilled sample should be decontaminated inside the BSC and debris removed prior to reuse.
- Always follow the manufacturer's instructions when operating the centrifuge and balance the buckets, tubes, and rotors properly before centrifugation.
- Avoid decanting or pouring off supernatant; unless the supernatant must be retained, use a vacuum aspirator with appropriate in-line reservoirs and filters.
- Work in a BSC when re-suspending pelleted material. Use a swirling rotary motion rather than shaking. If shaking is necessary, wait a few minutes to permit the aerosol to settle before opening the tube.
- Small, low-speed centrifuges may be placed in the BSC during use to reduce the aerosol escape. High-speed centrifuges pose additional hazards. Precautions should be taken to filter the exhaust air from vacuum lines, to avoid metal fatigue resulting in disintegration of rotors, and to use proper cleaning techniques and centrifuge components. Manufacturers' recommendations must be meticulously followed to avoid metal fatigue, distortion, and corrosion.
- Avoid the use of celluloid (cellulose nitrate) tubes with biohazardous materials. Celluloid centrifuge tubes are highly flammable and prone to shrinkage with age. They distort on boiling and can be highly explosive in an autoclave. If celluloid tubes must be used, an appropriate chemical disinfectant must be used.

Utilization of Cryostats
Use of cryostats is very common in many research laboratories. These devices may pose potential hazards associated with sharp cutting edges and cold environments and should be handled with extra care.

The following guidelines should be followed when using cryostats:

- Frozen sections of unfixed human tissue or animal tissue infected with an etiologic agent pose a risk because freezing tissue does not necessarily inactivate infectious agents. Use of freezing propellants under pressure is not recommended with frozen sections because they may cause spattering of droplets of potentially infectious material.
- Appropriate gloves should be worn during preparation of frozen sections.
- When working with human or infected animal tissue, consider the contents of the cryostat to be contaminated and decontaminate it frequently with 70% alcohol.
- Ribbons and trimmings from the frozen tissue samples can accumulate in the cryostat during its use. The machine should be cleaned up and decontaminated routinely.
- Defrost and decontaminate the cryostat with a tuberculocidal hospital disinfectant once a week and immediately after use with tissue known to contain bloodborne pathogens, *M. tuberculosis,* or other infectious agents.
- Use disposable knife blades. Handle microtome knives or blades with extreme care. Cut-resistant gloves with stainless steel mesh or similar gloves should be worn when changing knife blades.
- Solutions used for staining potentially infected frozen sections should be considered contaminated.
- Always use the safely lock of the equipment before mounting or unmounting tissues or replacing the blade.

Utilization of Inoculating Loops
Flaming inoculating loops can result in spatter and the release of aerosols and droplets. Use of an electric microincinerator, or disposable loops are the preferred alternative, to minimizing this issue.

Use of Absorbent Materials
Work surfaces should be covered with absorbent paper or "diaper" sheets to absorb splashes and drips and to minimize the spread of contamination. The absorbent paper should be changed at the end of the laboratory procedure as part of the final cleanup, or at least daily during use.

Utilization of Miscellaneous Aerosol-Producing Devices and Activities
Use of any of the devices listed below results in considerable aerosol production. Blending, cell-disrupting, and grinding equipment should be used in a BSC when working with biohazardous materials.

Blenders
Safety blenders, are designed to prevent leakage from the bottom of the blender jar. They provide a cooling jacket to avoid biological inactivation and can withstand sterilization by autoclaving.

- Safety blender rotors used for infectious materials should be leak-proof. They should initially be tested with sterile saline or dye solution prior to use with any biohazardous material.
- The use of glass blender jars is not recommended because of the potential for breakage. If they must be used, glass jars should be coated with a polypropylene to prevent spraying of glass and contents in the event the blender jar breaks. The blender must be operated within a secondary containment basin.
- A towel moistened with disinfectant should be placed over the top of the blender during use.
- When opening blenders, be cognizant of potential contamination hazards in the form of droplets that might become airborne or fall on the surfaces; liquid residue on the cap; and possible expansion of the volume due to aeration.

- Before opening the blender jar, allow the unit to rest for at least one minute to allow the aerosol to settle.
- Placing the blender in a BSC will provide protection against airborne hazards and placement of a tray lined with absorbent pads would assist with contamination control.
- The device should be decontaminated promptly after use.

Lyophilizers
Depending on type and model, potential aerosol production may occur when material is loaded into or removed from the lyophilizer unit.

- If possible, sample material should be loaded in a BSC.
- The vacuum pump exhaust should be equipped with a filter to filter out any hazardous agents or, alternatively, the pump can be vented into a BSC.
- After lyophilization is complete, all surfaces of the unit that have been exposed to the agent should be disinfected.
- If the lyophilizer is equipped with a removable chamber, it should be closed off and moved to a BSC for unloading and decontamination.
- Handling of cultures should be minimized and vapor traps should be used wherever possible.

Sonicators
Sonication is the use of sound-wave energy for dispersion, disruption, or inactivation of biological materials, such as viruses. Sonicators generate sound waves at very high frequencies (~20,000 + Hz range), which is outside normal hearing range. The following are hazards associated with sonicators:

- *Noise*: Although the 20,000-Hz frequency is outside normal hearing range, there are other sources of noise, such as vibration from any loose equipment or other items on the bench or the liquid itself. If the noise levels are high, hearing protection devices should be worn.
- *Aerosols*: Aerosols present a more serious potential hazard and must be taken into consideration. Precautions listed for blenders and lyophilizers should be observed.

Ampoules
Glass ampoules have been widely used in packaging cultured materials. Opening ampoules containing liquid or lyophilized cultured material should be performed in a BSC to control any aerosol produced. Sealed-glass ampoules used to store biohazardous material in liquid nitrogen have exploded, causing eye injuries from glass microparticles in the snap of the ampoule. The use of polypropylene tubes (cryovials) eliminates this hazard. These tubes are available dust-free or pre-sterilized and are fitted with polyethylene caps with silicone washers. Heat-sealable polypropylene tubes are also available.

- Individuals should be trained on the safe handle and opening of glass ampoules.
- Gloves and protective eyewear must be worn when opening ampoules or cryovials.
- To open a sealed-glass ampoule, nick the neck of the ampoule with a file, wrap it in disinfectant-soaked disposable towel, hold the ampoule upright, and snap it open at the nick.
- Reconstitute the contents of the ampoule by adding liquid slowly to avoid aerosolization of the dried material.
- Mix the contents without bubbling and withdraw it into a fresh container. Discard the disposable towel and the ampoule's top and bottom as medical waste.

Loop Sterilizers and Bunsen Burners
Sterilization of inoculating loops or needles in an open flame generates small-particle aerosols that may contain viable microorganisms.

- Alternatively, disposable plastic loops and needles may be used for culture work where electric incinerators or gas flames are not available.
- Continuous flame gas burners should not be used in a BSC. These burners can produce turbulence that disturbs the cabinet's protective airflow patterns. Additionally, the heat produced by the continuous flame may damage the HEPA filter. If a gas burner must be used, one with a pilot light should be selected. Electric sterilizers should also be considered.

Personal Protective Equipment (PPE)

Personal protective equipment (PPE) must be provided without cost to personnel. Although not a substitute for the use of BSCs and good laboratory practices, PPE is considered a primary barrier to infectious agents and proper use will reduce the likelihood of infection. PPE is the least-desirable exposure control method because its failure results in direct exposure to the agent.

PPE is most effective when used to supplement primary control methods such as biological safety cabinets, safety centrifuge cups, and other containment devices. Appropriate clothing may also protect the experiment from contamination

The following PPE requirements apply to all individuals visiting research and teaching laboratories:
- Full-length pants, or equivalent must be worn at all times;
- Closed toe footwear, that covers the top of the foot, must be worn at all times; and
- Long sleeves or laboratory coat covering both arms.

All other individuals entering laboratory space must follow the PPE requirements described above for the visitor, as well as the following:
- Laboratory coats must be worn over personal clothing at all times;
- Long hair and facial hair must be secured or tied back;
- Flame resistant laboratory coats must be worn when working with pyrophoric chemicals, water reactive chemicals, and high volumes of flammable chemicals;
- Disposable gloves that are protective against the hazardous or potentially hazardous materials being used must be worn. Gloves must be replaced when soiled, contaminated or damaged; and
- Eye protection must be available and used when danger to splashing of hazardous or potentially hazardous materials could occur.

Respirators
Respirators are selected based on the hazard involved and the protection factor required. Certain laboratory and clinical situations require respiratory protection to prevent inhalation of infectious agents. Regulations, as well as good safety practice, require that personnel be medically evaluated, specifically trained, and fit tested **prior** to wearing respiratory protective equipment.

Contact EHS if respiratory protective equipment is required or if there are questions about the respiratory protection program.

Note: ***Use of respirators requires completion of the OSHA Respiratory Questionnaire for medical clearance from the ROHP, and fit testing by EHS***.

Further guidance on the use of PPE can be found in the Personal Protection Equipment in Laboratories Policy and Chemical Hygiene Plan.

Storage and Labeling of Biological Agents

Biological agents must be stored using leak proof and sealed containers. Containers must be clearly labeled with the identity of the agent and should include the universal biohazard symbol (see below) as physical space on the container permits. At a minimum, secondary (or outside) containers must include the universal biohazard symbol (identity of contents is also desirable).

Freezers, refrigerators, and other storage areas must also be labeled with the biohazard symbol; exceptions to this policy will be considered on an individual basis by the IBC. Waste and contaminated equipment or other objects to be decontaminated must also be labeled with the biohazard symbol.

Universal Biohazard Symbol

The OSHA Bloodborne Pathogen Standard specifically requires that containers of human blood or other potentially infectious material (OPIM), contaminated waste, and refrigerators, freezers, and other storage containers used to store or transport blood or OPIM be labeled with the universal biohazard symbol (fluorescent orange or orange-red):

Biohazard Labels and Signs

Each laboratory must have a sign at the entrance that provides safety information to visitors and service personnel. Room signs must contain designations for all laboratory hazards in use within the laboratory (carcinogens, acutely toxic agents, reproductive hazards, biohazards, radioactive materials, lasers, and magnetic fields). EHS will prepare the signs for each door in accordance with the requirements of NFPA 704 and BSL3.

Biohazard signs will be posted at the following:

- Entrances to laboratories that use agents classified as BSL2, BSL3 or BSL4.
- Entrances to animal rooms used for housing animals infected with ABSL2, ABSL3, or ABSL4 agents.

For examples of BU door signage, see Appendix S.

Certain other areas and pieces of equipment within a laboratory may also require signs. Refrigerators, freezers, cabinets, and other storage facilities require the biohazard symbol whenever they are used to store infectious agents of Risk Group 2 or higher; human blood or blood products; unfixed tissues; cell or organ cultures; body fluids; or excreta. Large pieces of equipment for handling such materials (e.g., centrifuges, biological safety cabinets) must be similarly labeled.

Chapter 6
Laboratory Training

Training is a critical component of any integrated biological safety program. Training is intended to provide the understanding, technical knowledge, and tools that the trainee can use to improve his or her daily laboratory safety practices.

At a minimum, all personnel working with biological materials must have training in the following areas prior to the start of their experiments:

- Knowledge of this biosafety manual;
- Knowledge of hazards of the agent or sample being used:
- Experimental procedures to be performed;
- Safe use of laboratory equipment:
- Proper use of personal protective equipment:
- Procedures to follow in the event of an exposure incident;
- Decontamination and spill clean-up procedures;
- Safe handling methods for any infectious agent and/or recombinant DNA (rDNA) they might be handling;
- Proper methods for transporting infectious agents and other biohazardous materials;
- Proper waste handling, storage. and disposal;
- Procedures to follow and reporting after an injury;
- Bloodborne Pathogens Standard (if they work with human blood or blood products, unfixed tissue, body fluids, organ, or primary tissue and/or samples contaminated with bloodborne pathogens);
- BPHC requirements (see Appendix O for a summary); and
- Other specialized training as deemed appropriate by the IBC or the BSO.

The PI is responsible for ensuring that his or her employees receive proper training in the biohazards and controls specific to his or her laboratory and the safe conduct of the experimental procedures to be used. The Biosafety Program provides different types of training associated with the BU biological, chemical, and radiological safety programs. Each of these has its own driver and emphasis.

The ROHP is available as a resource to the IBC, PI's and the BSO to complement required training in the areas of biosafety and specific agents.

Biosafety Training
All research laboratory workers (e.g., faculty, staff, students, and visiting scientists) must complete the necessary biosafety training prior to engaging in any laboratory activities. Attendance at the EHS new employee orientation does not fulfill this requirement. The training should be specific to the unique hazards, equipment, and procedures for a given laboratory and includes, but is not limited to, laboratory safety practices, biosafety, chemical safety, bloodborne pathogens, and hazardous waste operations.

It is the responsibility of the PI, supervisor, or laboratory manager to administer, document, and track training of laboratory personnel. This training is mandated and must be provided by the PI or laboratory manager on a periodic basis to all laboratory personnel. Documentation of the training is required and must include, at minimum, the date and duration of training, name and position of the trainer, topics covered, and names of the trainees.

Additional training may be required by law or BU policy, and in some cases, completion of such training must be documented with the BSO or EHS.

Laboratory Safety Training
Laboratory Safety Training satisfies the basic competency and regulatory requirements for those working in labs and must be completed annually. This training requirement must be fulfilled before engaging in any laboratory activities and on an annual basis thereafter. The Laboratory Safety Training requirement can be fulfilled by attending a ninety minute in person session "Classroom Laboratory Safety Training" or completing online "Laboratory Safety Training". The online training requires the completion of the Laboratory Safety Training module and additional modules assigned by job activities by the researcher's Principal Investigator based on expected laboratory procedures. Those modules are Biosafety Training Level 1 & 2, Chemical Safety Training and Bloodborne Pathogens Safety training. All the training is available on BioRAFT through Kerberos login.

Please note that this training does not satisfy the need for department-specific training, shipment of infectious agents, select agents, Biosafety Level 3 or 4 work, or other specialized training.

Training and knowledge of the NIH Guidelines and IBC policies
All PIs listed on an active IBC protocol and all individuals listed on an active IBC protocol involving recombinant or synthetic nucleic acids are required to complete the online "IBC Policy / Recombinant DNA Training" and Quiz before engaging in any protocol activities and at the time of three-year renewal before continuing to engage in the protocol activities. This is a requirement for all PIs and individuals listed on an active IBC protocol regardless of whether or not they currently work with recombinant or synthetic nucleic acids.

Mandated Specific Training
Mandated specific training may also be required by law or BU policy. In some cases, it is administered and tracked by the BSO or EHS, who must maintain the training records. Examples of mandated specific training include, but are not limited to: non-human primate users training; agent specific trainings or other specific training required by the IBC or BPHC. Individuals working in laboratories classified as BSL3 and above, or who are potentially exposed to specific zoonotic diseases, must also undergo training.

HIV/HBV Laboratory Training
Personnel who work in research laboratories that culture, produce, or otherwise perform microbiological manipulation of human immunodeficiency virus (HIV) or hepatitis B virus (HBV) must receive additional training beyond the standard bloodborne pathogen training. The PI is responsible for ensuring that this training is provided and completed prior to working with HIV or HBV. Laboratory workers must demonstrate proficiency in standard microbiological techniques, and in the practices and techniques specific to the laboratory. Additionally, workers must have prior experience in handling human pathogens before working with HIV or HBV.

Personnel who do not have experience with human pathogens must be trained in the laboratory before working with HIV or HBV. Initial training must not include the use of infectious agents; rather, training and work activities should be progressive as proper techniques are demonstrated. Workers are permitted to handle infectious agents only after demonstrating proficiency to the laboratory supervisor's satisfaction.

Packaging and Shipping of Infectious Agents Training

Personnel who package and ship infectious agents and diagnostic specimens such as microorganisms, blood samples, and clinical samples for pathological testing are required by federal and international regulations to receive training every two years. EHS offers this training monthly, online and upon request. The training is valid for 2 years and must be retaken prior to the expiry date for persons responsible for shipping of these materials.

Training dates and locations can be found by Sign Up in BioRAFT under Classroom Shipping Biological training. Online training is also available in BioRAFT as Shipping Biologicals.

Biosafety Level 3 and Level 4 Training
Specialized BSL3/4 training is required for individuals who work in a BSL3/4 containment lab or in the ABSL3/4 biocontainment facility (see Appendix F, BSL3 Biosafety Manuals and BSL4 Biosafety Manual). This training must be completed annually. Contact the BSO for more information.

The "BSL 3/4 Annual Training" can be found in the list of available trainings at the BioRAFT Research Management Platform.

Select Agents Training
Personnel authorized to use select agents are required to receive training. This training is designed to meet the specific requirements of 42 C.F.R. Part 73, 7 C.F.R. Part 331, and 9 C.F.R. Part 121 requirements and must be completed prior to any individual starting work with select agents; all individuals must also complete the training annually to continue working with select agents. EHS and the lab will maintain copies of the training records for reference. Contact the BSO for more information.

Agent-Specific Training
Personnel authorized by the IBC to work with specific agents designated as biological agents with an increased potential to cause Laboratory Acquired Infection (LAI) are also required to receive agent specific training (see Appendix G for a List of Biological Agents with an increased Potential to Cause LAI that are in use at Boston University). ROHP is available to assist PIs with this training requirement.

In addition, personnel working with select agents must complete the applicable "Agent-Specific Training" for the select agent that they work with in the lab (e.g., *Francisella tularensis*, *Yersinia pestis, Ebola virus, etc.*) and Shipping Biologicals Training. Agent Information Sheets (AIS) and Agent Specific Identification Cards must be made available to individuals using biological agents with the potential to cause Laboratory Acquired Infection ("LAI").

Laboratory-Specific Training
Individual laboratories are required to develop specific training for the particular agents and procedures that personnel will perform in that laboratory. This training should be specific to the hazards in the laboratory and to each person's laboratory duties. Each person in the laboratory must understand the hazards associated with the agent and laboratory operations, how to prevent exposures to biological and chemical agents (see Chemical Hygiene Plan), and be trained on the laboratory standard operating procedures. Laboratory-specific training should not duplicate the general biosafety training, but instead should supplement it.

Laboratory safety training records are maintained by BioRAFT for the courses offered on the system. If lab specific training needs to be documented use the Miscellaneous Training Roster on the Documents tab of the lab home page in BioRAFT and upload the training record with name, date and training objective. Ongoing training is required as new hazards and procedures are introduced into the laboratory.

Other Safety Training
Personnel who utilize other materials such as radioisotopes, controlled substances, or x-ray generating devices must complete additional laboratory safety trainings. These trainings can be found in the course directory in BioRAFT under Training.

Non-user Training
Individuals employed in high and maximum containment facilities (e.g., BSL3 and BSL4) but are not working with biological materials (e.g., administrative staff, facilities, security, etc.) are also required to complete the mandatory training programs. The scope and content of these training programs will be developed based on the needs of each facility. Contact the BSO for more information

Refresher Training
All laboratory workers and certain categories of building occupants will be subject to periodic mandatory refresher training. The scope and details of these refresher trainings is based on the risk of the agent and procedures performed and will range from annually to every three years based on regulatory requirements such as Bloodborne Pathogen Standard or Select Agents Rule. All laboratory personnel must also complete the annual Laboratory Safety Training.

Chapter 7
Decontamination and Sterilization

Decontamination is a process or treatment that renders a device, instrument, or work surface safe to handle. A decontamination procedure can range from sterilization by autoclave or ethylene oxide to simple cleaning with soap and water. Sterilization, disinfection, and antisepsis are all forms of decontamination.

Sterilization is the use of a physical or chemical procedure to destroy all microbial life, including highly resistant bacterial endospores.

Disinfection eliminates virtually all pathogenic, non-spore-forming microorganisms but not necessarily all microbial forms on inanimate objects (work surfaces, equipment, etc.). Effectiveness is influenced by the types and extent of organisms, the amount of organic matter, and the surface type (i.e. porous or smooth) of the object to be disinfected and chemical exposure time, temperature, and concentration.

Antisepsis is the application of a liquid antimicrobial chemical to skin or living tissue to inhibit or destroy microorganisms. It includes using germicidal solutions for swabbing an injection site on a person or animal and for handwashing. Although some chemicals may be utilized as either a disinfectant or an antiseptic, adequacy for one application does not guarantee adequacy for another. Manufacturers' recommendations for appropriate use of germicides should always be followed.

General Procedures

Decontamination of cultures and objects contaminated by biological agents is routinely performed in microbiological laboratories. Decontamination is a vital component of microbiological safety practice and serves to protect laboratory personnel (as well as others) from contamination and potential infection and the release of infectious organisms to the outside environment (primarily through person-to-person transmission). Decontamination of media, work surfaces, and equipment is also necessary to prevent contamination of cultured organisms.

- Infectious wastes such as contaminated liquid and solid will be handled, treated and disposed of according to biological waste policies and procedures. Liquid wastes such as bacterial or viral culture media from BSL2 labs will be treated with appropriate disinfectant prior to sink disposal. Solid wastes from the BSL2 laboratories will be segregated and placed in biohazard containers lined with biohazardous waste bags and disposed of as biological wastes. This waste is sealed by the laboratory and shipped off-site for sterilization (see Waste Chart posted in the laboratory for more information).
- All wastes from the BSL3 laboratories will be inactivated before disposal from the laboratory (see Chapter 9)
- A disinfectant should be chosen that is appropriate for the organism in use.
- All liquid biological cultures should be deactivated with appropriate disinfectant.
- All solid biological waste should be disposed of in the biohazard waste containers.
- Waste created in BSL3 laboratories is required to be autoclaved prior to removal from the laboratory (see Chapter 9).

Methods of Decontamination

The three main categories of physical and chemical decontamination are heat, liquid disinfection, and vapors and gases.

Heat: Wet heat is the most dependable method of sterilization. Autoclaving (saturated steam under pressure of approximately 15 psi to achieve a chamber temperature of at least 250° F for a prescribed time) is the best method of rapidly achieving destruction of all forms of microbial life.

- In addition to proper temperature and time, prevention of entrapped air is critical to achieving sterility because of air's poor heat transfer properties.
- Material to be sterilized must come into contact with steam and heat. Indicators of proper autoclave operation (e.g., autoclave tape or autoclave-sensitive labels) must be used with each load to visually indicate successful processing.
- Use of autoclave tape alone is not an adequate monitor of the sterilization's success.
- The Massachusetts Department of Public Health Medical Waste Management Act has specific quality-control requirements for autoclaves used for sterilization of medical waste. Appendix D describes the procedures for such tests.

Liquid disinfection: A liquid disinfectant (e.g., 1:10 solution of household bleach yielding a final hypochlorite concentration of 0.5%) is used to wipe or soak potentially contaminated materials for a period of time to kill all pathogenic agents present. Each disinfectant requires varying amounts of contact time.

Gas and vapor: Potentially contaminated articles are exposed to a sterilizing gas (e.g., ethylene oxide, or ETO) or vapors from a chemical (e.g., formaldehyde, vaporized hydrogen peroxide). Because of the hazardous nature of the gases and vapors used, this requires specially designed equipment and facilities.

Autoclaving

Autoclaving uses saturated steam under pressure (approximately 15 psi) to achieve a temperature in the autoclave of at least 121^0 C (250^0 F). Autoclaving can be used to destroy vegetative bacteria, bacterial spores, and viruses. When decontaminating biohazardous waste, it is recommended that the temperature **in the waste** reach a minimum of 115^0 C for a minimum of 20 minutes. The total processing time required to meet these conditions depends on several loading factors (see below); however, it is recommended that a minimum autoclave cycle of one hour be used when decontaminating waste. Please note that waste that has been designated by the IBC for autoclave treatment must be treated by autoclaving prior to disposal in biohazardous waste boxes and shipped off as regulated biohazardous wastes. The autoclaving process makes them safer for handling and transport, it does not change the disposal endpoint.

When using an autoclave, the following guidelines should be taken into consideration:

- Biohazardous materials should not be left inside the autoclaves overnight in anticipation of autoclaving the next day.
- Autoclaves should not be operated by untrained personnel.
- Special precautions should be taken to prevent accidental removal of material from an autoclave before it has been sterilized or the simultaneous opening of both doors on a double door autoclave.
- Always use the appropriate PPE when operating the autoclave including lab coat, disposable gloves, heat resistant gloves and face protection.
- Dry hypochlorite, or any other strong oxidizing material, must not be autoclaved with organic materials such as paper, cloth, or oil: **WARNING! OXIDIZER + ORGANIC MATERIAL + HEAT = POSSIBLE EXPLOSION**

Three factors in combination determine the effectiveness of autoclaving:

Temperature: an autoclave uses steam under a pressure of approximately 15 psi to achieve a chamber temperature of at least 121°C. Although the autoclave chamber may reach 121°C, this does not necessarily mean that the interior of the load will reach this temperature.

Time: a minimum autoclave cycle time of 20 minutes at a chamber temperature of 121°C (time does not begin as soon as the autoclave cycle is initiated) is commonly recommended for sterilization of clean items. However, the total processing time required to achieve decontamination depends on several loading factors, including the load container (heat transfer properties); the amount of water added to the load; and the weight of the load. For increased loads, an increased cycle time will be required to ensure effective decontamination.

Contact: steam saturation is essential for maximum heat transfer. Steam must contact all areas of the load. Autoclave bags and other containers should be left partially open (or otherwise permit entry of steam) to ensure adequate contact. Studies have shown that adding water to the interior of the bag improves the time-temperature profile of the autoclave cycle, thereby increasing the autoclave's sterilization efficiency.

Dry Heat

Dry heat method requires a higher temperature and longer contact time. It is less effective than moist heat (autoclaving). Nevertheless, dry heat is preferable to moist heat for decontamination of anhydrous materials and closed containers because the moisture component of the steam used in an autoclave will not effectively penetrate anhydrous materials and closed containers.

The highest dry heat equivalent temperature that these materials will reach in an autoclave is 121°C. The highest temperature that material will reach in a dry heat oven will be the actual temperature inside the oven. A temperature of 160°-180°C for three to four hours is recommended for decontamination of waste using a dry heat oven.

Chemical Disinfection

Disinfection is the decontamination of work surfaces, equipment, biological safety cabinets, and other inanimate objects using antimicrobial agents. Several chemical agents are used as disinfectants. Laboratory workers should remember that there are hazards associated with all of these chemical disinfectants.

- Inhalation and skin contact should be minimized, and contact with eyes avoided.
- Appropriate gloves and safety eyewear should always be worn when handling these chemicals.

Pertinent information for some of the common chemical disinfectants is summarized in table format at the end of this chapter.

Summary of Chemical Disinfectants

Disinfectant	Use Parameters	Effective Against[a]					Important Characteristics	Potential Application
		Vege-tative cells	Lipo-philic viruses	Tuberc le bacilli	Hydro -philic viruses	Bacter ial spores		
Alcohol (ethyl, isopropyl)	*conc.*: 70-85% *contact time*: 10-30 min.	+	+	+	±		Eye irritant, toxic, flammable, inactivated by organic matter.	Surfaces: work and equipment
Chlorine Compounds	*conc.*: 0.05-0.5% (commercial bleach 0.5%) *contact time*: 10-30 min.	+	+	+	+	±	May leave residue; corrosive; skin, eye and respiratory irritant; inactivated by organic matter; make up at least weekly.	Spills, equipment surfaces, instruments, glassware, water baths
Quaternary Ammonium Compounds	*conc.*: 0.1-2% *contact time*: 10-30 min.	+	+				Toxic, inactivated by organic matter.	Surfaces (work and equipment), BSCs, floor maintenance, glassware, instruments
Phenolic Compounds	*conc.*: 0.2-3% *contact time*: 10-30 min.	+	+	+	±		Leaves residue; corrosive; skin, eye and respiratory irritant; toxic; inactivated by organic matter.	Surfaces (work and equipment), BSCs, floors, spills, glassware, instruments, water baths
Iodophor Compounds	*conc.*: 0.47% *contact time*: 10-30 min.	+	+	+	±		Leaves residue; corrosive; skin and eye irritant; toxic; inactivated by organic matter.	Surfaces (work and equipment), BSCs, glassware, water baths
	conc.: 4-8%	+	+	+	+	±		

Disinfectant	Use Parameters	Effective Against[a]					Important Characteristics	Potential Application
		Vege-tative cells	Lipo-philic viruses	Tuberc le bacilli	Hydro -philic viruses	Bacter ial spores		
Formaldehyde[b] (Formalin)	*contact time*: 10-30 min.						Leaves residue; skin, eye and respiratory irritant; toxic (carcinogen).	Less effective than other disinfectants but can be used for equipment surfaces, glassware, instruments
Glutaraldehyde	*conc.*: 2% *contact time*: 10-60 min.	+	+	+	+	+	Leaves residue; skin, eye and respiratory irritant; toxic.	Equipment surfaces, glassware, instruments

a: + = very positive response, ± = less positive response. A blank denotes a negative response or not applicable.
b: due to its irritating characteristics and status as a carcinogen, formaldehyde should not be used without good local exhaust ventilation.

From *Laboratory Safety: Principles and Practices*, second edition, Diane O. Fleming, John H. Richardson, Jerry J. Tulis, and Donald Vesley, eds., American Society for Microbiology, Washington, D. C.

Chapter 8
Biohazardous Spill Response

Even with the most careful planning and implementation of a research project, the possibility of an incident or spill involving biological materials exists. The following procedures are intended to provide a planned response to such rare events.

In any spill scenario, the priority of actions is determined by the "PEP" rule - **P**eople, **E**nvironment and **P**roperty. The highest priority is to provide aid to injured personnel and prevent spill area access to others.

Note: the following are the general requirements and guidelines for Biohazardous Spill Response; each BSL3 and BSL4 facility will develop site-specific procedures**.**

Preplanning for Biohazardous Spill Cleanup

All spills of biohazardous materials do not represent the same risk to personnel and the environment, making each spill somewhat unique. There are several factors that must be considered, including but not limited to: the pathogenicity of the agent; route of exposure, volume of a spill, the quantity, and other aspects such as sharps.

The following should also be considered when conducting an assessment:

- Location (e.g., biohazard cabinet, countertop, floor, equipment);
- Nature (e.g., tip-over, aerosolizing (spray/splash), drop from a height);
- Toxicity/infectivity of the spilled material;
- Volatility and viscosity of the spilled material;
- Other properties of material (e.g., pH, normality, temperature);
- Nature of affected surfaces (e.g., absorbent, porous or smooth-pitted. Additional challenges (e,g broken glass or sharps, clothing, mixing with other materials); and
- Susceptibility of spilled material to neutralization/disinfection

Preplanning of spill response will lower the risk associated with cleaning up a spill and will increase the likelihood that the spill is handled appropriately. Principal Investigators or Laboratory Directors should prepare their laboratory for typical spill scenarios expected in the laboratory. Laboratory workers should be informed of the hazards of the biological agents used in the laboratory, the risk associated with these agents during spill scenarios, how to safely clean up the agents, and how to properly dispose of cleanup materials.

Spill Cleanup Materials

Each laboratory area should have spill cleanup materials available to respond to the largest spill anticipated for that area. At a minimum, the following spill cleanup materials should be available in the laboratory:

- Disposable gloves (thick, chemical-resistant gloves or double pair of thin, nitrile gloves are recommended);
- Safety goggles and masks or a full-face shield (strongly recommended to avoid splashes to the nose and mouth);
- Lab coat or smock to protect clothing and body;

- Absorbent pads;
- Disinfectant appropriate for the agents used in the laboratory;
- Forceps or other devices to pick up contaminated material (especially sharps);
- Sharps disposal container; and
- Autoclavable biohazard bags
- Respirators as required

The spill kits distributed by EHS to laboratories may not be adequate for the response to a biological spill. Additional items needed for the cleanup of biohazardous agents can be maintained in the laboratory.

Biohazardous Spill Cleanup Risk Assessment

Several factors must be considered when assessing the risk that a spill represents:

- Volume and concentration of the spilled material;
- The infectivity of the spilled material and routes of exposure;
- Location of the spill;
- Aerosolization potential of the agent resulting from the spill;
- Susceptibility of the spilled material to disinfection;
- Nature of the affected surface(s) and its ability to "hide" organisms from disinfection; and
- Immune status of immediate personnel

As with any spill scenario (biological, chemical, or radiological), **the safety of personnel is the most important consideration**. Cleanup is to begin only after it is determined that the personnel who will clean up the spill have appropriate knowledge, training, and equipment.

Biological Material Spill Cleanup Procedures

The following are general biohazardous spill cleanup procedures that are appropriate for most spill scenarios; however, the appropriate response to any spill is based on an assessment of the risk associated with that particular situation.

If in doubt, immediately call the Medical Campus Control Center at (617) 358-4144 for the CRC EHS emergency telephone at (617) 353-2105. Both response lines are active 24/7/365.

Biohazardous Spills Inside Biological Safety Cabinets
If a biohazardous spill occurs inside a Biological Safety cabinet, the following procedures should be followed:

- Wear a laboratory coat (disposable is recommended when available), safety glasses, and gloves (appropriate for the biological agent and the chemical disinfectant) during cleanup.
- Allow the BSC to run continually during cleanup.
- Surround the affected spill area with absorbent material to prevent spread of the spill.
- Apply disinfectant appropriate for the biological agent and allow a minimum of 20 minutes of contact time (or as directed by manufacturer's instructions). Alcohol or other flammable liquids are not recommended.
- Wipe up the spill with a paper towels soaked with disinfectant.
- Wipe the BSC's walls and work surface, as well as any equipment in the cabinet, with a

disinfectant-soaked paper towels.
- Place contaminated items in an appropriate container (biohazard waste bag, sharps container, or autoclavable pan with lid for reusable items) for autoclaving or disposal in biohazardous waste box.
- Allow items to have a minimum of 20 minutes of contact time with the disinfectant (or as directed by manufacturer's instructions) before removing them from the BSC.
- Remove disposable protective clothing, gloves and place in a biohazard waste bag.
- Thoroughly wash hands and forearms with soap and water.
- Allow BSC to run for a minimum of 10 minutes before resuming work in the cabinet or shutting off the cabinet.

Biohazardous Spills in the Laboratory, Outside the Biological Safety Cabinet
If a **BSL1 agent** or **less than 100 ml of a BSL2** agent is spilled, the following procedures should be followed:

- Remove any contaminated disposable protective clothing and place in a biohazard waste bag. Wash the hands and other areas affected by skin contact with soap and water.
- Wear a long-sleeved gown or lab coat (disposable is recommended), shoe covers, safety glasses (face shield also recommended), and gloves (appropriate for biological agent and disinfectant).
- Place absorbent pads over the spill (to absorb liquid), then place a second layer of disinfectant-soaked absorbent pads over the spill.
- Pour additional disinfectant around the spill, being careful to minimize any splatter or aerosolization, and work from the periphery toward the center, ensuring thorough contact between the spill and the disinfectant. Disinfect all items in the spill area.
- Allow a minimum of 20 minutes contact time (or as directed by manufacturer's directions) with the disinfectant.
- Wipe down all equipment, tools, etc., with disinfectant.
- Place contaminated items in an appropriate container (biohazard waste bag, sharps container, or autoclavable pan with lid for reusable items) for disposal as biohazardous waste or for autoclaving as necessary.
- Remove disposable protective clothing and place in a biohazard waste bag.
- Thoroughly wash hands, forearms, and face with soap and water. It is recommended that cleanup personnel shower as soon as possible.

If the spill involves a **BSL3/4 agent**, or **greater than 100 ml of a BSL2 agent**, **immediately evacuate all personnel from the affected area.** Wait for aerosol to settle (usually a minimum of 30 minutes) before entering the spill area. **Exception:** If the laboratory is not under negative pressure, cleanup should begin as soon as possible to minimize the spread of aerosols.

In addition, the following procedures should be followed:

- Contact the BUMC Control Center at 4-4444 and notify EHS immediately for assistance with the cleanup.
- Remove any contaminated clothing and place in a biohazard waste bag for disposal or autoclaving as necessary and wash all areas affected by skin contact with soap and water.
- Wear a long-sleeved gown or lab coat (disposable recommended), shoe covers, safety glasses (face shield also recommended), and gloves (appropriate for biological agent and disinfectant). For cleanup of a BSL3 agent, a HEPA-filtered respirator may be required and

for BSL4 agents, a full body pressurized suit.

- Place absorbent pads over the spill (to absorb liquid), then place a second layer of disinfectant-soaked absorbent pads over the spill.
- Pour additional disinfectant around the spill, being careful to minimize aerosolization, and work from the periphery toward the center, ensuring thorough contact between the spill and the disinfectant. Disinfect all items in the spill area.
- Allow a minimum of 20 minutes contact time (or as directed by manufacturer's directions) with the disinfectant.
- Wipe down all equipment, tools, etc., with disinfectant.
- Place contaminated items in an appropriate container (biohazard waste bag, sharps container, or autoclavable pan with lid for reusable items) for disposal as biohazardous waste or for autoclaving and necessary.
- Remove protective clothing and place in a biohazard waste bag for autoclaving.
- Thoroughly wash hands, forearms, and face with soap and water. It is recommended that cleanup personnel shower as soon as possible.

Biohazardous Spills Inside a Centrifuge

If a biohazardous spill occurs inside a centrifuge, the following procedures should be followed:

- Clear the area of all personnel and allow aerosol to settle (usually a minimum of 30 minutes) before re-entering the area.
- Wear a laboratory coat (disposable recommended), safety glasses, and gloves during cleanup. For a BSL3 agents, a HEPA-filtered respirator may be required and for BSL4 agents, a full body pressurized suit is required.
- Transfer and open the centrifuge rotor and buckets in a BSC for cleanup.
- Using an appropriate disinfectant, thoroughly disinfect the inside of the centrifuge, the rotor, and buckets.
- Discard cleanup materials and protective clothing as biohazardous waste.
- Thoroughly wash hands, forearms, and other parts of the body with soap and water.

Biohazardous Spills Outside the Laboratory During Transport

When transporting biological materials between laboratories in the same campus, the samples must be contained in an unbreakable, leak-proof, primary container. The primary container must be placed inside a secondary container with absorbent material that is well-sealed and leak-proof container (see Chapter 11 for transportation guidelines). Both the primary and secondary containers must be labeled with the universal biohazard symbol with the identity of the agent. In the event a transport container drops and its contents are spilled, the following procedures should be followed:

- If necessary, clear the area of all personnel and secure the area.
- Cleanup should be initiated as soon as possible to prevent the release of potentially infectious aerosol. Attempt cleanup **only** if appropriate cleanup materials and protective clothing are available
- Notify the Medical Campus Control Center at 617-358-4144 or the CRC EHS emergency telephone at 617-414-4075. Both response lines are active 24/7/365.

Note: *Employees should become familiar with other non-spill emergencies, such as fire and medical emergencies. EHS has developed special emergency flip charts that are located in every lab and provide quick references to employees. Employees should review the charts so that in the event of an emergency, they are familiar with their location and content.*

Site-Specific Spill Procedures
BSL3 and BSL4 facilities have site-specific emergency response and spill response procedures that are part of the facility Plans, SOPs and ERPs.

Note: BPHC is notified of all emergencies in BSL3 and 4 Facilities.

Spill Response

When responding to a spill, the following rules should be followed:

- **Tend to the injured**: Ensure receipt of immediate medical care and do not attempt to move the injured individual(s) unless ambient conditions become life-threatening. Individuals splashed, sprayed with, or otherwise exposed to human blood or other body fluids or tissues during a spill will need to remove contaminated clothing and utilize basic first aid, washing any wounds immediately.
- **Await assistance**: Unless laboratory personnel are trained and properly supplied and equipped with appropriate personal protective equipment, **DO NOT** attempt to clean up the spill. Personnel should immediately call the Medical Campus Control Center at 617-358-4144 or the CRC EHS emergency telephone number, 617-414-4075. Both response lines are active 24/7/365.
- **Isolate the spill**: Evacuate the immediate spill area or the entire room in the case of an aerosolizing (splashing or spraying) spill or a spill of volatile material. Prevent others from entering the spill area with barricades or, if necessary, a sentry.
- **Contain the spill**: Place absorbent material around, on, or in the flow path of the spilled material *only if it can be done safely*.
- **Provide information**: Provide the information requested by the Control Center or EHS personnel and wait for the arrival of the emergency provider.
- **Clean up**: Clean up should take place **ONLY** if laboratory personnel are trained, properly supplied with personal protective equipment, and otherwise able to clean up and disinfect the spill safely.

Chapter 9
Biohazardous and Medical Waste Disposal

In the Commonwealth of Massachusetts, biohazardous waste is governed by the Department of Public Health regulation 105 CMR 480, "Storage and Disposal of Infectious or Physically Dangerous Medical or Biological Waste, State Sanitary Code Chapter VIII." Boston University has biological waste management guidance documents for each campus which are reviewed annually and posted on the EHS website. The information below is a brief summary of the instruction provided in the guidelines.

The regulation defines biohazardous waste as ***infectious or physically dangerous medical or biological waste*** that because of its characteristics may cause, or significantly contribute to, an increase in mortality or an increase in serious irreversible or incapacitating reversible illness; or pose a substantial present potential hazard to human health or the environment when improperly treated, stored, transported, disposed of, or otherwise managed.

The following types of waste are identified and defined as infectious or physically dangerous medical or biological waste, and shall be subject to the requirements of 105 CMR 480.000:

- **Blood and blood products**: Discarded bulk human blood and blood products in free draining, liquid state; body fluids contaminated with visible blood; and materials saturated with blood.
- **Pathological waste**: Human anatomical parts, organs, tissues, and body fluids removed and discarded during surgery or autopsy, or other medical procedures, and their containers.
- **Cultures and stocks of infectious agents and associated biologicals**: All discarded cultures and stocks of infectious agents and associated biologicals, biotechnological by-product effluents, cultures of specimens from medical and pathological laboratories, cultures and stocks of infectious agents from research laboratories, wastes from the production of biologicals, and discarded live and attenuated vaccines intended for human use.
- **Contaminated animal carcasses, body parts and bedding**: The contaminated carcasses and body parts and bedding of all research animals known to be exposed to pathogens.
- **Sharps**: Discarded medical/research articles that may cause puncture or cuts, including but not limited to all, used and discarded hypodermic needles and syringes, Pasteur pipettes, broken medical glassware, scalpel blades, disposable razors, and suture needles.
- **Biotechnological by-product effluents**: Any discarded preparations made from genetically altered living organisms and their products. Infectious or physically dangerous medical or biological waste shall be referred to as "Waste" in the subsequent provisions of 105 CMR 480.000.

Biohazardous Waste

Proper handling and disposal of biohazardous waste is necessary to prevent infection of personnel (laboratory workers, custodians, laboratory visitors, etc.) and release to the environment. OSHA and Commonwealth of Massachusetts regulations (105 CMR 480.000) require that biohazardous waste be properly labeled, stored, and disposed of.

Labeling Biohazardous Waste

At a minimum, all biohazardous waste must be labeled with the universal biohazard symbol and the word 'Biohazard'. Additional information, such as the type of waste (such as "sharps" or "liquid waste") and origin of the waste, is recommended.

Handling and Disposal of Biohazardous Waste

Sharps

Sharps include **all** syringes, lancets, scalpels, and other similar medical instruments (whether or not contaminated), as well as contaminated Pasteur pipettes and broken glass, and other instruments or materials that can cut or puncture personnel.

- Sharps must be collected in rigid containers that are leak-proof and resistant to puncture from the sharps. Sharps containers must be designed so that sharps can be safely introduced into the container but not easily retrieved.
- Containers must be red or orange in color and labeled with the universal biohazard symbol and the word 'Biohazard'. When the sharps container is approximately 3/4 full, personnel should seal the waste container and it will be picked up by the building facilities custodian or appropriate service personnel. CRC personnel should seal the waste container and fill out a pick-up request on the EHS website . Waste will be picked up by a waste management vendor that is contracted by EHS.

A licensed vendor retrieves the waste from each building at pre-determined intervals to process the waste with an approved sterilization method.

Uncontaminated Laboratory Glassware and Broken Glass

Collect uncontaminated laboratory glassware and broken glass in rigid containers (separate from other waste) that will prevent cuts and punctures to personnel. Containers should be labeled "broken glass." Broken glass is to be disposed of as ordinary trash.

Solid Biohazardous Waste

Solid biohazardous waste includes cultures of microbiological agents, tissue culture, and contaminated material (such as petri dishes, pipettes, contaminated glass, etc.). These materials are collected in a cardboard box lined with two red bags with biohazard symbols. The cardboard box is labelled with the biohazard symbol.

- Personnel should close and seal the biohazard waste box with tape for pick up by the building facilities custodian or appropriate service personnel. Each box must be labelled with the building and room number (a Sharpie or similar permanent marker if appropriate) on the top of the box to identify its origin.
- CRC personnel should seal the waste container and fill out a pick-up request on the CRC website. The building and room number should be written (a Sharpie or similar permanent marker is appropriate) on the top of the box to identify its origin.

A licensed vendor retrieves the waste from each building at pre-determined intervals to process the waste with an approved sterilization method. Medical Waste Tracking forms are maintained by EHS.

Liquid Biohazardous Waste

Liquid biohazardous waste includes all blood and liquid waste from humans or animals, and all other liquid biohazardous waste (such as microbial cultures). Collect liquid waste in closeable, rigid, plastic, leak-proof containers labeled with the universal biohazard symbol and the word "Biohazard".

- Human and animal blood and body fluids can be disposed of by flushing directly to the sanitary sewer (wear laboratory coat, safety glasses and face shield, and gloves, and be careful to minimize splashing).
- All other liquid waste must be autoclaved or treated with a disinfectant prior to sink disposal.
- Liquid waste treated with small quantities of bleach or other household disinfectants can be disposed of by flushing directly to the sanitary sewer after sufficient contact time. Liquid waste treated with other (wescodyne, for example) chemical disinfectants must not be disposed in the sink and must be collected and disposed of as hazardous chemical waste through EHS.

In BSL3 laboratories, liquid biological waste disinfection events must be documented on a log sheet provided by EHS.

Animal Carcasses, Body Parts, Tissue and Bedding
All animal carcasses and parts, regardless of whether they have been experimentally infected or not , are disposed of as pathological waste.

- Animal carcasses and parts should be stored in a freezer or cold storage area prior to disposal. Ensure to secure any bones, **limbs and sharp parts from puncturing the bag and protruding to prevent injuries.**.
- Animal tissues and animal bedding must be disposed of as pathological waste if the source animal was infected with a BSL2 agent or higher.

All animal wastes that are collected as biohazardous must be sent for incineration via a licensed vendor who retrieves the waste from each building at pre-determined intervals. A yellow 'pathological' or 'incinerate only' sticker must be affixed to the closed biohazardous waste box if it contains animal carcasses, parts, tissues or bedding. Medical Waste Tracking disposal forms are maintained by EHS.

Animal carcasses from ABSL3/4 are treated by autoclaving. Quality control of autoclaving is done prior to disposal as biohazardous wastes. Animal carcasses that are autoclaved from the ABSL4 are disposed by tissue digestion process or incineration via licensed vendor.

Chapter 10
Federal Select Agent Program

The U.S. Department of Health and Human Services (DHHS) and the U.S. Department of Agriculture's (USDA) regulations require institutions that possess, use, or transfer certain biological agents and toxins (known as "select agents") be registered and approved by the Federal Select Agent Program (FSAP). The FSAP have identified specific biological agents and toxins they consider to be a severe threat to public health and safety because of their potential use as bioterrorism agents. These materials are referred to as "Select Agents". Their transfer, possession, use, and disposal are strictly regulated. On December 4, 2012, the CDC and APHIS (now the FSAP) implemented the amendment to the regulation and identified certain select agent and toxins as Tier I. These Tier I agents have additional requirements on security, biosafety and occupational health.

This chapter will refer to all these agents as "Select Agents." The current list of select agents is provided at the end of this chapter. Because the list of select agents may be revised, it is recommended that the Federal Select Agent Program website be checked before acquiring pathogenic agents and biological toxins.

The regulations associated with select agents are very complex and strict, and significant monetary fines and criminal penalties are associated with non-compliance. The information in this chapter is a summary of the select agent regulations; it is not a complete description of the regulatory requirements. **Investigators must review and understand the select agent regulations and their responsibilities prior to acquiring or working with any select agent** (for regulatory information, see the CDC website.

Responsible Official and Authorization

Responsible Official (RO)

Select agent regulations require that a RO be designated for each institution that possesses and uses select agents. **The RO has institutional responsibility for the biosafety, security, and regulatory compliance of select agents, and as such, must be contacted *prior* to obtaining any select agents.**

Authorization to Possess and Use Select Agents

Prior to personnel obtaining any select agent, the IBC must review and approve any proposed work. In addition, PIs who want to acquire, possess, or use any biological agent or toxin listed as a select agent **must be registered and approved with the FSAP *prior* to obtaining the agent(s) or toxin(s)**.

The FSAP must approve both the institution and the individual laboratory. Investigators who want to possess and use select agents must contact the RO for assistance with the registration application process. Approval by the FSAP can take several months, and PIs should plan research projects accordingly.

The select agent regulations contain very strict requirements regarding biosafety, training, emergency response, security and accountability, as well as other requirements. Investigators wanting to acquire select agents should thoroughly review the Federal select agent regulations before initiating the registration application process.

Exemptions and Exclusions

Diagnostic labs that do not maintain select agents are largely excluded from the Federal select agent regulations; however, notification and possession time limits and other requirements do apply. Additionally, the FSAP can grant exclusions for temporary public health emergency situations and other

special circumstances. Consequently, any laboratory that conducts diagnostic or verification testing for any select agent must identify itself by contacting the RO as soon as possible. **Identification of any select agent in a specimen or isolate must be reported to the RO immediately. The RO will assist the diagnostic laboratory with reporting to FSAP immediately after identification. Laboratories must fill out and submit "Report of the Identification of a Select Agents or Toxin" (Form 4) within 7 days of the identification. Form 4 can be found on the FSAP website.**

Several specific select agent microbial strains and toxin forms have been determined not to present a severe threat to public health and safety and are therefore excluded from the Federal select agent regulations. The list of excluded biological agents and toxins is dynamic and the most current list is available on the FSAP select agent website. Permissible amounts of the listed biological toxins do not fall under the regulation as long as they meet the threshold quantities. **Laboratories maintaining these exempt quantities of select agent toxins must register their toxin with the IBC and keep an accurate inventory of toxin amounts to verify that total quantities are below the threshold.**

Security, Incident response and Biocontainment requirements

Each select agent laboratory must develop and implement three written plans: security; incident response; and biosafety; that address safety issues associated with that specific select agent.

Security Requirements

Each select agent laboratory must have a written security plan that addresses the following topics:

- Site-specific security risk assessment
- Information system security control
- Storage control and inventory audits of select agents
- Select agent shipping and transfers
- Roles and responsibilities and training
- Reporting of unauthorized persons, suspicious activities and missing materials
- Access control and escort provisions for cleaning, maintenance, and repairs

Any theft or loss of select agents must be immediately reported to the RO, BU Police and EHS, which will notify the FSAP. In addition, the BPHC will be notified of such events. BU in collaboration with City Agencies (BPHC, Boston Fire Department, Boston Police Department and EMS) has developed an Emergency Notification and After-Action Guideline High Risk Materials Matrix outlining the list of agencies and events for which they will be notified.

This plan must be available and up-to-date during a CDC inspection.

The Department of Justice must approve all persons who will have access to any select agent. Approval requires that each individual successfully pass a background security check (conducted by the FBI in accordance with the USA Patriot Act) and submit fingerprints to the FBI. Anyone who has not been approved for access to select agents must be denied access unless escorted by an approved person. Everyone who enters a laboratory where select agents are accessible must have security approval or be accompanied by an approved person. This includes visiting scientists (on or off-campus), maintenance workers, custodians, and vendors.

Please see the CDC/USDA Security Plan Guidance document for more information.

Incident Response

Each laboratory that possesses or uses select agents must develop a written emergency plan that is laboratory specific and coordinated with department, building, and Institutional emergency plans. The plan must address the following:

- Loss, theft, or release of a select agent or toxin
- Inventory discrepancies
- Security breaches (including information systems access controls to select agents and toxins)
- Severe weather and other natural disasters
- Workplace violence
- Bomb threats and suspicious packages
- Emergencies such as fire, gas leak, explosion, or power outage
- Planning and coordination with emergency responders
- Building evacuation, site security, and control
- Decontamination and emergency medical treatment, and other emergency response issues

Any exposure or potential exposure should be reported immediately, and the BU Incident Response Plan for Select Agent Laboratories and the Biological Spill Response Plan for Select Agent Laboratories implemented.

Affected personnel should immediately contact the ROHP for medical evaluation and treatment by calling (617) 358-7647(ROHP).

Please see the CDC/USDA Incident Response Plan document for more information.

Laboratory personnel should become familiar with these plans.

Biocontainment

All persons approved for access to select agents must receive documented training covering the following:

- Hazardous characteristics of select agents and their safe handling, use, and disposal
- Safeguards for protecting against exposure to select agents, requirements and procedures
- Biological safety and personal protective equipment (PPE) requirements
- Disinfection, decontamination or destruction of select agents
- Handling select agents and in shared spaces

For more information on biocontainment, please see the CDC and USDA's Select Agents and Toxins Biosafety/Biocontainment Plan Guidance

Training of Personnel

Training in all aspects of delineated in the Security, Incident Response and Biosafety Plans is required before beginning work with select agents and annually thereafter.

Transfers of Select Agents

Select agents can only be transferred to, or between, entities that are currently approved by the FSAP to possess and use select agents. All transfers of select agents require *prior* approval of the FSAP.

Both the sender and recipient must complete a common transfer form (Form 2), and the recipient must submit the form 2 request to the FSAP for approval. Form 2 requires the signature of the RO at both the sender and recipient facilities. When the select agent is consumed or destroyed, the recipient must notify FSAP through an update of their registration.

Inventory and Disposal of Select Agents

An accurate record of all select agents, from receipt to destruction or disposal, must be maintained. The inventory must include specific information on individual containers and vials, as well as a record of each use, and ultimate disposal. The select agent inventory must be verified twice a year to account for all quantities and containers of select agents. Any discrepancies between the inventory record and the actual inventory must be reported immediately to the RO.

For more information, please see Guidance on the Inventory of Select Agents and Toxins.

Records Required for Select Agents

Select agent regulations require that several records be maintained, including the following:

- Biocontainment certifications
- Laboratory notebooks
- Institutional Biosafety and Animal Use Committees minutes
- Records associated with occupational health and suitability programs
- Training records
- Transfer documents (Form 2)
- Safety and security incident reports

Each laboratory/institution is responsible for maintaining these records. The recordkeeping requirements are complex, and therefore the FSAP regulations should be reviewed for a complete description of the recordkeeping requirements.

Recordkeeping for Select Agent Laboratories

The following is a list of required recordkeeping for all select agent inventory and access records, per FSAP regulations.

Inventory Records

The Logbook Inventory must contain the following elements:

- Name, characteristics, designation data;
- Quantity acquired, source, date;
- Where stored (e.g., building, room, and freezer);
- Quantity, volume, used, purpose of use, destroyed or disposed of date, individual;
- Transfers: quantity, date, individual;
- Current quantity held;
- Lost, unaccounted for, stolen;
- Written explanation of any discrepancy.

Access Records
Access Records must contain the following elements:

- Access to SA: Name, SA, date Access to Area: Name, date, and time entered and left area; uncleared individuals must be accompanied by approved individuals and recorded as such.

Records are reviewed routinely by the RO and EHS to ensure that they are being maintained and updated appropriately. Records must be maintained for three (3) years.

Further information regarding select agents and records will be given to laboratories working with select agents in specialized safety training by laboratory personnel authorized to work with such agents.

Procedures for Select Agent Procurement and Receipt

Procedure Description
The BSL3 / BSL4 Transportation Plan establishes the BU procedures to be followed when obtaining biological agents and toxins that have been designated as "Select Agents" under Federal Regulation (42 CFR 73.0, 7 CFR 331, 9 CFR 121).

For the transportation of Select Agents, Boston University follows the regulations of other international, federal, state, and local authorities including the Department of Transportation, the FSAP/CDC, International Air Transportation Authority, and World Health Organization on the transportation of Select Agents to ensure pathogens are safely shipped to and from the labs. The general requirements are issued by the US Department of Transportation, which sets down strict requirements for packaging, labeling, and documentation of the materials, and requires training for employees involved in shipping.

All transportation of Select Agents will involve Department of Transportation (DOT) compliant triple packaging and will be placed in a non-crushable, liquid-tight, solid container for an added layer of safety. These packages will be transported via exclusive-use vehicles and will be secured in the transport vehicle away from potential impact on outer walls. In addition, shippers will adhere to pre-determined travel routes and strictly defined schedules for pick-ups and deliveries, and both package and vehicle will be monitored by BU and local emergency responders using GPS.

For more information, please see the Boston Public Health Commission website.

The FSAP/CDC also regulates the shipment of Select Agents. Qualified carriers must meet all federal, state and local regulations to transport select agent materials. There will be notifications to the Boston Public Health Commission, Boston Police and Fire Departments, and Boston Emergency Medical Services in advance of shipments and GPS monitoring of the vehicle and package. The transportation of Select Agents is tightly controlled, and BU has worked closely with city, state, and federal authorities to ensure that our transportation plan complies with all regulations. Boston University's Select Agent transportation plan significantly exceeds requirements and standards in place.

This SOP incorporates the requirements of the BU Materials Transportation Management Policy.

The BU Select Agent Transportation Plan outlines the procedures for the transfer of select agents between BSL-4 laboratories. *For more information about select agent transportation contact the BSO.*

Approval and Transportation Process

Initial Request for Select Agent

- PI notifies the BUBSO that a select agent needs to be ordered at least two weeks before anticipated use date.
- PI obtains any applicable USDA permits that may be required for the interstate transport of the select agent, and provides permits to RO.

BSO's Review

- Upon receipt of request to acquire select agent, the BSO:
- Confirms that the PI is an authorized select agent user.
- Confirms that IBC approvals, training, and inspection status are valid and current. Confirms that appropriate laboratory and storage facilities are available.

RO's Approval

- RO or Alternate RO completes Section 1 of the Form 2 requesting the transfer of select agents and submit it for approval by the Federal Select Program (FSAP).
- For imported select agents, the RO or Alternate RO works with the PI to obtain any needed CDC Import permit, USDA and/or U.S. Public Health Service (PHS) permit.

Federal Approval

- APHIS/CDC issues an approval authorization number that is good for 30 days. Faxes approved Form 2 to Recipient (BU RO) and Sender RO.

Shipping Process

Order Placement

- BSO designates a transporter to be used who meets the selection criteria of the BU Materials Transportation Policy described in Chapter 11.
- The BSO, upon approval of Form 2 and authorization number from the RO, coordinates transport of the select agent with the shipper to use a method that tracks the movement of the select agent being shipped and is in accordance with the BU Materials Transportation Policy. Coordinates shipment details and tracking with transporter.
- Sender RO/ARO complete Section 2 of the Form2 and coordinates shipment details with BU RO and BSO. Packages, labels, and ships select agent in accordance with all federal regulations.

Note: All transportation must be in accordance with the specifics of the BU Materials Transportation Policy in effect at the time of the transportations.

Notifications

The BSO notifies the following of shipment, date, and time of delivery:

- RO
- PI/Authorized User (Recipient)
- Executive Director of Public Safety
- City of Boston and Boston Public Health Commission

- Manager of Emergency Planning and Response

Transportation

- Transporter accepts, stores, loads and delivers package(s) to the approved location, using approved access routes.
- Transporter reports any and all violations of law, regulation, and/or policy.
- Transporter will contact BSO for any problem or incident that may occur during transit with select agents.

Receipt

Steps Prior to Arrival

- RO, BSO, and PI verify that appropriate laboratory and/or storage facilities are available.
- RO and Executive Director of Public Safety or designee review security procedures for receipt and transfer prior to the day of scheduled arrival, which includes the means for securing of the loading dock.
- The Executive Director of Public Safety or designee will ensure that a BU public safety officer provides escort for the RO and subject materials package.

Arrival and Receipt

- Upon the transporter's arrival, the RO and Executive Director of Public Safety or their designee(s) verify identity of drivers and accuracy of the shipping papers.
- RO or designee instructs drivers to wait until the package contents are verified.
- The public safety officer will escort the RO or designee to the approved select agent laboratory.

Note: if the shipment appears to be damaged the delivery truck will be stopped from moving from the premises and BU ERT will evaluate the situation to determine the best course of action. Public agencies (e.g. BPHC, BFD, BPD) will also be notified immediately.

The actual course of action will depend on whether or not there is any sign of obvious leakage, the extent of the damage or suspicion that the integrity of the internal packaging container has been compromised. The action taken may include:

- Over-packing of the package and removal to the laboratory to check the contents to check the integrity of the inner package
- Leaving the container in place for further evaluation by public agencies for additional course of action
- Containment of any leakage within the transport vehicle will be achieved by use of appropriate (i.e. effective for the agent) absorbent materials and disinfectants.

Verification of Shipment

- After donning appropriate personal protection equipment and following established laboratory procedures, the PI and RO or their designee(s) take the unopened package to a previously designated biological cabinet (in a laboratory appropriate for a select agent).
- The PI and RO or their designee(s) examine the package for any signs of tampering, damage, or leakage and then open the package and verify contents.
- The public safety officer will wait outside the laboratory while verification of the shipment occurs.

- If all is in order (no non-conformities) and the contents are verified, the RO or designee finalizes the transporter's shipping papers.

Notification and Documentation

- The RO then completes Section 3 of Form 2 *within 24 hours of receipt*, and submit it to the FSA.
- The PI enters the select agent into inventory per established procedure.

Discrepancies

Notification

In the event of non-conformity with the shipment, the RO will immediately notify:

- The Executive Director of Public Safety to hold the transporter.
- FSAP, BPHC and local law enforcement and the Department of Justice in the event of theft or loss.
- RO/ARO complete and transmit a loss or release of select agent Form3 to the FSAP.

References

- APHIS/CDC Guidance Document for Report and Transfer of Select Agents and Toxins (APHIS/CDC Form 2)
- APHIS/CDC Guidance Document for the Report of Theft, Loss or Release of Select Agents and Toxins (APHIS/CDC Form 3):
- Federal Select Agent website
- BU Materials Transportation Management Policy

List of Select Agents*

HHS and USDA Select Agents and Toxins

The following biological agents and toxins have been determined to have the potential to pose a severe threat to both human and animal health, to plant health, or to animal and plant products. An attenuated strain of a select agent or an inactive form of a select toxin may be excluded from the requirements of the Select Agent Regulations. Excluded agents and toxins are listed separately.

1. Abrin [6]
2. *Bacillus cereus* Biovar *anthracis* [1]
3. Botulinum neurotoxins [1][6]
4. Botulinum neurotoxin producing species of *Clostridium* [1]
5. Conotoxins (Short, paralytic alpha conotoxins containing the following amino acid sequence $X_1CCX_2PACGX_3X_4X_5X_6CX_7$) [6]
6. *Coxiella burnetii*
7. Crimean-Congo haemorrhagic fever virus
8. Diacetoxyscirpenol [6]
9. Eastern Equine Encephalitis virus [4][5]
10. Ebola virus [1]
11. *Francisella tularensis* [1]
12. Lassa fever virus
13. Lujo virus
14. Marburg virus [1]
15. Monkeypox virus [4]
16. Reconstructed replication competent forms of the 1918 pandemic influenza virus containing any portion of the coding regions of all eight gene segments (Reconstructed 1918 Influenza virus)
17. Ricin [6]
18. *Rickettsia prowazekii*
19. SARS-associated coronavirus (SARS-CoV) [5]
20. SARS-CoV/SARS-CoV-2 chimeric viruses resulting from any deliberate manipulation of SARS-CoV-2 to incorporate nucleic acids coding for SARS-CoV virulence factors
21. Saxitoxin [6]

South American Haemorrhagic Fever viruses:

22. Chapare
23. Guanarito
24. Junin
25. Machupo
26. Sabia

27. Staphylococcal enterotoxins (subtypes A,B,C,D,E) [6]
28. T-2 toxin [6]
29. Tetrodotoxin [6]

Tick-borne encephalitis complex (flavi) viruses:

30. Far Eastern subtype [5]
31. Siberian subtype [5]
32. Kyasanur Forest disease virus [5]
33. Omsk hemorrhagic fever virus [5]
34. Variola major virus (Smallpox virus) [1]
35. Variola minor virus (Alastrim) [1]
36. *Yersinia pestis* [1]

Overlap Select Agents and Toxins

37. *Bacillus anthracis* [1]
38. *Bacillus anthracis* Pasteur strain
39. *Brucella abortus*
40. *Brucella melitensis*
41. *Brucella suis*
42. *Burkholderia mallei* [1]
43. *Burkholderia pseudomallei* [1]
44. Hendra virus
45. Nipah virus
46. Rift Valley fever virus
47. Venezuelan equine encephalitis virus [4][5][8]

USDA Veterinary Services (VS) Select Agents and Toxins

48. African horse sickness virus
49. African swine fever virus
50. Avian influenza virus [4]
51. Classical swine fever virus [5]
52. Foot-and-mouth disease virus [1][5]
53. Goat pox virus
54. Lumpy skin disease virus
55. *Mycoplasma capricolum* [4]
56. *Mycoplasma mycoides* [4]
57. Newcastle disease virus [3][4]
58. Peste des petits ruminants virus
59. Rinderpest virus [1]
60. Sheep pox virus
61. Swine vesicular disease virus [5]

USDA Plant Protection and Quarantine (PPQ) Select Agents and Toxins

62. *Coniothyrium glycines*
    (formerly Phoma glycinicola and Pyrenochaeta glycines)
63. *Peronosclerospora philippinensis*
    (Peronosclerospora sacchari)
64. *Ralstonia solanacearum [7]*
65. *Rathayibacter toxicus*
66. *Sclerophthora rayssiae [7]*

67. *Synchytrium endobioticum*
68. *Xanthomonas oryzae*

Xanthomonas oryzae

[1] Denotes Tier 1 Agent
[2] C = Cysteine residues are all present as disulfides, with the 1st and 3rd Cysteine, and the 2nd and 4th Cysteine forming specific disulfide bridges; The consensus sequence includes known toxins a-MI and a-GI (shown above) as well as a-GIA, Ac1.1a, a-CnIA, a-CnIB; X1 = any amino acid(s) or Des-X; X2 = Asparagine or Histidine; P = Proline; A = Alanine; G = Glycine; X3 = Arginine or Lysine; X4 = Asparagine, Histidine, Lysine, Arginine, Tyrosine, Phenylalanine or Tryptophan; X5 = Tyrosine, Phenylalanine, or Tryptophan; X6 = Serine, Threonine, Glutamate, Aspartate, Glutamine, or Asparagine; X7 = Any amino acid(s) or Des X and; "Des X" = "an amino acid does not have to be present at this position." For example if a peptide sequence were XCCHPA then the related peptide CCHPA would be designated as Des-X.
[3] A virulent Newcastle disease virus (avian paramyxovirus serotype 1) has an intracerebral pathogenicity index in day-old chicks (Gallus gallus) of 0.7 or greater or has an amino acid sequence at the fusion (F) protein cleavage site that is consistent with virulent strains of Newcastle disease virus. A failure to detect a cleavage site that is consistent with virulent strains does not confirm the absence of a virulent virus.
[4] Select agents that meet any of the following criteria are excluded from the requirements of this part: Any low pathogenic strains of avian influenza virus, South American genotype of eastern equine encephalitis virus, west African clade of Monkeypox viruses, any strain of Newcastle disease virus which does not meet the criteria for virulent Newcastle disease virus, all subspecies Mycoplasma capricolum except subspecies capripneumoniae (contagious caprine pleuropneumonia), all subspecies Mycoplasma mycoides except subspecies mycoides small colony (Mmm SC) (contagious bovine pleuropneumonia), and any subtypes of Venezuelan equine encephalitis virus except for Subtypes IAB or IC, provided that the individual or entity can verify that the agent is within the exclusion category.
[5] For determining the regulatory status of nucleic acids that are capable of producing infectious forms of select agent viruses, please reference guidance here.
[6] For determining the regulatory status of Recombinant and/or Synthetic nucleic acids that encode for the toxic form(s) of any select toxins if the nucleic acids (i) can be expressed in vivo or in vitro, or (ii) are in a vector or recombinant host genome and can be expressed in vivo or in vitro; please reference guidance here.
[7] Select agents or toxins that meet any of the following criteria are excluded from the requirements of this part: Any subspecies of *Ralstonia solanacearum* except race 3, biovar 2 and all subspecies of *Sclerophthora rayssiae* except var. *zeae,* provided that the individual or entity can identify that the agent is within the exclusion category.
[8] Modified Venezuelan Equine Encephalitis Virus TC-83(A3G) strain is a select agent.

Chapter 11
Transportation of Biological Materials

Training is required prior to shipping of materials off campus. This does not count as training.

The packaging and transportation of biological materials are subject to strict local, state, federal, and international regulations. This is particularly so if the material is transported through the "public domain," namely, those roadways, airways, and sea lanes accessible to the public.

Therefore, unless the material is being moved within a specific campus, legal requirements governing packaging, labeling, and handling must be followed.

The intent of the packaging and transportation regulations is to prevent accidental exposure of personnel who may handle the material during its shipment. Therefore, certain general criteria apply to all possible transportation scenarios.

Prior to transporting any biological materials, the following controls must be in place:

- Emergency procedures (e.g., contact names and information, spill cleanup, disinfection protocols, etc.) must be known to the person carrying the materials.
- Container must be appropriate for the material being transported.
- Material must be packed so that it will stay upright during transportation.
- The containers must be properly labeled.
- Proper PPE must be worn during the packaging of the material.
- Hands should be washed after handling materials.
- Open cuts or other wounds should be covered before handling the materials.
- Aerosol generation must be avoided when handling and packing the materials.
- The person packaging the material must ensure that the exterior surfaces of each package are free of any potential contamination by the packed material.

Transportation within a Campus

The following requirements must be observed during the transportation of biological materials within a campus (e.g., between two laboratories):

- At a minimum, all laboratory materials must be transported in a secondary container that is sealed, shatterproof, and leak-proof. Materials should never be carried in hands or pockets.
- The secondary container should be closeable and easy to decontaminate; an absorbent pad (or similar material) should be placed inside the secondary container to absorb any spills.
- A laboratory coat should be worn during transport.
- Label information must include the identity of the biological material or agent, the universal biohazard symbol (if the material or agent is in, or above, Risk Group 2.
- Each individual container must have enough label information to identify its contents. Other information should be on the outside of the package.
- The container should be carried directly to the intended laboratory and not taken to offices, cafeterias, or other public or inappropriate locations.
- Upon delivery, the receiving laboratory personnel should be informed and the material properly stored.
- The package should be carefully inspected for signs of leakage or other contamination and, if

necessary, decontaminated before opening.

Transportation between Campuses (Ground)

Transportation of biological samples between campuses (e.g., BUMC and CRC) is subject to the general conditions described above. Biological materials should not be transported on the Boston University Shuttle (BUS). In addition, because the transportation takes place through the public domain, the following other conditions apply:

- All biological samples must be packed according to Department of Transportation/International (DOT)/International Air Transport Association (IATA) regulations; this includes triple-packaging all samples, even if exempt materials.
- The specimen should be placed inside a primary container with a tight-fitting, leak-resistant top (e.g., full round-threaded screw cap with seal or stopper).
- The primary receptacle or secondary container should be labeled with the universal biohazard symbol if it contains bloodborne pathogen materials, as per required under the OSHA Bloodborne Pathogen standard 29 CFR 1910 1030.
- The primary receptacle is placed within a secondary (outermost) container that must meet the following specifications:
    - Enough extra space to hold absorbent and cushioning materials around the primary receptacle.
- Label information must include the category of the infectious biological material or agent, (e.g. Category B or exempt human or animal specimen), and the sending and receiving laboratory identification. Category A CANNOT be transported by hand between laboratories.
- Each individual container must have enough label information to identify its contents. In addition, a sheet containing a description of contents should be placed inside the container between the outer and secondary packaging.
- Any dry ice or other coolant can now be added between the secondary and outer packaging layers. This coolant material should be placed in a shipping box that contains a styrofoam liner or other appropriate material to ensure that the outer box is not damaged by moisture from cold packs or other coolants.
- All required DOT/IATA labeling and marking information should be on the outside of the package.
- The BU shuttle system, MBTA, taxi cabs, driving services, or other payment for transport methods must not be used for transportation of infectious agents or other biohazardous materials.
- If the package contains exempt human or animal specimens, or materials that fall under the "Category B Infectious Substances" category, the package may be moved over U.S. roadways by a member of the laboratory. This exclusion, called "Materials of Trade"(MOT) by the U.S. Department of Transportation, allows some materials that are exempt or Category B Infectious materials to be transported by a research or clinical laboratory personnel. Courier services fall under the "Exclusive Use" Exemption under DOT. This exclusion does not apply to Category A infectious substances or other categories of Dangerous Goods. This individual must have undergone shipping training in the last two years. This package must follow all requirements as described above. Contact the Office of Research Safety, EHS for further information and questions about these DOT exemptions.
- The container should be shipped directly to the intended laboratory and not taken to offices, cafeterias, or other public or inappropriate locations.
- Upon delivery, the receiving laboratory personnel should be informed and the material properly stored. The package should be carefully inspected for signs of leakage or other contamination and, if necessary, decontaminated before opening.

Air Transport of Materials

Occasions do arise when a PI must either ship or receive biological materials from another institution. Such activities are governed by strict federal and international guidelines. See Appendix A for detailed requirements pertaining to international (import/export) shipments. Before exporting biological material, you should check 1) whether the particular material requires an export permit by reviewing the Commerce Control List, Category 1; 2) check the recipient against the "Restricted Parties Lists"; 3) verify whether license is needed for the country of import; and 4) verify that the material will not be used to design weapons of mass destructions or another military development. After determining U.S. export control requirements, you should verify the import requirements for the destination country and apply for import permits if required. Boston University's Export Control Officer can provide assistance with this process.

All anticipated purchases/shipments of materials subject to the International Traffic in Arms Regulations (ITAR) must be reported to the Export Control Officer in advance of the purchase to ensure that laboratories are briefed on the licensing requirements for the use of such materials.

In addition to U.S. export regulations, you are required to review the dangerous goods shipping requirements outlined below.

The International Civil Aviation Organization (ICAO) is the United Nations entity that governs all international civil aviation matters. The ICAO's *Technical Instructions for the Safe Transport of Dangerous Goods by Air* govern the shipping of dangerous goods. These technical instructions have been incorporated into U.S. law and are an acceptable method of transport in the United States (49 CFR 175).

Packaging and shipping biological materials involve certain risks with numerous potential liabilities. The International Air Transport Association's (IATA) *Dangerous Goods Regulations* (DGR), latest edition, is the worldwide gold standard for shipping. The IATA regulations apply to *all* air transport, both domestic and international flights. Following IATA's DGR ensures that a package will also meet U.S Department of Transportation requirements for ground transport.

All responsibilities for packaging and shipment of these agents have been assigned to the shipper. Only properly trained personnel may offer infectious materials for transport. The following is only a summary of the requirements for packaging and shipping infectious agents. All persons must complete the shipping training prior to the packaging and shipment of their materials.

Definitions and Applicability

Dangerous goods: articles or substances capable of posing significant risk to health, safety, property, or the environment when transported by surface or air. Most infectious or biological materials are considered dangerous goods and therefore are subject to shipping regulations.

Infectious substances: substances known or reasonably expected to contain pathogens. Pathogens are defined as micro-organisms (including bacteria, viruses, rickettsiae, parasites, fungi) and other agents, such as prions, which can cause disease in humans or animals. For the purposes of shipping classification, infectious substances are broken into two categories:

> **Category A**: an infectious substance transported in a form that, when exposure to it occurs, is capable of causing permanent disability or life-threatening or fatal disease in otherwise healthy

humans or animals.

Category B: an infectious substance that does not meet the criteria for inclusion in Category A.

Biological products: those products derived from living organisms manufactured and distributed in accordance with the requirements of national governmental authorities (e.g., the FDA). They may have special licensing requirements and are used either for prevention, treatment, or diagnosis of disease in humans or animals, or for developmental, experimental, or investigational purposes related thereto. Biological products manufactured and packaged in accordance with the requirements of appropriate national authorities that are transported for the purposes of final packaging or distribution and for personal health-care use by medical professionals are NOT subject to dangerous goods regulation. However, biological products not governed by national authorities and that are known or reasonably believed to contain infectious substances MUST be classified and shipped according to dangerous goods regulations.

Dry Ice: Commonly used a refrigerant.

Exempt Patient/Animal Specimens: patient or animal specimens for which there is a minimal likelihood that pathogens are present are exempt from most of the shipping regulations. However, they must be marked with the words "exempt human specimen" or "exempt animal specimen" and must be triple-packed as described below.

Genetically Modified Micro-Organism/Organisms (GMMO/GMO): materials in which genetic materials have been altered through genetic engineering which does not occur naturally.

Completely Exempt Substances: materials that are totally exempt for consideration under the shipping regulations:

- Substances containing micro-organisms that are non-pathogenic to humans or animals
- Substances in a form so that any present pathogens have been neutralized or inactivated such that they no longer pose a health risk (the chemical itself may be regulated – Contact EHS prior to shipping)
- Environmental samples (including food and water samples) that are not considered to pose a significant risk of infection, and
- Dried blood spots, collected by applying a drop of blood onto absorbent material, fecal occult blood screening tests, blood or blood components intended or prep to be used for transfusion, and tissues or organs intended for transplantation.

Classification and Identification

The substance to be shipped must be classified as completely exempt from regulation, an exempt patient/animal specimen, or a Category A or B infectious substance. Once classified, proper shipping names and identification numbers can then be assigned to the material. Exempt patient specimens require shipping names. However, Category A and B materials are assigned the following names and numbers:

- **Category A**: assign one of two identifiers, depending on whether or the material infects humans:

  • UN 2814 Infectious substance affecting humans
  • UN 2900 Infectious substance affecting animals

Note: *If a material infects both humans and animals, use the Infectious substance affecting human code, UN 2814.*

- **Category B:** UN 3373 biological substance category B
- **Dry Ice:** Un 1845 Dry Ice
- **GMMO/GMO:** UN 3245 Genetically Modified Micro-Organism/Organisms
- **Exempt Materials:** Exempt Human or Animal Specimen

Packaging

All regulated infectious substances, including Category A, Category B, and exempt patient specimens, must be triple packed:

- The innermost primary receptacle(s) is leak-proof.
- A leak-proof secondary receptacle with absorbent material and cushioning material placed between the primary and secondary receptacles to prevent the release of liquid during transport and to shield multiple primary receptacles from coming in contact with one another.
- Rigid, tertiary outer packaging that is at least 100 mm (4 in) in its smallest external dimension.

Additionally, shipments of Category A and Category B materials must be packaged according to IATA Packing Instructions 620 and 650, respectively. Those guidelines require the following:

- Shipments must be prepared in such a way that they arrive at their destination in good condition and present no hazard to persons, animals and/or environment during shipment.
- Outer packaging must meet structural strength requirements and carry defined specification markings.
- Packages must be at least 100 mm (4 in) in their smallest external dimension.
- An itemized list of contents must be enclosed between the secondary container(s) and the outer packaging.
- All packages containing infectious substances must be marked durably and legibly on the outside of the package with the name and telephone number of a person responsible for the shipment.
- The shipper must make advance arrangements with the recipient and the operator to ensure the shipment can be transported and delivered without unnecessary delay.
- Substances shipped at ambient temperatures or higher must be in primary receptacles made only of glass, metal or plastic, with a positive means of ensuring a leak-proof seal. Screw caps must be reinforced with adhesive tape.
- Substances shipped refrigerated or frozen must carry the refrigerant between the secondary container and outer packaging. Wet ice is not recommended for shipping as it may cause the package to leak during transport, thus delaying or causing rejection of the package by the transporter. If dry ice is used, the packaging must permit the release of CO_2 gas.
- Primary and secondary containers must meet temperature and pressure requirements set out in the regulations.

Category A shipments require UN Spec packaging.

Labeling

Package labeling is in the form of standardized pictures that must be affixed to the outside. The color and design of each label is prescribed in the IATA regulations. All labels must be at least 4 inches on the smallest side.

For the purposes of infectious substances, five different labels must be considered:

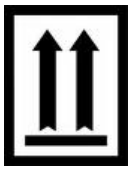
Category A:

Category B:

Dry Ice:

Cargo Aircraft Only: must be affixed if shipping volumes greater than 50 ml of a Category A substances can be halved for use on a smaller category A box.

Orientation Arrows: if shipping liquids, two such labels must be affixed to the package, on opposing sides.



Marking

Markings are the words and numbers required to be on the outside of a package. The following markings must be present on any package containing a Category A or Category B material:

- *UN Number and Proper Shipping Name*:
  - UN 2814 Infectious substance affecting humans
  - UN 2900 Infectious substance affecting animals
  - Biological substance category B
  1. Genetically Modified Micro-organisms/Organisms

Note: *The UN number is part of the label for Category B substances.*

- *Contact Information*
  - Name and telephone number of the responsible person
  - 24-hour emergency telephone number in case of transportation emergency
  - "To" and "from" information

If shipping a material under dry ice, the following additional marking is required:

- UN 1845 Dry Ice (the weight in kilograms of the dry ice present should also be noted)

If shipping an exempt patient or animal specimen, the only marking required is:

- Exempt Human Specimen

or

- Exempt Animal Specimen

Training Requirements

Those involved in the packaging and shipping of infectious substances must undergo training every two years or when regulations change. It is the department's responsibility to ensure training is completed. The Office of Research Safety, EHS can provide this training. The shipper is obligated to receive further qualification when shipping hazardous materials of a class or division (chemical, radiological, Li-Ion Battery, etc.) where current training is insufficient or contact EHS for more information.

S	INSTRUCTIONS
1	Shipper's: Name Address Phone number
2	Receiver's: Name Address Phone number
3	Line out the item that does not apply. Passenger aircraft can only be used to ship quantities less than 50 ml. Cargo aircraft must be used to ship quantities between 50 ml and 4 L.
4	Line out the item that does not apply.
5	Proper Shipping Name (infectious substance, affecting humans or infectious substance, affecting animals) Identify the specimen by name in parenthesis *ex. Infectious substance, affecting humans (rabies virus)*
6	Class or Division * Always 6.2
7	UN Code * UN 2814 or UN 2900 (UN 3373 does not require shippers dec.)
8	Packaging Group * There is no packaging group for biological agents.
9	Identify by stating the number of containers by the quantity in each container. (e.g., 5 X 10ml) Identify type of outer container for the shipment
10	Packaging Instructions * 602 or 650 (also 904 if dry ice included)
11	24-hour emergency contact number for the shipper (PI, Lab Supervisor), The statements, "Prior arrangements as required by the IATA Dangerous Goods Regulations 1.3.3.1 have been made." And "Prepared according to ICAO/IATA."
12	Name and Signature of the shipper.

* As described in the latest edition of the IATA Dangerous Goods Regulations

Note*:*

- *When shipping biomaterials on dry ice, remember that dry ice is itself considered a dangerous good and must also be listed on the shipping documents as UN1845, Packing Group III, Packing Instruction 954.*
- *BU has adopted additional shipping requirements for "high hazard materials" with strict requirements for approved carriers, including a dedicated vehicle, point-to-point delivery, and specified shipping routes. For more information, contact EHS.*
- *The transportation must also meet the NIH guidelines.*

BU Materials Transportation Management Policy

Purpose and Applicability

The purpose of this policy is to define the procedures used to manage the shipping, receiving, and transportation of items determined to be high-risk by EHS in accordance with Boston University policies and procedures and all applicable laws and regulations.

This policy applies to all items determined to be high -risk and to all employees and staff, including those who are visiting users of Institutional facilities and those who are contracted services involved in the shipping, receiving, handling or other use of subject materials as described below.

This policy defines the protocols for the selection of contracted services to be used in the shipping, receiving, and transport of subject materials. It also includes standards for packaging, transporting, delivery routes and the quality controls to be utilized to ensure that all those involved in the management of subject materials transport adhere to these standards.

Definitions

Subject Materials: A substance or material in a quantity and form that may pose a high level of risk to health, safety or property when received, transported and/or stored. These materials include, but are not limited to, toxic/infectious substances (including select agents), radioactive materials, chemicals, compressed gases, and any other materials that EHS deems a material that should be managed throughout its transport.

Select Agents: Biological agents and toxins that have the potential to pose a threat to public health and safety if used for bioterrorism purposes. The list includes over 80 bacteria, viruses, toxins, rickettsia, and fungi. The program is regulated by the Department of Health and Human Services (DHHS) and Department of Agriculture (USDA) under the Federal Regulation for Select Agents [42 CFR 73.0; 7 CFR 331; 9 CFR 121].

Shipper: The shipper is the person who packages the subject material and signs the shipper's declaration form. This person is responsible for the material to be classified, identified, packaged, marked and labeled, with all appropriate documentation included with the package. This individual is required to have shipping training and notify the receiver regarding the planned shipment of high-risk material.

Transporter: The transporter is the individual, operator or contracted service that obtains the package from the shipper, verifies it has been packaged correctly, and carries the package to the receiver.

Receiver: The receiver, for the purposes of this policy, is the individual who receives the package. This individual is required to have shipping training. The receiver notifies the shipper upon receipt of the planned delivery of high-risk material.

Shippers Declaration Form: The documentation that a high-risk material will be shipped. These documents will be maintained in accordance with all laws, regulations and BU policies including standards for the maintenance of original forms to be maintained by the shipper, the transporter and the receiver.

Qualified Vendor: A vendor who meets or exceeds the criteria in Section 6.

Roles and Responsibilities

EHS
The EHS is responsible for the management and oversight of the Materials Transportation Management Policy and for ensuring compliance with the procedures outlined within this policy by all employees and staff, visiting users of BU facilities and contracted services including associated transporters.

Office of Mail Services
The Office of Mail Services will provide support to EHS and Department of Public Safety with the screening/examination of delivered packages, with the staffing of designated locations, and with the management of contracted services.

Office of Purchasing Services
The Office of Purchasing Services will be responsible for facilitating the selection of contracted service providers who are capable of providing services in accordance with this policy and in compliance with all applicable laws and regulations. The Office of Purchasing Services will select, monitor, manage and discharge all contracted services that are involved in the management and transport of subject materials.

Research Compliance
The Export Control Officer will assist with export license applications, international shipping documentation and will submit classification requests to the respective governmental agency if export classification is unclear.

Department of Public Safety
The Department of Public Safety (DPS) will, through its Investigations Unit, initiate, conduct and/or participate in audits and conduct investigations as necessary. DPS, through its Systems and Operations Units, will be responsible for maintaining the security of locations determined to be appropriate for the receiving, shipping and storage of designated materials as well as the screening and examination of vehicles, packages and personnel. DPS will provide security at the point of receipt of the high hazard material and escort the package from the point of entry to the final destination in the BUMC. Transport of select agents from one location to another outside of a contained area may require security escort to verify that the transporter is BUMC select agent authorized.

Office of Emergency Planning and Response
The Office of Emergency Planning and Response (OEPR) will provide to EHS, Facilities Management and Planning, the Department of Public Safety and members of the Emergency Response Team recommendations related to emergency management planning, training and response coordination. In addition, the OEPR will participate in the development and implementation of emergency response plans, exercises, risk reduction initiatives and risk prevention measures; and serve as the liaison to the Boston Mayor's Office of Emergency Preparedness, the Massachusetts and Federal Emergency Management Agencies.

The Shipper
The Shipper will be responsible for ensuring that the material being shipped is appropriately packaged including classifying, identifying, marking, labeling and providing appropriate documentation with the package. The shipper must be trained in accordance with all applicable laws, regulations and BU policies including those that address the type and frequency of training and necessity of additional training should laws, regulations or BU policies change at any time.

The Transporter
The Transporter will be required to do the following: accept, store, load, inspect and deliver packages to an approved location using approved access routes; report any and all violations of law, regulation or policy; retain all records; and have proper shipping training. The inspection of packages includes requirements involving damage to packages, reporting guidelines and immediate communication to the shipper and receiver, public health and regulatory authorities. In addition to these requirements, transport companies may have their own specific safety requirements for subject material transport.

Procedures

EHS and DPS will determine the best location for the receipt, control, audit, transport, and shipping of all items under this policy. Such location(s) will be operated or provided with oversight by representatives of EHS and other related user departments. These areas will be routinely audited. Transport to and from this location will be by major routes of travel that immediately border BUMC and are limited to Albany Street, Massachusetts Avenue and the highway/connector system in the rear of BioSquare.

EHS will train all users of the laws, regulations, polices and requirements involved in the shipping and receiving of subject materials and will manage the tightly controlled, pre-approved, scheduling of shipment and delivery times. EHS will train all BU users in the approved procedures for the packaging of materials, the approved contracted services to be used in the transport of such materials and the penalties of failing to follow all aspects of this policy.

EHS and DPS will ensure that BU staff involved in the high-risk materials shipping / receiving areas undergo a background clearance check, as appropriate, consistent with the select agent regulatory requirements prior to being approved to work in these locations.

EHS and DPS will determine the packaging requirements to be used in the shipping and receiving of subject materials. These requirements will comply with all applicable regulatory standards. These mandated packaging requirements would only be altered after obtaining any required approval from all relevant regulatory authorities.

Transport of select agents will be done in accordance with all laws and regulations including the approval from the U.S. Department of Health and Human Services/ Center for Disease Control and Prevention (HHS/CDC) or United States Department of Agriculture/Animal and Plant Health Inspection Service (USDA/APHIS), prior to shipment, and notification within 24 hours of receipt. The transport will also include the utilization of appropriate forms and the reporting of registration numbers of all parties involved in shipping, transporting and receiving packages.

EHS, DPS and the Office of Purchasing will select contractors for the transportation of subject materials based on criteria including, but not limited to, the following:

- Past performance on similar contracts.
- Ability to provide services as a qualified vendor for transport of all subject materials.
- Ability to provide transport services in accordance with all applicable regulatory standards.
- Ability to provide transport services in accordance with all applicable BU standards.
- BU requires that the DOT-compliant triple packaging be placed in a non-crushable liquid tight solid container for an added layer of safety.
- BU requires that packages be secured in the vehicle away from potential impact on outer walls.
- Ability to provide staffing that has undergone, and continues to undergo on an annual basis, appropriate background checks.
- Ability to provide courier services that may require that a single individual pick up and deliver packages.
- Ability to provide GPS tracking of packages or vehicles as determined appropriate and approved by BU.
- Ability to provide vehicles that are inspected in accordance with all applicable inspection standards at least every six months.

- Ability to provide customized services that require adherence to BU determined routes of travel, audit procedures and strictly defined schedules for both pick-ups and deliveries.
- Ability to maintain and to provide an all-inclusive chain of custody document upon delivery of each package.
- Ability to provide resources to participate in BU audits of services.
- Any transportation vendor personnel having relative proximity to the package must report all occurrences of illness to the BPHC for a period of three weeks from the delivery departure date.

Tracking Shipments: EHS will schedule all deliveries and will track the delivery with the contracted service performing the transportation by means of contractor-provided tracking methods. BU will initiate its own tracking methods at its discretion and will determine the type of packaging that the shipper, receiver and transportation company uses, and that it is in compliance with all laws and regulations.

Prior to the transport of a shipment to the NEIDL of a select agent, the Director of Emergency Planning and Response will ensure that the appropriate Commonwealth and Boston emergency response departments having jurisdiction are notified.

Off Peak Delivery: EHS will schedule all deliveries to arrive at off peak traffic hours through the City of Boston to ensure transport and reduce the possibility of accident or delay due to traffic congestion.

Clear Loading Dock: DPS will ensure that the loading dock or other facility where the transporter is delivering the high hazard material is free and clear of all parked vehicles to enable safe, secure transfer and receipt. Areas used for deliveries will include secure loading or vehicle inspection areas in which the delivery vehicle can be isolated from movement.

Delayed Receipt: Failure to receive package within the specified time range of delivery will result in an immediate investigation involving the transport contractor, the shipper, BU and all applicable regulatory personnel.

Receipt of Packages: Packages delivered to BU will be inspected, verified, documented and transported to the appropriate location within BU by EHS.

Prior to receipt of the package, the RO will verify with the driver that the package's integrity is intact. In the event that the package's integrity is compromised, the transport compartment will be sealed and the transporter's emergency protocols will be followed. OEPR will notify all appropriate local response agencies and initiate the BU Emergency Response Plan, the BU Select Agent Incident Response Plan, and Incident Command System.

Problems or Incidents On-Route: The transporter will contact the relevant law enforcement agency having jurisdiction for any problem or incident that may occur during transit or transport of the subject material. The transporter will also notify BU immediately of any such event.

The transporter will ask that the public safety agency having jurisdiction notify the local emergency responders having jurisdiction where any incident occurs.

Upon notification of an incident enroute to BU, OEPR will ensure that the local emergency response departments having jurisdiction are notified.

The transporter will have a reputable hazardous materials cleanup contractor available on a 24-hour by

seven days a week basis for response for a biological incident mitigation. The contractor will coordinate those mitigation efforts with the local emergency responder incident commander.

Notice of Successful Transport: Upon the successful receipt of a shipment under this policy, OEPR will notify all the appropriate public safety agencies of the conclusion of the transport.

Key References and Resources

- U.S. Department of Health and Human Services, *Biosafety in Microbiological and Biomedical Laboratories,* 6th Edition, June 2020
- U.S. Department of Transportation, 49 CFR Part 171 Final Rule, 03/18/05
- Current Revised International Air Transport Authority, Dangerous Goods Regulations
- U.S. Public Health Service (HHS)/ CDC 42 CFR Part 73.0, "Possession, Use & Transfer of Select Agents and Toxins," 03/18/05
- Morbidity and Mortality Weekly Report Vol. 1 No. RR-19, "Laboratory Security and Emergency Response Guidance for Laboratories Working with Select Agents" 12/06/02
- National Institutes of Health *Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*

Website References

BU EHS

BUMC, Public Safety Department

BU, Purchasing

Centers for Disease Control and Prevention Import Permit Program

Federal Select Agent Program, Laboratory Registration

Federal Express, Dangerous Goods Program

International Air Transport Authority

MA Department of Public Health-State Lab Institute

United Parcel Service, Hazardous Materials Support Center

United States Postal Service

United States Public Health Service

U.S. Department of Transportation

U.S. Department of Commerce

Appendix A
Importation and Exportation of Infectious Biological Agents

Multidisciplinary and multi-institutional research is a common practice that involves collaboration among faculty from various institutions and countries. At times it is necessary to share biological samples or materials with collaborators. Federal regulations strictly control the importation and exportation of infectious biological agents, equipment and technologies used for study and processing of these agents. The following outlines two major requirements that must be followed.

Note: All importation and exportation of infectious biological agents must be processed through the Biosafety Program. Contact the EHS office for assistance in this matter. Laboratories that will import infectious or potentially infectious materials must first be registered with the IBC before the sample can be obtained and stored in the laboratory.

CDC Etiologic Agent Import Permit Program

Infectious biological agents are those microorganisms and microbial toxins that cause disease in humans and include bacteria, bacterial toxins, viruses, fungi, rickettsiae, protozoans, and parasites. These disease-causing microorganisms may also be referred to as infectious agents. Arthropods and other organisms that transmit pathogens to animals (including humans) are called vectors.

Infectious biological agents, vectors, and materials containing infectious biological agents are recognized as hazardous materials. Materials containing infectious biological agents are regularly transported from one location to another by common land and air carriers. Materials containing infectious biological agents must be appropriately packaged to prevent breakage or leakage in order to avoid exposing the package contents to package handlers, transporters, and the general public. Materials containing infectious biological agents must be packaged, labeled, and transported in accordance with all applicable regulations. Material containing infectious biological agents being imported into the United States must be accompanied by a U.S. Public Health Service importation permit.

Importing Biological Agents and Materials into the United States

Before you decide to import biological materials or equipment associated with biological research into the United States, ensure that you review the U.S. import requirements to determine if an import permit or license is required. Securing an import permit may take months so it is critical that you start this process early. It is recommended that you contact the Export Control Officer and the Office of EHS in connection with license application.

All imports into the United States must be processed by a licensed Customs Broker. Most freight forwarders such as World Courier, FedEx etc. have customs brokers on staff to help you. Boston University customs broker is Watchpoint Logistics.

Contact information:
Linda Amiro
International Import Manager
Watchpoint Logistics Inc.
100 Griffin Brook Drive
Methuen, MA 01844
Phone: (617) 567-6800

Email:Linda.Amiro@Watchpointlogistics.com

Contact the University Export Control Officer if you need assistance with import shipments. Link here on detailed guidelines on Importing into the United States by US Customs and Border Protection.

You have approximately 10 days to file import paperwork with US Customs and Border Protection after your shipment has arrived into United States. If you don't have permits and documentation in place, your shipment will be placed into Customs storage and you will be charged daily fees and penalties. The ultimate issue with biological shipments, of course, is that your materials may get destroyed during this process before you are able to secure an import permit.

Import Permits
Import permits are issued only to the importer of record, which must be located in the United States. Import Permits may take several months and must be secured prior to the importation of any material. The permit, with the proper packaging and labeling, will help expedite ensure clearance of the package of infectious materials through the U.S. Public Health Service Division of Quarantine and release by U.S. Customs.

The importer is legally responsible for ensuring that the foreign personnel package, label, and ship the infectious materials according to federal and international regulations. Shipping labels with the universal biohazard symbol, the importer's address, the permit number, and the expiration date are also issued to the importer with the permit. The importer must send the labels and one or more copies of the permit to the shipper. The permit and labels inform the U.S. Customs and Border Protection and U.S. Division of Quarantine personnel of the package contents.

Boston University researchers are encouraged to contact the Office of EHS and the Export Control Officer prior to submitting permit application.

Federal Regulation
The importation of infectious biological agents is governed by the following federal regulation: USPHS 42 CFR - Part 71 Foreign Quarantine. Part 71.54 Import regulations for infectious biological agents, infectious substances and vectors.

A person may not import into the United States, nor distribute after importation, any etiologic agent or any arthropod or other animal host or vector of human disease, or any exotic living arthropod or other animal capable of being a host or vector of human disease unless accompanied by a permit issued by the CDC Director.

Any import coming within the provisions of this section will not be released from custody prior to receipt by the District Director of U.S. Customs Service of a permit issued by the Director (Centers for Disease Control and Prevention).

Items Requiring Permits

Infectious Biological Agents
It is impractical to list all etiologic agents in this document. In general, an import permit is needed for any infectious agent known or suspected to cause disease in humans.

Biological materials
Unsterilized specimens of human and animal tissues (such as blood, body discharges, fluids, excretions,

or similar material) containing an infectious biological agent may require a permit in order to be imported.

If you are importing biological materials that are not infectious, you may be required to submit such declaration to U.S. Customs at the time of the import. This document should be on a sender's university/hospital/company letterhead and signed by an individual who can legally bind the entity. It should accompany all import shipments into the United States to expedite Customs clearance.

Hosts and vectors

- *Animals*: any animal known or suspected of being infected with an organism capable of causing disease in humans requires a permit issued by CDC. Importation of live turtles of less than 4 inches in shell length and live nonhuman primates is regulated by the CDC's Division of Global Migration and Quarantine.
- *Bats*: all live bats require an import permit from the CDC and the U.S. Department of Interior, Fish and Wildlife Services. The application for a CDC import permit for live exotic bats is at CDC Importation of Animals website**.**
- *Arthropods*: any living insect or other arthropod that is known or suspected of containing an infectious biological agent requires a CDC import permit.
- *Snails*: snail species capable of transmitting a human pathogen require a CDC permit.

Packaging Requirements

Infectious materials imported into this country must be packaged to withstand breakage and leakage of contents and be labeled, as specified in the following federal regulations:

- DOT 49 CFR PART 173 - General Requirements for Shipments and Packaging
- For international shipments, the International Air Transport Association's (IATA) *Dangerous Goods Regulations* must be consulted.

Importation of Animal Pathogens and related biological materials

USDA and APHIS permits are required for infectious agents of livestock and biological materials containing animal material. Tissue culture materials and suspensions of cell culture-grown viruses or infectious biological agents containing growth stimulants of bovine or other livestock origins are controlled by the USDA because of the potential risk of introduction of exotic animal diseases into the United States. For more information, contact USDA/APHIS at their website:

Principal Investigators must submit USDA/APHIS permit applications via IBC staff. More information about the application process can be found in the IBC Policies page.

Principal Investigators must submit USDA/APHIS permit applications via IBC Staff More information about the application process can be found in the IBC Policies page.

Importation of Wildlife and Animals

U.S. Fish and Wildlife Service permits are required for certain live animals, including bats. For more information, call (800) 344-WILD or visit their website here.

Importation of Select Agents

Individuals wishing to import select agents and toxins must be registered with the Federal Select Agent Program (FSAP) in accordance with 42 CFR Part 73 (Possession, Use, and Transfer of Select Agents and

Toxins; Interim Final Rule) for the select agent(s) and toxin(s) listed on the import permit application. Also, in accordance with 42 CFR Part 73.16(a), an FSAP Form 2 must be completed and submitted to the Federal Select Agent Program and granted approval prior to the shipment of the select agents or toxins under the import permit. Additional information can be found at Form 2 Transfer Guidance.

Importation of Research Equipment
Research equipment: Some equipment used in biological and medical research must be approved by the Food and Drug Administration (FDA) and must have appropriate safety certificates. Before purchasing equipment abroad, ask the manufacturer if this equipment requires FDA approval and if the company has such approvals in the United States.

Exportation of Infectious Materials

There are two sets of export controls that govern the export of biological materials: the Export Administration Regulations (EAR) and the International Traffic in Arms Regulations (ITAR). The EAR govern the export of dual-use agents, genetic material, vaccines and equipment used in biological research. Prior to the export, you should review the Commerce Control List (CCL) (Category 1) to determine if your material is controlled under an Export Control Classification Number (ECCN). If the material is listed on the CCL, contact the Export Control Officer to help you determine if a license is required. Licensing requirements are based on the material, customer and end-use. If the material is not listed on the CCL and is not controlled under the U.S. Munitions List, it is designated as EAR99. EAR99 material can be exported abroad without an export license unless your collaborator is listed on the "Restricted Parties Lists;" or you ship to a country where U.S. maintains a comprehensive embargo administered by the Office of Foreign Assets Control; or the end use will be weapons of mass destructions or military end use.

If you are unable to determine the ECCN of your material, the Export Control Officer will submit commodity classification request with the Department of Commerce, Bureau of Industry and Security on your behalf. Classification requests can take anywhere from few days to several months so it is important to plan ahead.

Biological agents, pathogens, toxins specifically modified, developed, configures or adapted for military use are controlled on the U.S. Munitions List (Category XIV) under the International Traffic in Arms Regulations (ITAR). Research with these agents is heavily regulated and licenses are required for you to share these materials with non-U.S. Persons whether abroad or in the United States. Contact the Export Control Officer before shipping ITAR controlled materials abroad as a license is required.

Link here for more information on export controls and biological materials. **Export controls regulate more materials/agents than CDC and USDA regardless of quantity or attenuation; therefore, it is critical that you review the Commerce Control List and the US Munitions List prior to any export shipment. DO NOT ASSUME THAT YOUR MATERIAL IS NOT REGULATED.**

In addition to the product/material based regulations, you may need an export license based on the destination and customer. Office of Foreign Assets Controls manages economic sanctions and embargoes and you may need an export license to ship to any of these countries. Before you make any export shipments, please verify by screening the Restricted Parties List that no license is required for the receiving researcher, entity or end-user. Some universities are on those lists.

Research Compliance developed guidelines to help you determine whether an export license is required. Please review the Export Control Website, International Shipping Training or contact the University Export Control Officer to provide assistance.

Export licenses or requests for material classifications may take months so you are encouraged to start this process early.

In addition, to the licensing requirements, you should understand that you will need to complete export shipping paperwork. Standard documents include Commercial Invoice and Air Waybill; however, additional documentation may be required depending on the importing country requirements. You should also verify the requirements of the importing country for licensing biological materials prior to dispatching export shipments. Contact the receiving entity or your freight forwarder to provide assistance with foreign country import requirements.

Foreign Trade Regulations

All export shipments valued over $2,500 per commodity classification or subject to an export license must be reported via the Automated Export System to U.S. Census Bureau prior to the export. Your freight forwarder will be able to handle the reporting, alternatively, you should contact the University Export Control Officer to provide assistance.

Recordkeeping

All shippers are required to keep records on file five (5) years from the date of the export or expiration of an export license whatever period is longer.

Appendix B
Laboratory Ventilation and Containment for Biosafety

Laboratory-ventilated containment equipment fall into three (3) major categories:

Laboratory Chemical (Fume) Hoods
Traditional laboratory chemical (or fume) hoods are designed to capture and control chemical vapors and pull them away from the worker. Although the inward flow of air protects the user, chemical hoods do not protect the product (the desired organism being manipulated).

Other Local Exhaust Ventilation (LEV) Systems

Horizontal Laminar Flow Clean Bench
With horizontal laminar flow clean benches, HEPA-filtered air flows horizontally across the workspace directly toward the user. These clean benches provide product protection and were originally designed to provide a particulate-free environment for the manufacture of semiconductor components.

Clean benches provide product protection against microbial contamination, but they *do not* provide personal or environmental protection. In fact, the horizontal flow of air will blow biological agents directly toward the user and into the laboratory. Clean benches are not a biological safety cabinet, and they should not be used with any materials (biological, chemical, or radiological) requiring containment for protection of personnel or the environment.

Clean benches are acceptable for use with materials that do not present risks to the laboratory workers (including immunocompromised individuals who may frequent the lab). Human cell lines and nonhuman primate cell lines are generally considered to be BSL2 agents and would not be suitable for use in a clean bench.

Biological Safety Cabinets

Biological safety cabinets (BSCs) are divided into Class I, II, and III (see schematic below). Class II BSCs are subdivided into type A and type B. All BSCs provide personnel and environmental protection, with Class II BSCs also providing product protection.

- Personnel protection is achieved by inward airflow through the front of the cabinet.
- Product protection is achieved by downward HEPA-filtered airflow from the top of the cabinet.
- Environmental protection is achieved by HEPA filtration of exhaust air.

New NSF Classification (Adopted 2002)	Previous NSF Classification	**General Description**
A1	Class II, Type A	- Maintain minimum average inflow velocity of 75 ft/min (0.38 m/s) through the work access opening; - have HEPA/ULPA filtered downflow air that is a portion of the mixed downflow and inflow air from a common plenum (i.e., a plenum from which a portion of the air is exhausted from the cabinet and the remainder supplied to the total work area; - may exhaust HEPA/ULPA filtered air back into the laboratory or to the environment through an external exhaust system connected to the cabinet with a canopy connection; and - have all biologically contaminated ducts and plenums under negative pressure or surrounded by negative pressure ducts and plenums. If using chemicals with toxic vapors, the unit shall be connected to an external exhaust system. Type A1 cabinets may be used for work with volatile chemicals if deemed appropriate by a chemical risk assessment NOTE — Type A1 BSCs manufactured prior to 2010 are not suitable for work with volatile chemicals due to the contaminated positive pressured plenums that are not surrounded by negative pressure plenums.
A2	Class II, Type (formally Class II A/B3) When exhausted to the environment were formally designated Type B3	- Maintain a minimum average inflow velocity of 100 ft/min (0.51 m/s) through the work access opening; - have HEPA/ULPA filtered downflow air that is a portion of the mixed downflow and inflow air from a common exhaust plenum; - may exhaust HEPA/ULPA filtered air back into the laboratory or to the environment through an external exhaust system connected to the cabinet with a canopy connection; and - have all biologically contaminated ducts and plenums under negative pressure or surrounded by negative pressure ducts and plenums. If using chemicals with toxic vapors, the unit shall be connected to an external exhaust system. Type A2 cabinets may be used for work with volatile chemicals if deemed appropriate by a chemical risk assessment

B1	Class II, Type B1	- Maintain a minimum average inflow velocity of 100 ft/min (0.51 m/s) through the work access opening; - have HEPA/ULPA filtered downflow air composed largely of uncontaminated recirculated inflow air; - exhaust contaminated downflow air from a region of the total work area via an internal dedicated exhaust plenum and through HEPA/ULPA filter(s) to a dedicated external exhaust system for BSCs with a direct connection and exhausted to the atmosphere; - recirculate the balance of the downflow and inflow air through a supply HEPA/ULPA filter(s); and - have all biologically contaminated ducts and plenums under negative pressure or surrounded by negative pressure ducts and plenums. Type B1 cabinets may be used for work with volatile chemicals if permitted by a chemical risk assessment
B2	Class II, Type B2	- Maintain a minimum average inflow velocity of 100 ft/min (0.51 m/s) through the work access opening; - have HEPA/ULPA filtered downflow air drawn from the laboratory or the outside air (i.e., downflow air is not recirculated from the cabinet exhaust air); - exhaust all inflow and downflow air to the atmosphere through a dedicated external exhaust system for BSCs connected to the cabinet with a direct connection after filtration through a HEPA/ULPA filter without recirculation in the cabinet or return to the laboratory; and - have all contaminated ducts and plenums under negative pressure or surrounded by directly exhausted (non-recirculated through the total work area) negative pressure ducts and plenums Type B2 cabinets may be used for work with volatile chemicals if permitted by a chemical risk assessment
C1	Class II, Type C1	- Maintain a minimum average inflow velocity of 100 ft/min (0.51 m/s) through the work access opening; - have HEPA/ULPA filtered down-flow air composed largely of uncontaminated recirculated inflow air; - exhaust contaminated down-flow air from a region of the total work area via an internal dedicated exhaust plenum and blower, and then through HEPA/ULPA filter(s); - recirculate the balance of the down-flow and inflow air through a supply HEPA/ULPA filter(s); - have all biologically contaminated ducts and plenums under negative pressure or surrounded by negative pressure ducts and plenums; and - may exhaust HEPA/ULPA filtered air either back into the laboratory or via a canopy connection to an external system that exhausts to the atmosphere. If working with volatile chemicals, the unit must be connected to an external exhaust system. Type C1 cabinets may be used for work with volatile chemicals if permitted by a chemical risk assessment

Certification of BSCs

Generally, BSCs are tested by the cabinet manufacturer in accordance with National Sanitation Foundation (NSF) criteria. Cabinets that meet the NSF 49 criteria for performance characteristics, including biological containment, ventilation, cabinet leakage, and HEPA filter leakage, are NSF certified.

Field certification of BSCs is also required to ensure that the cabinet still performs as it did when it obtained NSF certification at the factory. NIH requires field certification under the following circumstances: (1) upon installation of a new BSC; (2) annually thereafter; (3) after repair or maintenance is performed; and (4) after the BSC is moved and relocated.

CDC recommends that BSCs be recertified annually to ensure for proper function. They will also be recertified after being moved to ensure that they have not been damaged. Laboratories are responsible for ensuring that the BSCs are recertified in a timely manner. Laboratories at CRC will contact EHS at (617) 353-4094. Laboratories at BUMC will contact the certification contractor directly. The contact information to reach the contractor is indicated on the certification sticker affixed on the front of the BSC.

NSF standard 49 provides criteria for construction of BSCs, testing by manufacturers (including biological containment testing), and field certification. NSF has also established a certification program for field certifiers to ensure a minimum level of competency and professionalism. It is recommended that NSF field certifiers be used for field certification of BSCs. Field certification tests include:

Primary tests (BSC performance):

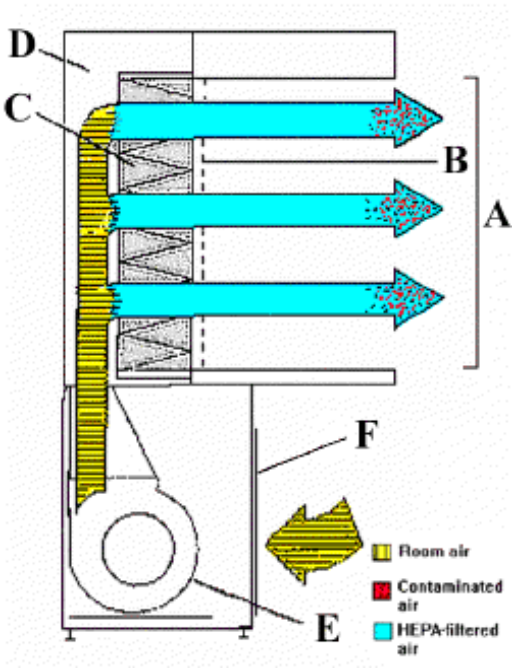
- Inflow test
- Down-flow test
- Smoke pattern test
- HEPA filter leakage
- Cabinet leakage (when BSC is newly installed, relocated, or maintenance has been
- performed that involved removal of access panels)

Additional tests (worker comfort and safety), performed at discretion of certifier:

- Noise
- Vibration
- Lighting
- Electrical leakage, polarity, and ground circuit resistance

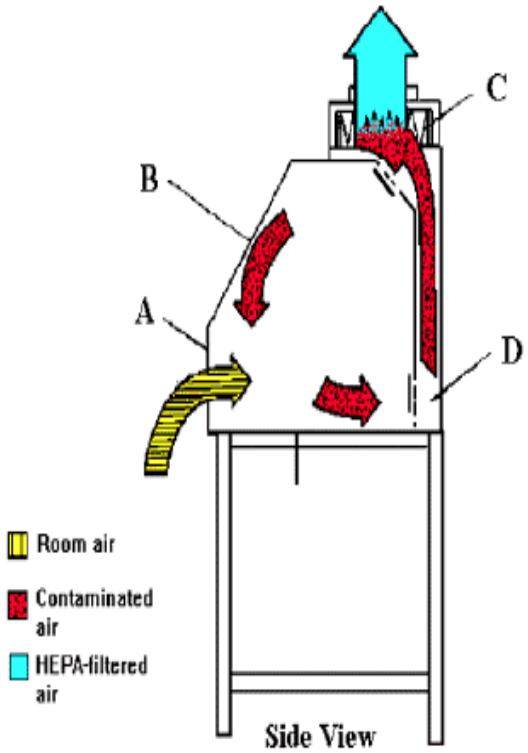
Horizontal Flow "Clean Bench"

A. front opening
B. supply grille
C. supply HEPA filter
D. supply plenum
E. blower
F. grille

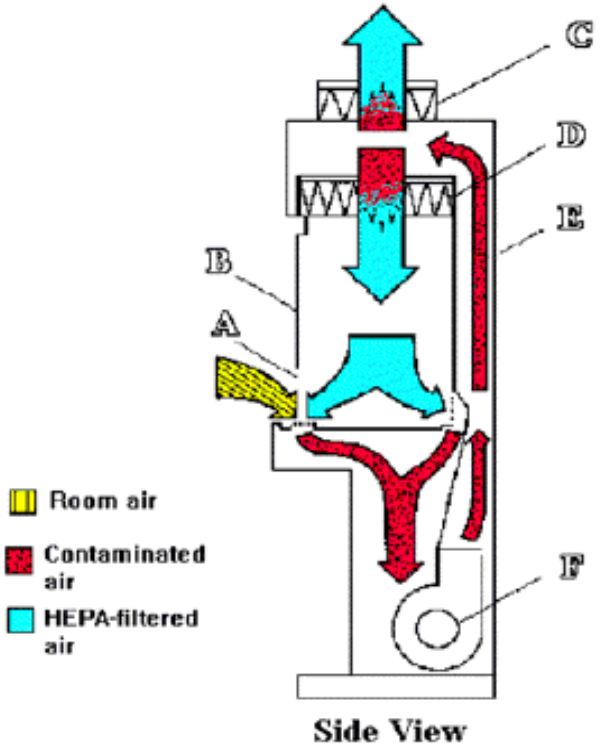


Class I BSC

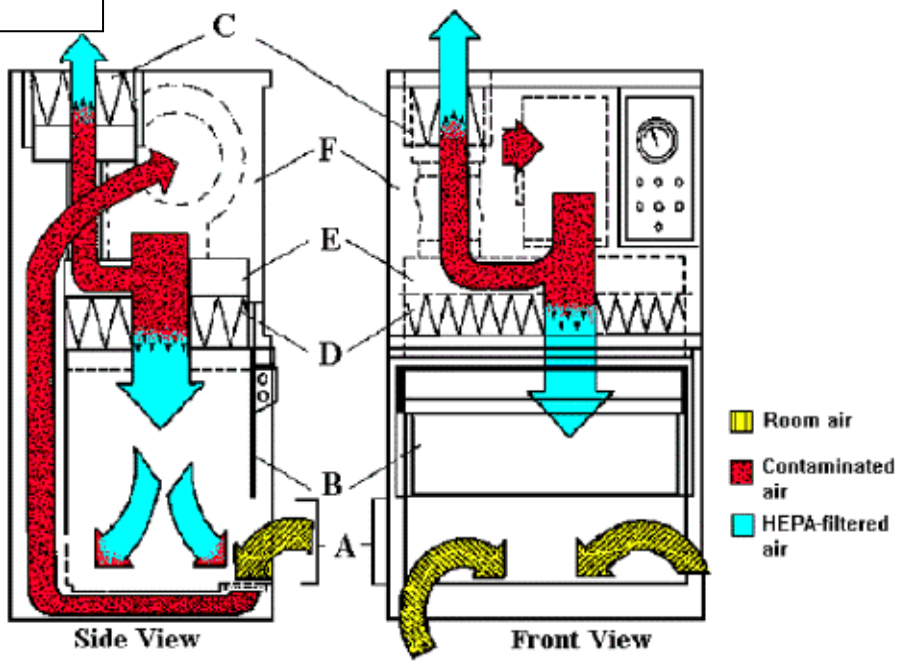
A. front opening
B. sash
C. exhaust HEPA
D. exhaust plenum

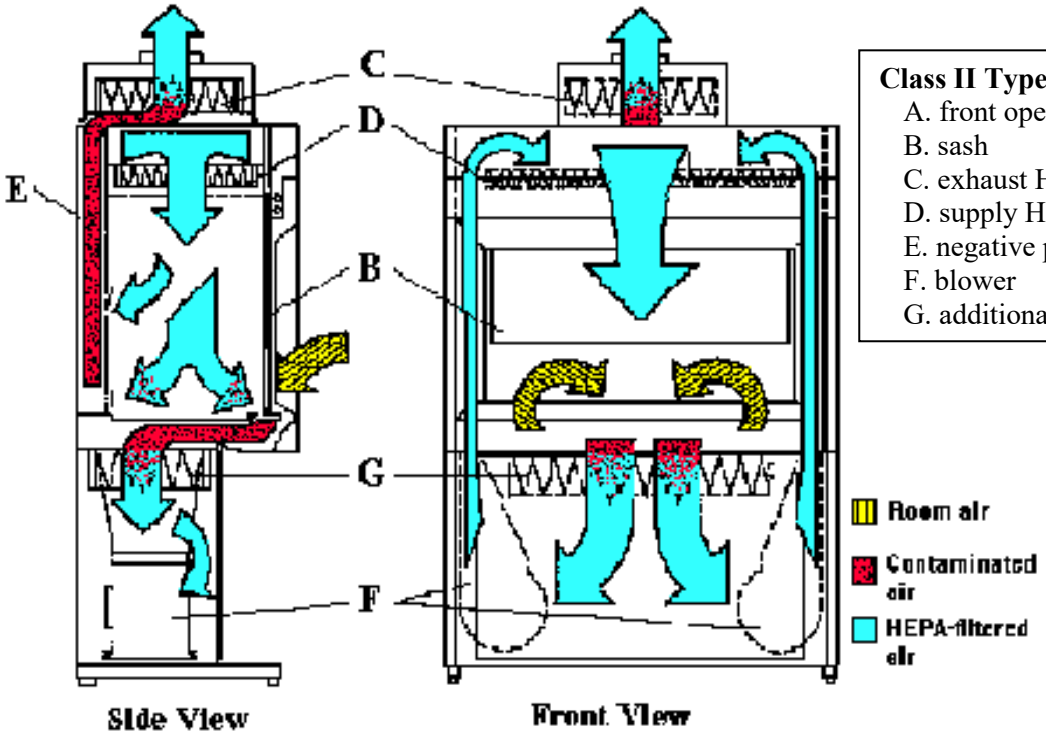


Class II Type A BSC
A. front opening
B. sash
C. exhaust HEPA filter
D. rear plenum
E. supply HEPA filter
F. blower



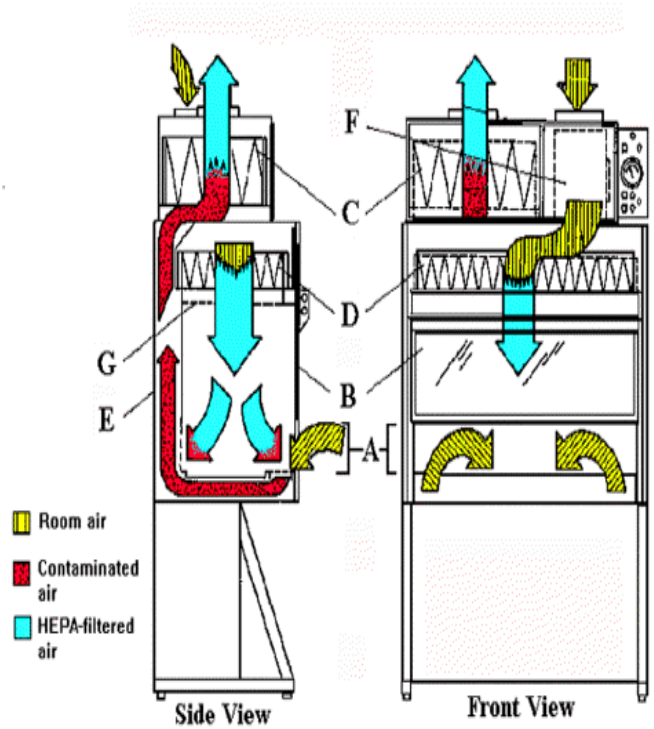
Class II Type B3 BSC (Tabletop model)
A. front opening
B. sash
C. exhaust HEPA filter
D. supply HEPA filter
E. positive pressure plenum
F. negative pressure plenum





Class II Type B1 BSC
A. front opening
B. sash
C. exhaust HEPA filter
D. supply HEPA filter
E. negative pressure exhaust plenum
F. blower
G. additional HEPA filter for air supply

Class II Type B2 BSC
A. front opening
B. sash
C. exhaust HEPA filter
D. supply HEPA filter
E. negative pressure exhaust plenum
F. supply blower
G. filter screen



Appendix C
Autoclave Quality Assurance Program

Autoclaving is an accepted procedure for the decontamination of certain biohazardous waste. Biological cultures and stocks, contaminated solid waste, and liquid waste can be sterilized through autoclaving. After sterilization in a steam autoclave, these materials are considered non-infectious. All autoclaved waste is placed into the solid biohazard waste stream. Wastes from the BSL4 and BSL3 containment laboratories are first autoclaved before being disposed as biological waste. Materials that contain hazardous chemicals or radioisotopes are not to be autoclaved. To ensure that biohazardous waste is properly decontaminated during autoclaving, the following procedures should be followed by laboratory personnel

1. Infectious waste must be treated in an autoclave for a **minimum of 30 minutes at 121°C (250°F)**; however, the total processing time required to decontaminate infectious waste depends on the specific loading factors (container type, water content, quantity, etc.) A total processing time of 60 minutes is recommended for gravity displacement autoclaves and 10 minutes for vacuum-type autoclaves (132° C).

    - Sterilization by autoclaving is accomplished through exposure and penetration of the contaminated material by superheated steam for an adequate amount of time. Because steam will not penetrate a sealed plastic autoclave bag, the bags containing dry loads must not be tightly sealed (rubber band closures will allow bags to "breathe") to allow the steam to enter the bag or an adequate amount of water must be added to the load. Consult the manufacturer's instructions for sterilizing materials inside plastic autoclave bags. Liquid waste may also be autoclaved in lieu of adding an appropriate chemical disinfectant and disposed of in the sink. Animal carcasses from the ABSL3 and ABLS4 will be autoclaved inside an autoclavable bag.

2. All autoclaved waste must include a chemical sterilization indicator (the use of biohazard bags with a "built-in" indicator is recommended).

3. Steam autoclaves used to treat infectious waste must operate at a minimum temperature of 121° C. The operating temperature of the autoclave must be verified for each run by maintaining a record of the temperature either as a chart or paper tape recording or a manual recording in a logbook.

4. On a monthly basis, confirm that adequate sterilization conditions are being met through the use of Biological Indicators ("BI") containing heat-resistant spores (e.g. Geo*bacillus stearothermophilus*) placed in the center of an autoclave load. In conjunction with the BI testing, measure and record the maximum temperature achieved during the autoclave cycle through the use of a maximum registering (or "holding") thermometer or calibrated data logger for full cycle.

5. Maintain records of BI testing and maximum autoclave temperature recordings for a minimum of one year (see Autoclave QC Log at end of appendix).

Monthly Spore Testing Procedure

1. Place BI spores and holding thermometer or data logger in the center of an autoclave load.

2. Process the load under normal operating procedures.

3. The highest temperature indicated on the holding thermometer is entered on the Autoclave QC Log. If this temperature is less than 121°C, the autoclave is not to be used to treat infectious waste until it has been repaired and passes retesting. In the interim, tag the autoclave as "Not Approved for Infectious Waste."

4. Incubate the autoclaved BI and a non-autoclaved, control BI according to the manufacturer's instructions (normally 55°-60°C overnight).

5. If a color change (cell growth) occurs, the sterilization process was unsuccessful. Discontinue use of the autoclave until it is checked, repaired as needed. and passes retesting. Tag the autoclave as "Not Approved for Infectious Waste" until the autoclave passes retesting.

6. Indicate test results on Autoclave QC Log available from EHS and retain for at least three years.

Appendix D
Biosafety Level 2 (BSL2) Requirements

Biosafety Level 2 (BSL2) is suitable for experiments involving agents of moderate potential hazard to personnel and the environment.

For example:

- Microorganisms of low biohazard potential, such as those in Risk Group 2 or BSL2.
- Recombinant DNA activity requiring BSL2 physical containment including animal studies that involve the construction of transgenic animals.
- Non-recombinant cell and/or tissue culture systems that require this level of containment.
- Oncogenic viral systems classified as low risk.
- Production activities with Risk Group 1 organisms.

The control of potential biohazards at the BSL2 level is provided by use of standard microbiological practices with the addition of personnel protective equipment (lab coat and gloves).

The following are procedures used with BSL2 containment requirements. They are based on the recommendation of the *Biosafety in Microbiological and Biomedical Laboratories* (BMBL) 6th Edition, 2020 and BU policies and procedures.

Standard Microbiological Practices

- Access to the laboratory is limited or restricted at the discretion of the laboratory director when experiments are in progress.
- Persons wash their hands after they handle viable materials, after removing gloves, and before leaving the laboratory.
- Eating, drinking, smoking, handling contact lenses, and applying cosmetics are not permitted in the work areas. Food is stored outside the work area in cabinets or refrigerators designated for this purpose only.
- Personnel who use contact lenses will consult with EHS if required to use eye protection in the lab.
- Use of personal electronic devices such earbuds and cell phones should not be practiced when working in the lab.
- Mouth pipetting is prohibited; mechanical pipetting devices are used.
- Policies for the safe handling of sharps are instituted.
- All procedures are performed carefully to minimize the creation of splashes or aerosols.
- Work surfaces are decontaminated upon completion of work, or at the end of the day, and after any spill or splash of viable material with disinfectants that are effective against the agents of concern.
- An insect and rodent control program is in effect.

Special Practices

Access to the laboratory is limited or restricted by the laboratory director when work with infectious agents is in progress. In general, persons who are at increased risk of acquiring infection, or for whom infection may have serious consequences, are not allowed in the laboratory or animal rooms. For

example, persons who are immunocompromised or immunosuppressed may be at increased risk of acquiring infections. The laboratory director in consultation with ROHP has the final responsibility for assessing each circumstance and determining who may enter or work in the laboratory or animal room.

The Principal Investigator or Laboratory Director establishes policies and procedures whereby only persons who have been advised of the potential hazards and meet specific entry requirements (e.g., immunization) may enter the laboratory.

A biohazard sign must be posted on the entrance to the laboratory when etiologic agents are in use. Appropriate information to be posted includes the agent(s) in use; the biosafety level; the required immunizations; the investigator's name and telephone number; any personal protective equipment that must be worn in the laboratory; and any procedures required for exiting the laboratory.

Laboratory personnel receive appropriate immunizations or tests for the agents handled or potentially present in the laboratory (e.g., hepatitis B vaccine or TB skin testing).

Biosafety procedures are incorporated into standard operating procedures or in a biosafety manual adopted or prepared specifically for the laboratory by the laboratory director. Personnel are advised of special hazards and are required to read and follow instructions on practices and procedures.

The Principal Investigator or Laboratory Director ensures that laboratory and support personnel receive appropriate training about the potential hazards associated with the work involved; the necessary precautions to prevent exposures; and the exposure evaluation procedures. Personnel receive annual updates or additional training as necessary for procedural or policy changes.

A high degree of precaution must always be taken with any contaminated sharp items, including needles and syringes, slides, pipettes, capillary tubes, and scalpels.

Needles and syringes or other sharp instruments should be restricted in the laboratory for use only when there is no alternative, such as parenteral injection, phlebotomy, or aspiration of fluids from laboratory animals and diaphragm bottles. Plasticware should be substituted for glassware whenever possible.

Only needle-locking syringes or disposable syringe-needle units (e.g., needle is integral to the syringe) are used for injection or aspiration of infectious materials. Used disposable needles must not be bent, sheared, broken, recapped, removed from disposable syringes, or otherwise manipulated by hand before disposal; rather, they must be carefully placed in conveniently located puncture-resistant containers used for sharps disposal. Non-disposable sharps must be placed in a hard-walled container for transport to a processing area for decontamination, preferably by autoclaving.

Syringes that re-sheathe the needle, needleless systems, and other safety devices are used when appropriate.

Broken glassware must not be handled directly by hand, and must be removed by mechanical means such as a brush and dustpan, tongs, or forceps. Containers of contaminated needles, sharp equipment, and broken glass are decontaminated before disposal according to any local, state, or federal regulations.

Cultures, tissues, specimens of body fluids, or potentially infectious wastes are placed in a container with a cover that prevents leakage during collection, handling, processing, storage, transport, or shipping.

Laboratory equipment and work surfaces should be decontaminated with an effective disinfectant on a routine basis; after work with infectious materials is finished; and especially after overt spills, splashes, or other contamination by infectious materials. Prior to its removal from the facility, contaminated equipment must be decontaminated according to any local, state, or federal regulations before it is sent for repair or maintenance or packaged for transport in accordance with applicable local, state, or federal regulations.

Spills and accidents that result in overt exposures to infectious materials are immediately reported to the Principal Investigator and Laboratory Director. Medical evaluation, surveillance, and treatment are provided as appropriate, and written records are maintained.

Sinks in the BSL2 area should be made free of clutter and cleaned routinely with appropriate disinfectant such as a 10% bleach solution and flushed down with running water after a few minutes. Water baths and all water reservoirs should be washed periodically with a suitable chemical decontaminant.

Once a month, work spaces should be cleaned and disinfected, as well as other lab areas where clutter accumulates (e.g., storage areas).

The laboratory will set up a routine schedule to perform surface cleaning with appropriate chemical disinfectant of large equipment (such as incubators) as part of laboratory good practices.

Supplies should be rotated and outdated material discarded. Unlabeled material should be eliminated.

Eliminate and clean clutter.

Custodial services: only personnel with appropriate authorization may enter a BSL2 facility while BSL2 research activity is in progress.

Animals not involved in the work being performed are not permitted in the lab.

Safety Equipment (Primary Barriers)

Properly maintained biological safety cabinets, preferably Class II, or other appropriate personal protective equipment or physical containment devices are to be used when:

- Procedures that have the potential to create infectious aerosols or splashes are conducted. These may include centrifuging, grinding, blending, vigorous shaking or mixing, sonic disruption, opening containers of infectious materials whose internal pressures may be different from ambient pressures, inoculating animals intranasally, and harvesting infected tissues from animals or embryonate eggs;
- High concentrations or large volumes of infectious agents are used. Such materials may be centrifuged in the open laboratory with sealed rotor heads or sealed centrifuge safety cups are used, and if these rotors or safety cups are opened only in a biological safety cabinet;
- Face protection (goggles, mask, face shield, or other splatter guard) is used for anticipated splashes or sprays of infectious or other hazardous materials to the face when the microorganisms must be manipulated outside the BSC;
- Protective laboratory coats, gowns, smocks, or uniforms designated for lab use are worn while in the laboratory. This protective clothing is removed and left in the laboratory before leaving for non-laboratory areas (e.g., cafeteria, library, administrative offices). All protective clothing is

either disposed of in the laboratory or laundered by the institution; it should never be taken home by personnel;

- Gloves are worn when hands may contact potentially infectious materials, contaminated surfaces, or equipment. Wearing two pairs of gloves may be appropriate. Gloves are disposed of when overtly contaminated and removed when work with infectious materials is completed or when the integrity of the glove is compromised. Disposable gloves are not washed, reused, or used for touching "clean" surfaces (keyboards, telephones, etc.). They should not be worn outside the lab. Alternatives to powdered latex gloves should be available. Hands are washed following removal of gloves.

Procedures for Receiving and Inspecting Samples

The PI will designate a responsible person for the purchase of all infectious materials to be used in the BSL2 lab.

Infectious materials will be shipped to the laboratory in accordance with the appropriate Department of Transportation (DOT) and the International Air Transportation Association (IATA) standards for shipping of infectious biological materials.

Upon receipt of the package, it will be placed on a tray covered with absorbent material and opened in the Biological Safety Cabinet prevent any potential exposure to personnel in case the container leaked during transport.

Personnel assigned to open packages will wear lab coat, gloves, and eye protection.

If any containers are found to be damaged, leaking or otherwise contaminated, they will be immediately isolated into a plastic bag along with all packaging materials. The spill will be disinfected and cleaned up. The Principal Investigator, lab director or designee will be notified immediately. The incident will be reported to EHS and as necessary, to other appropriate agencies.

If, after inspection, the samples are intact, they can be placed into labeled secondary containers (unbreakable plastic containers or metal tubes) and then transferred to a storage area.

Only staff who are authorized to do so can remove samples from storage. Removal and use of all such materials must be entered into the logbook.

Unused cultures can be returned to storage after the outer container has been properly disinfected.

Laboratory Facilities (Secondary Barriers)

In a BSL2 lab, the following conditions are to exist:

- Doors that can be locked and secured should be installed for facilities that house restricted areas.
- Consideration should be given to locating new laboratories away from public areas.
- Each laboratory contains a sink for handwashing.
- The laboratory is designed so that it can be easily cleaned. Carpets and rugs in laboratories are inappropriate.
- Bench tops are impervious to water and resistant to moderate heat and the organic solvents, acids, alkalis, and chemicals used to decontaminate the work surfaces and equipment.

- Laboratory furniture is capable of supporting anticipated loading and uses. Spaces between benches, cabinets, and equipment are accessible for cleaning. Chairs and other furniture used in laboratory work should be covered with a non-fabric material that can be easily cleaned and decontaminated.
- Biological safety cabinets should be installed in such a manner that fluctuations of the room's air supply and exhaust air do not cause them to operate outside their parameters for containment. Locate BSCs away from doors, windows that can be opened, heavily traveled laboratory areas, and other potentially disruptive equipment to avoid disruption of the BSC's air flow parameters.
- An eyewash station is readily available for use.
- Illumination is adequate for all activities, avoiding reflections and glare that could impede vision.
- There are no specific ventilation requirements. However, planning of new facilities should consider mechanical ventilation systems that provide an inward flow of air without recirculation to spaces outside of the laboratory. If the laboratory has windows that open to the exterior, they are fitted with fly screens.

Appendix E
Biosafety Level 3 (BSL3) and Biosafety Level 4 (BSL4) Requirements and Practices

Biosafety Level 3 and 4 (BSL3/4) is the recommended containment for work with agents or toxins that may cause serious or potentially fatal disease through inhalation exposure. Work at BSL3/4 requires enhanced facility design, operational controls and special practices, which are outlined in the BSL3 Biosafety Manual and BSL4 Biosafety Manual.

BSL3/4 facilities are designed and verified with facility and ventilation features to accommodate the safe handling and containment of risk group 3/4 agents. The architectural and engineering plans, commissioning testing documents, and equipment validations and verifications for BSL3/4 facilities is reviewed and approved in advance by EHS to ensure that they in compliance with the CDC/NIH's *Biosafety in Microbiological and Biomedical Laboratories* (BMBL) 6th edition requirements. Facility-specific standard operating procedures (SOPs) and annual containment verifications are reviewed by EHS and research protocols are reviewed and approved by the BU IBC to determine adequacy for the use of the proposed biological agents. Additionally, all work with BSL3 and above agents must be registered with the BPHC.

The BSL3 and BSL4 Biosafety Plans outline the general requirements for BSL3 and BSL4 facilities at Boston University. Special requirements dealing with Select Agents and Select Agent facility documentation are covered in the NEIDL-specific Laboratory Manuals.

Appendix F
Guidelines for Work with Toxins of Biological Origin

Biological toxins are poisons, either naturally produced by living organisms including animals, plants, or microbial sources that cause death or severe incapacitation at relatively low exposure levels. Biological toxins do not replicate and are not infectious. In amounts used most typically in biomedical research laboratories, biological toxins can be handled safely by trained laboratory personnel and they are a low risk to the local community. Biological toxins are difficult to transmit from person-to-person, they are non-volatile, and usually are not dermally active (mycotoxins are an exception). They tend to be more toxic per weight than many chemical agents. These guidelines are intended for biological toxins recommended to be handled under BSL2 conditions. Personnel using biological toxins listed by CDC and USDA under the Federal Select Agent Program (such as Botulinum neurotoxins, Staphylococcal enterotoxins, ricin, tetrodotoxin and selected low molecular weight toxins), should follow additional safety, handling and inventory practices appropriate for the higher biosafety level and detailed elsewhere under BSL3 practices. The federal list of select agents and toxins and exemptions can be found here.

A PI should expect that storage and use of a biological toxin(s), including the select agent toxins, will need approval by the IBC. Please check with IBC if you have questions on a particular biological toxin.

Select agent toxins are not regulated under the Federal Select Agent Program if the amount stored and possessed by the lab at any given time does not exceed the permissible toxin amounts. The permissible amount for each select agent toxins is listed here.

The following guidelines are intended to provide general safety requirements for the use of such toxins.

General Information

Working with biologically-derived toxins may present health risks due to routes of exposure that are not always taken into consideration. The laboratory facilities, equipment, and procedures for work with toxins must reflect the intrinsic level of hazard posed by a particular toxin, as well as the potential risks inherent in the operations being performed. If both toxins and infectious agents are used, both must be considered when containment equipment is selected and policies and procedures are written. If animals are used, animal safety practices must also be considered. IBC will evaluate all such uses and determine if the proposed safeguards are adequate or not.

Standard Practices

Provide all laboratory personnel with biosafety training specific for the toxins being used. Training is documented and repeated annually or as needed for new personnel before use. Toxin-specific training should include description of the toxin, its importance to public health and/or research priorities, medical consequences of any exposure, appropriate lab safety measures including decontamination policies, and instructions for how to deal with accidental exposure. If needed and when requested by the PI, toxin-specific training can be provided by the ROHP and the EHS.

For Select Agent Toxins and selected low molecular weight toxins, an inventory control system should be in place to account for toxin use and disposition according to the CDC BMBL (6th edition) Appendix I- Guidelines for Work with Toxins of Biological Origin. Select Agent Toxins require inventory detail to ensure that total quantities remain below the regulated amount. Select Agent Toxin inventories should include date and quantity of each acquisition (purchase, transfer, etc.), use and disposal. For other

biological toxins, an inventory control system is not required unless mandated by the IBC.

Biological toxins have varying susceptibility to inactivation and decontamination measures. For example, most are resistant to freeze-thaw, but susceptible to 10% (v/v) fresh bleach solutions. Refer to the CDC BMBL (6th Edition) Appendix I Guidelines for tables detailing toxin-specific inactivation and decontamination recommendations as appropriate.

Store toxin stocks in secured storage rooms, cabinets, or freezers with restricted access. If toxins are stored in the laboratory, containers should be sealed, labeled, and secured to restrict access; refrigerators and other storage containers should be clearly labeled and provide contact information for trained, responsible laboratory staff.

Dry forms of toxins present a high aerosol risk. Primary containers of dry forms of toxins should be handled in a chemical fume hood, a glove box, or a biological safety cabinet or equivalent containment system. All work should be done within the operationally effective zone of the hood or biological safety cabinet, and each user should verify the inward airflow before initiating work, and whenever possible, reconstitute entire vial of powdered toxin by injecting diluent through septum. HEPA and/or charcoal filtration of the exhaust air may be required, depending on the toxin.

If infectious agents and biological toxins are used together in an experimental system, consider both when selecting protective clothing and equipment.

Glove selection: If powdered toxin must be handled, select gloves that do not generate static electricity. Do not use latex. When handling toxins that are percutaneous hazards (irritants, necrotic to tissue, or extremely toxic from dermal exposure), select gloves that are known to be impervious to the toxin. Additional PPE such as disposable, long-sleeved gown may be necessary.

Standard practices listed under BSL2 and/or BSL3 should be reviewed and incorporated as appropriate into protocols for work with toxins.

Standard Laboratory Practices

Appropriate laboratory practices will depend on a number of parameters, such as the toxin used or the type of operations performed. General guidelines below are for biological toxins recommended to be handled under BSL2 conditions. In addition to standard BSL2 PPE, other protective equipment may be required depending on the characteristics of the biological toxin and the containment system. For example, additional respiratory protection may be necessary if aerosols may be generated and it is not possible to use containment equipment or other engineering controls.

Each laboratory should develop Standard Operating Procedures (SOPs) for toxin handling and policies (or a chemical hygiene plan specific to the toxin(s) used in that laboratory). If necessary, IBC will assist the PI with development of SOPs appropriate for the toxin(s). The SOPs should include:

- Description of hazards that will be encountered during expected use of the toxin and those that could be encountered in case of a spill or other accident. This is typically a summary of the biosafety training for that toxin.
- Policies and practices to be used to minimize risks such as:
  - Containment and personal protective equipment.
  - Toxin-appropriate methods for decontamination of PPE, equipment, and bench areas.

  - Transport of toxin outside the laboratory. Toxins should be transported only in leak-/spill-proof secondary containers.
  - Management of spills.
  - Medical surveillance.
  - Procedure for accidental exposure
- Safety receipt, inspection, storage, and disposal of the toxin used.

All high-risk operations (e.g., use of toxin at levels considered to be unusually high) should be conducted with two knowledgeable individuals present. Each must be familiar with the applicable procedures, maintain visual contact with the other, and be ready to assist in the event of an accident.

When biological toxins are in use, the room should be posted to indicate "Biological Toxins in Use - Authorized Personnel Only." Any special entry requirements should be posted at the entrance(s) of the room. Only personnel whose presence is required should be in the room while toxins are in use.

Laboratory Facilities

Laboratory facility recommendations listed under BSL2 and BSL3, as well as OSHA standards should be reviewed and incorporated as appropriate into protocols for work with toxins.

When vacuum lines are used with systems containing toxins, they should be protected with a HEPA filter to prevent entry of toxins into the lines. Water aspirators should be avoided.

Appendix G
List of Biological Agents with the Potential to Cause Laboratory Acquired Infection (LAI) in use at Boston University

The List of Biological Agents with the Potential to Cause Laboratory Acquired Infection (LAI) contains BSL4, BSL3, BSL4 and BSL2 agents in use within the research community. Principal Investigators and research staff listed on approved IBC protocols involving these biological agents with the potential to cause LAI must receive agent specific training, agent specific identification cards to be carried by those personnel, and Agent Information Sheets (AIS) providing safety and handling instructions.

The list of biological agents with the potential to cause LAI is dynamic and will be routinely reviewed by the LAI Committee for pathogens that researchers are proposing to use. As new agents approved by the IBC are introduced into the laboratory environment, they may be added to the list; agents that are no longer being used will be removed from the list. Contact the IBC Office at for the current list.

Appendix H
Prion Research/Creutzfeldt-Jacob Disease (CJD) Guidelines

Creutzfeldt-Jacob Disease (CJD) is one of a group of neurodegenerative diseases called *transmissible spongiform encephalopathies* (TSE) (or prion diseases) which affect humans (e.g., Kuru, Fatal Familial Insomnia and Gerstmann-Sträussler-Scheinker syndrome of humans) and a variety of domestic and wild animal species (e.g., Scrapie of sheep, "Bovine Spongiform Encephalopathy [BSE] or Mad Cow Disease" of cattle and dairy cows, Chronic Wasting Disease [CWD] of deer and moose). Long (months to years) incubation periods precede the onset of clinical illness, with chronic progressive pathology that may last weeks to months. CJD is characterized by progressive dementia, myoclonic fasciculations, ataxia, and somnolence. The clinical course of CJD usually lasts several months and is invariably fatal. No effective treatment is available, and there are no known cases of remissions or recoveries.

A central biochemical feature of prion disease is the conversion of normal cellular prion protein (PrP) to an abnormal, misfolded, pathogenic isoform PrP^{Sc} (named for "scrapie", the prototypic prion disease). The infectious agents that transmit prion disease are resistant to inactivation by heat and chemicals and thus require special biosafety precautions. Procedures involving brain tissue from patients with neurological degenerative disorders (such as CJD and Alzheimer's disease) pose special challenges in reducing potential exposure to prions. Such material should be handled with at least the same precautions as HIV-positive or HBV-positive human tissue and prion-specific disinfection methods are recommended.

Laboratory Safety and Containment Recommendations

The CDC classifies prions as Risk Group 2 agents requiring Biosafety Level 2 (BSL2) containment. All researchers working with these agents are required to have IBC approval before any research can be initiated. In the laboratory setting prions from human tissue and human prions propagated in animals should be manipulated at BSL2. BSE (Bovine Spongiform encephalopathy) prions can likewise be manipulated at BSL2. However, due to the recent history of transmission of BSE prion to humans, work involving direct contact with BSE-infected specimens may require the use of BSL3 facilities and practices. All other animal prions are manipulated at BSL2.

This appendix mainly covers the lab safety and practice for research with prions that has evolved from best practices used at many institutions, including the University of California, San Francisco and the University of California, San Diego, that have been engaged in such research for years and also from the BMBL 6th edition Section VIII-H: Prion. Precautions for clinical safety and/or surgical procedures on patients diagnosed with prion diseases are not described here but are outlined in an Infection Control Guideline for TSE developed by a consultation convened by the WHO in 1999.

Safety Procedures

Prion agent must be treated as biohazardous. An autoclave for treatment of solid wastes is required. All equipment that has come in contact with the agent, packaging, containers and all unused portions and derivatives from the agent will be treated before disposal.

All fixed, non-fixed, or frozen tissues that contain the agent must be placed within watertight containers and labeled with the universal biohazard symbol and the notation "Infectious Materials." The use of conventional autoclaving protocol as the sole treatment has not resulted in complete inactivation of

prions. The recommended autoclaving procedure is in table below. Formalin-fixed and paraffin-embedded tissues, especially of the brain, remain infectious.

Personnel working with the agent must not have contact with any animal colonies without IACUC approval in the laboratory complex or with susceptible animal species.

Personnel must wear gloves and gowns while handling tissues that are potentially contaminated. All protective clothing must be removed before leaving the laboratory. Eye protection is recommended depending on the procedure. Personnel working with the material are instructed on the procedures for handling the agent. Sonication or homogenization of tissues must be performed in a properly certified Class II Biological Safety Cabinet (BSC).

The main precaution to be taken by laboratory members working with prion-infected or contaminated material is to avoid accidental puncture of the skin. Persons handling contaminated specimens should wear cut-resistant gloves if possible. If accidental contamination of unbroken skin occurs, the area should be washed with detergent and abundant quantities of warm water (**avoid scrubbing**); brief exposure (1 minute) to 1N NaOH or a 1:10 dilution of bleach may be considered for maximum safety.

The PI must contact the BSO in writing regarding spills and accidents that result in overt exposure to tissues. The report must include the following:

- Specification of amount released, time involved, and explanation of procedures used to determine the amount involved.
- Description of the area involved and the extent of employee exposure.
- Report of medical treatment provided.
- Corrective action taken to prevent the reoccurrence of the incident.

Records

ROHP must maintain health records for a period of 30 years. Records must be provided upon request by representatives of the Chief and/or Director of NIOSH. Access to the laboratory must be restricted to trained personnel when work is being conducted on tissue.

Personnel handling tissue must be trained in the following:

- Nature of CJD
- Route of transmission of CJD
- Specific hazards associated with handling of the tissue.

Inactivation of Prions

Table 1. Prion Inactivation Methods for Reusable Instruments and Surfaces [BMBL 6th edition Section VIII-H: Prion Disease Table 4]

1. Immerse in 1 N NaOH or sodium hypochlorite (20,000 ppm available chlorine) for 1 hour. Transfer into water and autoclave (gravity displacement) at 121ºC for 1 hour. Clean and sterilize by conventional means. [Note: Sodium hypochlorite may be corrosive to some instruments, including autoclaves.]
2. Immerse in a pan containing 1 N NaOH, heat in a gravity displacement autoclave at 121ºC for 30 minutes. Clean-rinse in water and sterilize by conventional means.

3. Immerse in 1 N NaOH or sodium hypochlorite (20,000 ppm) for 1 hour. Remove and rinse instruments with water, transfer to open pan and autoclave at 121ºC (gravity displacement) or 134ºC (porous load) for 1 hour. Clean and sterilize by conventional means.
4. Surfaces or heat-sensitive instruments can be treated with 2 N NaOH or sodium hypochlorite (20,000 ppm) for 1 hour. Ensure surfaces remain wet for entire period, then rinse well with water. Before chemical treatment, it is strongly recommended that gross contamination of surfaces be reduced because the presence of excess organic material will reduce the strength of either NaOH or sodium hypochlorite solutions.
5. 2% Environ LpH® (EPA Reg. No. 1043-118; no longer commercially available) may be used on washable, hard, non-porous surfaces (such as floors, tables, equipment, and counters), items, such as non-disposable instruments, sharps, and sharp containers, and/or laboratory waste solutions (such as formalin or other liquids). This product is currently being used under FIFRA Section 18 exemptions in a number of states. Users should consult with the state environmental protection office prior to use. Items may be immersed for 0.5–16 h, rinsed with water, and sterilized using conventional methods.

Working Solutions 1 N NaOH equals 40 grams of NaOH per liter of water. Solution should be prepared daily. A stock solution of 10 N NaOH can be prepared and fresh 1:10 dilutions (1 part 10 N NaOH plus 9 parts water) should be prepared frequently enough to maintain a fully effective alkalinity.

20,000 ppm sodium hypochlorite equals a 2% solution. Many commercial household bleach sources in the United States contain 6.15% sodium hypochlorite; for such sources, a 1:3 v/v dilution (1 part bleach plus 2 parts water) would produce a solution with 20,500 ppm available chlorine. This relatively easy method provides a slightly more concentrated solution (extra 500 ppm) that should not pose a problem with decontamination procedures or significantly increase chemical risks in the laboratory. Bleach solutions can off-gas and working solutions should be prepared frequently enough to maintain adequate available chlorine levels.

CAUTION: Above solutions are corrosive and require suitable personal protective equipment and proper secondary containment. These strong corrosive solutions require careful disposal in accordance with local regulations. Sodium, hypochlorite and sodium hydroxide solutions may corrode autoclaves.

Precautions in using NaOH or sodium hypochlorite solutions in autoclaves: NaOH spills or gas may damage the autoclave if proper containers are not used. The use of containers with a rim and lid designed for condensation to collect and drip back into the pan is recommended. Aluminum should not be used. Persons who use this procedure should be cautious in handling hot NaOH solution (post-autoclave) and in avoiding potential exposure to gaseous NaOH; exercise caution during all sterilization steps; and allow the autoclave, instruments, and solutions to cool down before removal. Immersion in sodium hypochlorite bleach can cause severe damage to some instruments. Neutralization of hypochlorite with thiosulfate prior to autoclaving is recommended to prevent the release of chlorine gas.

Appendix I
Summary of Requirements for Biosafety Levels

Safety Guideline	BSL1	BSL2	BSL3	BSL4
Laboratory personnel must wash their hands after handling cultures, removing gloves, and before leaving the laboratory.	Y	Y	Y	Y
Eating, drinking, and application of cosmetics is prohibited.	Y	Y	Y	Y
Personnel must be familiar with basic biosafety procedures, including this manual.	Y	Y	Y	Y
Personnel should wear face protection such as goggles, face shields or other device providing protection against any possible splashes and aerosols.	Y	Y	Y	Y
Pipetting by mouth is prohibited.	Y	Y	Y	Y
All laboratory procedures should be performed to minimize aerosol generation.	Y	Y	Y	Y
Work surfaces must be decontaminated at least daily, after each use for infrequent users, and after any spill of viable materials.	Y	Y	Y	Y
Sharps must be placed in specially designed puncture- and leak-proof sharps containers and disposed of appropriately as medical waste.	Y	Y	Y	Y
Laboratories must be kept neat; good housekeeping procedures must be in place and in regular use.	Y	Y	Y	Y
All medical waste is decontaminated before disposal by an approved decontamination method and/or disposed of as medical waste.	Y	Y	Y	Y
Insect and rodent control programs are instituted.	Y	Y	Y	Y
Laboratory contains a sink for handwashing.	Y	Y	Y	Y
Laboratories are designed for ease of decontamination (e.g., no carpets, sealed surfaces, no unreachable areas, etc.).	Y	Y	Y	Y
Bench tops are impervious to water, moderate heat, and chemicals.	Y	Y	Y	Y
Laboratory furniture must be secured, and spaces between benches, cabinets, and equipment must be accessible for decontamination.	Y	Y	Y	Y
All laboratory windows must be fitted with fly screens.	Y	Y	Y	Y
Laboratory coats or gowns and gloves must be worn.	Y	Y	Y	Y
Autoclaves are required for waste treatment prior to disposal - biohazardous waste.	N	N	Y	Y
Autoclave quality control program is required for use specified above.	Y	Y	Y	Y
Instructions for safety precautions are posted by the Principal Investigator.	Y	Y	Y	Y

Safety Guideline	BSL1	BSL2	BSL3	BSL4
Animals not involved in the experiment are not permitted in laboratory.	N	Y	Y	Y
Biological safety cabinets are required and must be certified annually.	N	Y	Y	Y
Laboratory personnel require specific training in the handling of pathogenic materials.	N	Y	Y	Y
Safety centrifuge cups are required.	N	Y	Y	Y
Access to facility is limited or restricted during experiments.	N	Y	Y	Y
The universal biohazard symbol must be posted on the access door to the laboratory.	N	Y	Y	Y
Immunization and/or serological testing for agents to be handled may be required.	N	Y	Y	Y
All laboratory procedures must be performed in a properly certified biological safety cabinet.	N	N	Y	Y
Laboratory requires controlled entry, unidirectional air flow, and other special design features.	N	N	Y	Y
Windows must be closed and sealed.	N	N	Y	Y
No material or equipment can leave the laboratory unless it is autoclaved or decontaminated.	N	N	Y	Y
Autoclaves must be located inside the laboratory.	N	N	Y	Y
Access is through an airlock system.	N	N	N	Y

Appendix J
Summary of Requirements for Animal Biosafety Levels

Safety Guideline	ABSL1	ABSL2	ABSL3	ABSL4
Access is limited or restricted at the discretion of the laboratory for satellite laboratories or the Attending Veterinarian for all laboratories.	Y	Y	Y	Y
Personnel must wash their hands after handling cultures and animals, removing gloves, and before leaving the facility.	Y	Y	Y	Y
Eating, drinking, and application of cosmetics is prohibited.	Y	Y	Y	Y
Personnel must be familiar with basic biosafety procedures, including this manual.	Y	Y	Y	Y
Personnel should wear goggles or face shields if the possibility of splashes and aerosols exists.	Y	Y	Y	Y
Pipetting by mouth is prohibited.	Y	Y	Y	Y
All procedures should be performed to minimize aerosol generation.	Y	Y	Y	Y
Work surfaces must be decontaminated at least daily with an approved disinfectant, after each use for infrequent users, and after any spill of viable materials.	Y	Y	Y	Y
Sharps must be placed in specially designed puncture- and leak-proof sharps containers and disposed of appropriately as medical waste.	Y	Y	Y	Y
Facilities must be kept neat; good housekeeping procedures must be in place and in regular use.	Y	Y	Y	Y
All medical waste is decontaminated before disposal by an approved decontamination method and/or disposed of as medical waste.	Y	Y	Y	Y
Insect and rodent control programs are instituted.	Y	Y	Y	Y
Doors to animal rooms are kept closed when experimental animals are present.	Y	Y	Y	Y
Facilities are designed for ease of decontamination (e.g., no carpets, sealed surfaces, no unreachable areas, etc.).	Y	Y	Y	Y
Bedding materials from animal cages are removed in a manner that minimizes aerosol production and are disposed of as medical waste.	Y	Y	Y	Y
Instructions for safety precautions are posted by the Principal Investigator.	Y	Y	Y	Y
Facility windows and vents that open must be fitted with fly screens.	Y	Y	Y	Y
Laboratory coats or gowns and gloves must be worn.	Y	Y	Y	Y
Autoclaves are required for waste treatment prior to disposal as biohazardous waste.	N	Y	Y	Y

Safety Guideline	ABSL1	ABSL2	ABSL3	ABSL4
Autoclave quality control program is required for use specified above.	Y	Y	Y	Y
Cages are washed prior to release or reuse.	Y	Y	Y	Y
Air is exhausted to the outside without recirculation.	N	Y	Y	Y
Personnel baseline serum samples may be required.	N	Y	Y	Y
Facility personnel require specific training in the handling of pathogenic materials.	N	Y	Y	Y
Safety centrifuge cups are required.	N	Y	Y	Y
Access to facility is limited or restricted during experiments.	N	Y	Y	Y
The universal biohazard symbol must be posted on the access door to the facility.	N	Y	Y	Y
Immunization and/or serological testing for agents to be handled may be required.	N	Y	Y	Y
All procedures must be performed in a properly certified biological safety cabinet.	N	N	Y	Y
Facility requires controlled entry, unidirectional air flow, and other special design features.	N	N	Y	Y
Windows must be closed and sealed.	N	N	Y	Y
No material or equipment can leave the facility unless it is autoclaved or decontaminated.	N	N	Y	Y
Autoclaves must be located inside the facility.	N	N	Y	Y
Access is through an airlock system.	N	N	N	Y

Appendix K
Bloodborne Pathogen Standard

Avoiding occupational exposure to human blood, body fluids, and tissues is the primary way to prevent transmission of bloodborne pathogens. The goal of the initial and annual standard precautions training is to present information on how to prevent such exposures by administrative controls, workplace engineering controls, proper work practices, personal protective equipment, and a hepatitis B vaccine immunization program.

Personnel can be exposed to bloodborne pathogens by being stuck with contaminated needles, lacerations from contaminated sharp instruments, or being splashed with blood or body fluids on the mucous membrane of the eye, nose or mouth, or on abraded, non-intact skin (e,g., chapped skin or skin affected by dermatitis). Any direct contact (e.g., contact without barrier protection) to concentrated hepatitis B, hepatitis C, HIV, or any other infectious virus in a research laboratory or production facility is considered an exposure that requires clinical evaluation. All employees working with human cell cultures should be offered hepatitis B vaccination and be evaluated if an exposure occurs. Hepatitis B viral infection is one of the most frequent laboratory-associated infections, and laboratory personnel are recognized as a high-risk group for acquiring this infection (Centers for Disease Control and Prevention).

The OSHA Bloodborne Pathogens Standard applies to all employees who might come into contact with blood or other bodily fluids, including:

- Human blood
- Human blood components
- Products made from human blood, or other potentially infectious materials (OPIM) such as the following human body fluids:
    - Semen
    - Vaginal secretions
    - Cerebrospinal fluid
    - Synovial fluid
    - Peritoneal fluid
    - Amniotic fluid
    - Saliva in dental procedures
    - 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.
- Any unfixed tissue or organ (other than intact skin) from human (living or dead)
- HIV-containing cell or tissue cultures, organ cultures, and HIV-, HBV- or HCV-containing culture medium or other solutions; and blood, organs, or other tissues from experimental animals with HIV, HBV or HCV.

Program Elements

The Bloodborne Pathogens Standard requires that an Exposure Control Plan be written and implemented. The Exposure Control Plan must have the following elements:

- Policies and procedures for elimination, or minimization, of exposure
- Evaluation of employee exposure potentials
- Medical surveillance program
- Routine testing

The following is a general outline of the BU Exposure Control Plan.

Roles and Responsibilities

PI/ Laboratory Director/Employee Supervisor

The PI/laboratory director/employee supervisor must identify employees under his or her supervision who may be at risk. Upon identifying these employees, the supervisor must:

- Reduce potential risk by providing personal protective clothing and equipment;
- Provide HBV vaccinations at no cost to the employee;
- Complete the OSHA-required Bloodborne Pathogen Training;
- Train the employees;
- Ensure that the BU Exposure Control Plan manual is adopted by the lab and develop an effective hazard communication program;
- Ensure appropriate PPE, engineering controls, such as a biological safety cabinet or sharps container are available and used;
- Develop safe work practices and procedures, as well as internal notification procedures to report accidents;
- Review and evaluate safe alternatives for use of sharps with lab personnel;
- Ensure that all observation cited by EHS during lab inspection are addressed and closed-out;
- In conjunction with the academic department, review the list of at-risk employees on an annual basis to ensure that the list is current.

Laboratory Worker

- Complete required Bloodborne Pathogen Training initially on hire and annually thereafter;
- Complete training provided by the PI;
- Use required PPE when working in the lab;
- Report and follow procedures in the event of accidental exposure;
- Accept or decline the HBV vaccination upon offer. Complete the declination form when declining. Inform the PI and ROHP should the individual decide to take the vaccination previously offered at any time during employment;
- Review the lab Exposure Control Plan manual.

Environmental Health and Safety

- Inspect laboratories to verify the lab compliance with the OSHA Bloodborne Pathogen requirements;
- Review lab SOPs upon request by the lab;
- Conduct follow up investigation of exposure and incidents, Determine the root cause and provide recommendations to prevent or minimize the incident from recurring;
- Act as a liaison during inspections and visits by regulatory agencies;
- Prepare, maintain and implement the OSHA-required Bloodborne Pathogen Training for completion by the PI and lab personnel.

Key Definitions

Other potentially infectious materials (OPIM) are those listed above in Appendix K.

Regulated waste means liquid or semi-liquid blood or other potentially infectious materials and contaminated items that would release blood or other potentially infectious material in a liquid or semi-liquid state if compressed; items that are caked with dried blood or other potentially infectious materials and are capable of releasing these materials during handling; contaminated sharps; and pathological and microbiological wastes containing blood or other potentially infectious materials.

Sharps waste means any device having acute rigid corners, edges, or protuberances capable of cutting or piercing, including, but not limited to, all of the following:

Hypodermic needles, syringes, blades, and needles with attached tubing

Broken glass items, such as Pasteur pipettes and blood vials contaminated with other medical waste

At-Risk Employee Identification

The Exposure Control Plan requires each employer to identify, in writing, all tasks, procedures, and job classifications where occupational exposure to blood may occur and to document the methods of compliance that will minimize the potential of occupational exposure.

Incident Reporting

All incidents must be documented and a copy be kept in the laboratory and a copy forwarded to EHS. Accident response procedures are described in Chapter 8.

Written Policies and Procedures

This manual is intended to act as a primary source of policies and procedures designed to eliminate, or minimize, potential employee exposure to all biological materials, regardless of their hazard level. Employees are required to read and implement all sections of this manual that are relevant to their work environment and be fully familiar with standard precautions. Each PI must further develop site-specific SOP to address local programmatic needs.

Medical Surveillance

The OSHA Bloodborne Pathogens Standard requires that all personnel with potential exposure to bloodborne pathogens be offered immunization against the hepatitis B virus.

- HBV vaccinations must be offered to an employee within 10 days of assignment.
- Personnel must indicate their consent or declination for the Hepatitis B Vaccine using the ROHP Consent or Declination forms. Both forms are available from the ROHP. The ROHP must retain this form on file for the duration of the employee's employment plus thirty (30) years.
- An employee who declines hepatitis B vaccination may, at any time thereafter, change his or her mind and receive the vaccine. The acceptance statement must be signed at that time.
- The PI/laboratory supervisor must not make participation in a prescreening program a prerequisite for receiving the vaccination.
- The HBV vaccination is available at no cost to the employee.
- ROHP conducts thorough evaluation for risk of exposure to other blood borne pathogens such as HIV and HCV.

BPHC must also be notified of all presumptive exposures (See Appendix P for BPHC Medical Surveillance Reporting requirements).

- The PI must ensure that all employees with the potential for occupational exposure participate in a training program provided by EHS at no cost to the employee during working hours.
- Training must be given in accordance with the Bloodborne Pathogens Standard upon initial assignment, on an annual basis thereafter, or whenever modification of an existing job description may affect the employee's potential for occupational exposure.
- HIV/HBV research laboratories must ensure that their employees demonstrate proficiency in standard microbiological procedures prior to being allowed to work in the laboratory.
- Training must include a comprehensive discussion of this standard, including epidemiology, symptoms and transmission of bloodborne diseases; the Exposure Control Plan; the uses, limitations of, and procedures for using personal protective equipment; a discussion of the HBV vaccination (including the benefits of vaccination and efficiency of the vaccine to prevent disease); emergency procedures involving blood exposure or contamination and post-exposure follow-up procedures; hazard communication; and a question-and-answer discussion opportunity.

EHS provides Bloodborne Pathogens training on a regularly scheduled basis. For more information and scheduling, call (617) 358-7840 on the BU Medical Campus and 617-358-4094 on the Charles River Campus.

PI Responsibilities for Occupational Health Issues

In keeping with the OSHA Bloodborne Pathogen Standard, this policy requires annual standard precautions training, a hepatitis B immunization program, and a post-exposure medical management program.

It is the PI's responsibility to ensure that researchers, technicians, students, or volunteers who work in the laboratory and who have contact with animals, infectious agents, or bloodborne pathogens are medically evaluated prior to starting work and that anyone working with bloodborne pathogens is offered the hepatitis B vaccination series administered by ROHP in compliance with the Bloodborne Pathogen Exposure Policy. PIs are required to complete the Hepatitis B Vaccine Authorization available on ROHP's website at www.bu.edu/rohp/forms.

An appointment can be made with a medical provider by calling BU's ROHP at (617) 358-7647. If the research project is located at a facility at another institution, such as the VA Hospital or the Framingham Heart Study, the researcher should contact ROHP for assistance at 617-358-7647.

It is the PI's responsibility to ensure that any person present in a BU laboratory who has an incident involving potential exposure to an infectious agent is offered ***immediate*** access to a medical evaluation by or through the ROHP (listed below). An immediate evaluation is important, as efficacy of post-exposure medication for HIV and other infectious agents may be less effective if the initiation of treatment is delayed. Personnel working with non-human primates or their tissues may also require evaluation for post-exposure prophylaxis against herpes B virus.

If at any time, any employee has an exposure to bloodborne pathogens, they MUST immediately contact the ROHP at (617) 358-ROHP (7647). An immediate evaluation is important, as efficacy of post-exposure medication for HIV may be less effective if the initiation of treatment is delayed. For more information, call BU's ROHP at (617) 358-ROHP (7647).

Contacting the ROHP

ROHP is located on the Boston University Medical Campus at 72 East Concord Street, 8th Floor, Room 825. Our normal hours of operation are Monday through Friday from 8:00am to 4:30pm. Our phone number is (617) 358-7647 (ROHP) and is available and supported by medical staff 24 hours per day/7 days per week to triage and evaluate laboratory exposures and related illnesses. Based on injury severity, location and time of day, ROHP will refer people to the appropriate health care location.

- For lab exposures (e.g., needle stick, bite, cut, scratch, splash) involving animals or infectious agents on the Medical Campus or Charles River Campus, **call the ROHP 24/7 hour number (1-617-358-ROHP (7647) or 4-ROHP (7647) if calling from a Medical Campus location)** to be connected with the BU ROHP medical officer.

- For unexplained symptoms or illness **call the ROHP 24/7 hour number ((617) 358-ROHP (7647), or 4-ROHP (7647) if calling from a Medical Campus location)** to be connected with the BU ROHP medical officer.

When referred to a health care location under any of these scenarios, always inform the physician of your work in the laboratory and the agent(s) that you work with. If you have been given a wallet-size agent ID card, provide the agent ID card to the physician.

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Appendix L
Working Safely with Animals

Working with animals poses potential additional health and safety hazards that require extra precautions. The specific requirements will depend on the types of activities (e.g., surgery, feeding animals, use of anesthetic agents, etc.) and the specific species used. Personnel should follow the following guidelines:

- Follow the specific requirements established in the IACUC-approved protocol and the facility requirements.
- Follow procedures established by the Animal Science Center and IACUC for ABSL2 as appropriate.
- Wash hands after handling an animal, anything that an animal has touched, or before exiting the animal facility. The most common way of contracting an animal-transmitted infection is placing the infectious material directly into the mouth.
- Never smoke, drink, or eat in an animal area or before washing hands.
- Wear protective clothing as recommended/required by the facility for the species and operations: Protective laboratory coats, gowns, or uniforms are recommended to prevent contamination of personal clothing; Protective clothing helps prevent potentially contaminated material from leaving an animal area; and do not wear the protective clothing outside of the animal area and do not take protective clothing home;
- Use the personal protective equipment (PPE) recommended/required for the species and operations.
- Workers shall wear the appropriate PPE (e.g., gloves, face shields, masks, and respirators) when required and follow their supervisor's instructions scrupulously.
- Gloves are worn to prevent skin contact with contaminated, infectious and hazardous materials, and when handling animals.
- Gloves and personal protective equipment should be removed in a manner that minimizes transfer of infectious materials outside of the areas where infectious materials and/or animals are housed or are manipulated.
- Persons must wash their hands after removing gloves, and before leaving the areas where infectious materials and/or animals are housed or are manipulated.
- Eye and face and respiratory protection should be used in rooms containing infected animals, as dictated by the risk assessment.
- Participate in the ROHP medical surveillance program (See Appendix P) that provides medical evaluations, testing, immunizations, and periodic screenings for allergies, infections, and other medical problems related to animal exposure.
- Seek medical attention promptly when injured. Follow the specific recommendations for the facility.
- Workers engaged in work involving vertebrate animals should inform their physician of their work when seeking treatment for illness, even if uncertain whether the illness is work related. All animal care workers are provided wallet-sized agent identification cards. The card indicates the card carrier works in a laboratory setting at Boston University and may be exposed to hazardous materials. The card also contains ROHP contact information in the event the physician should choose to seek further information on potential occupational exposure. Physicians need such information to make an accurate diagnosis because many animal-transmitted diseases have flu-like symptoms.
- If there is any possibility of work-related illness or disease, the ROHP must be notified immediately at (617) 414-ROHP (7647).
- Get the appropriate training and contact a supervisor with any questions.

Basic Safety for the Necropsy of Infected Animals

- Ensure that the necropsy of infected animals is carried out in biological safety cabinets or designated necropsy space by trained personnel.
- Wear a surgeon's wrap-around gowns over laboratory clothing.
- Use a surgeon's mask and eye protection.
- Use other PPE recommended by the facility for the infectious agents present.
- Wear gloves.
- Wet the fur of the animal with a suitable disinfectant.
- Pin down or otherwise fasten small animals to metal in a tray.
- Before and after necropsy, disinfect the necropsy table, inside the BSC, and other potentially contaminated surfaces with a suitable germicide.
- Upon completion of necropsy, place all potential biohazardous materials in suitable containers and then sterilize the materials.
- Segregate contaminated mixed waste and store for appropriate disposal.
- Place contaminated instruments in a bath that contains a suitable disinfectant.
- Follow the facility requirements for sterilization.
- Clean contaminated rubber gloves in disinfectant before removal from the hands.
- Wearing gloves is not a substitute for handwashing; wash hands after necropsy and carcass disposal.
- Follow the facility's guidelines for the disposal of animal carcasses.

Appendix M
Procedures for Working in an Animal Biosafety Level 2 (ABSL2) Facility at BU

Before starting any Animal Biosafety Level 2 (ABSL2) work a PI must:

- Obtain IBC and IACUC approval
- Make appropriate housing arrangements with the ASC director

The following Standard Operating Procedures (SOP) have been developed to provide guidance to those individuals working in rooms in which animals involved in chemical and biological hazards determined to be ABSL2 are housed.

Definitions

ABSL2: Animal Biosafety Level 2 includes pathogenic agents of moderate hazard potential (CDC Biohazard Class 2) and chemical hazard agents of moderate hazard potential.

PPE: Personal protective equipment

EHS: Environmental Health and Safety

Parenteral: Taken into the body or administered in a manner other than through the digestive tract, as by intravenous or intramuscular injection.

Overview

Access to the room where the work with animals is to be conducted is restricted. Laboratory personnel must have training in aseptic micro-isolator techniques, when applicable, and use of biological safety cabinets, in addition to specific safety training in handling the pathogenic and/or chemical agent(s) with which they are working.

Research and Animal Science Center Facility (BUMC or CRC) personnel should receive appropriate immunizations or tests for any agents handled or potentially present in the room prior to initiating the ABSL2 portion of their project.

Procedures must be conducted in a Class II BSC.

Personal Protective Equipment

Minimum PPE:

- Solid front gown:
- Hair cover
- Shoe covers
- Mask
- Double gloves

In addition:

- N95 may be required
- Face shield or other specific eye or face protection may be required

Equipment and Supplies

- Biohazard stickers for cage cards
- MB-10 (chlorine dioxide) disinfectant or Virkon-S

Biological safety cabinet: Class II

Responsibilities

It is the responsibility of EHS to ensure that all necessary project-specific safety training is provided to research and LASC/LACF staff prior to any project being initiated. It is also the responsibility of EHS to provide documentation to the LASC/LACF of such training.

The PI and individuals working in the facility are responsible for ensuring they have received proper training and that they are adhering to this SOP, as well as to posted precautions and guidelines in the facilities.

Procedure

Entry

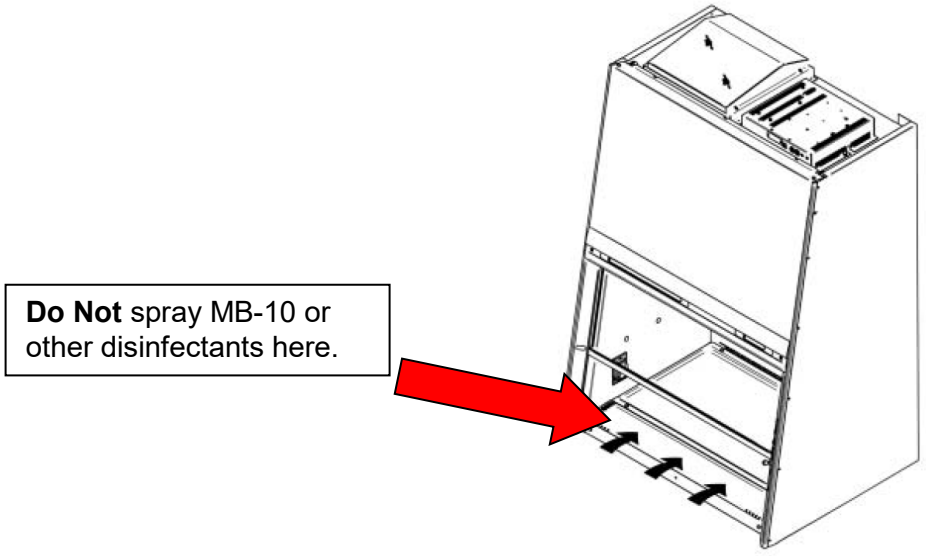
- Remove the lab coat worn in the ASC facility and hang it on the garment rack provided outside of designated ABSL2 animal space.
- PPE *must* be worn while working in ABSL2 animal housing and procedure space. PPE is provided just outside specific ABSL2 rooms. Don designated PPE prior to entry into the ABSL2 areas.
- Proceed into the designated ABSL2 room using an access card or key.

Conducting a Procedure

General Information:

- Investigators using the room will be assigned a cubicle and/or rack and shelf/shelves where their animals will be housed.
    - A cubicle or rack may hold cages belonging to more than one investigator.
    - Biohazard projects are not housed in cubicles that house ongoing chemical hazard projects.
- ASC personnel will perform daily health checks of animals on studies involving infectious agents if the animals are housed on racks not held in cubicles.
    - ASC personnel will perform daily health checks of animals on studies involving chemical agents by viewing the animals through the window of the isolation cubicle.
    - The ASC will notify PIs of any animal health issues.
    - All animal work will be conducted within the confines of the Class II BSC.
        - Always open animal cages in the Class II BSC using aseptic micro-isolator technique.
    - Hypodermic needles and syringes are used only for parenteral injection or aspiration of fluids from laboratory animals and bottles with plastic/rubber diaphragms.
        - Only needle-locking syringes (e.g. luer locking) or disposable needle syringe units (e.g., the needle is integral to the syringe) are used for the injection or aspiration of infectious fluids.

  - Needles should not be bent, sheared, replaced in the sheath or guard, or removed from the syringe following use.
  - The needle and syringe should be promptly placed in a puncture-resistant sharps container.
- Always spray or wipe down all interior surfaces of the Class II BSC with MB-10 or Virkon-S **before** and **after** working in the hood. Allow 10 minutes of contact time prior to wiping the surfaces with disposable towels. Do not spray the top grille of the Class II BSC (this is where the filter is located). Discard used towels in the waste container.



- Immediately following infection of animals with pathogenic agents, place a biohazard sticker on their cage card(s) (ASC provides these specific stickers). Fill out the following information on the biohazard sticker for cage cards:
  - PI name
  - 24-hour contact phone number
  - Protocol number
  - Pathogenic agent
  - Dose per animal
  - Date(s) infected
  - Husbandry by PI or ASC (circle one)
- Report all spills and accidents that result in overt exposure to infectious materials to a ASC Supervisor and the ASC office, (617) 638-4086 or LACF at (617) 353-5415

Removal of Dirty Cages and Bottles from Room

Biological agents

- Place a cage inside the BSC, remove the water bottle from the cage, and replace the lid.
  - Put soiled cage, wire lid, and bedding in a semi-clear biohazard autoclave bag and place on a cart.
  - Put water bottles in a separate, semi-clear biohazard autoclave bag on a cart.
- Closure ties are stored adjacent to the biohazard autoclave bags on the supply rack in the corridor outside rooms and in rooms.

- **Do not use** autoclave tape to close the bag.
- Thoroughly spray the exterior of all bags with MB-10 or Virkon-S after closing the bag with a nylon tie, beaded tie, or twist tie. Spray all surfaces and wheels of the cart(s).
- Cart(s) should be moved to the soiled side of the cage wash room.

Chemical agents

- Place a cage inside the BSC, remove the water bottle from the cage, and replace the lid.
  - Put soiled cage, wire lid, and bedding in a red biohazard bag and place on a cart.
  - Put water bottles in a separate red biohazard bag on a cart.
- Closure ties are stored adjacent to the biohazard autoclave bags on the supply rack in the corridor outside W-838/839 and in both rooms.
- **Do not use** autoclave tape to close the bag.
- Thoroughly spray the exterior of all bags with MB-10 after closing the bag with a nylon tie, beaded tie, or twist tie. Spray all surfaces and wheels of the cart(s).
- Cart(s) should be moved to the soiled side of the cage wash room on the 8th floor of W Building (W-8).

Disposal of carcasses

- Any dead animals must be removed from their cage (while in the BSC) and placed in a small, leak-proof red biohazard bag.
- Place a sticker with animal identification information on the outer bag, then thoroughly spray the bag with MB-10 or Virkon-S and place in the refrigerator. A cage card with a sticker showing the same animal identification information will be placed on the cage.
- The ASC will remove carcasses for incineration disposal three days after they are found in the refrigerator.

Exiting Procedures

- When work is complete and the BSC and all other work spaces have been decontaminated with MB-10 or Virkon-S, outer gloves should be removed and placed in the biohazard waste container.
- To exit the room, open the door and remove one shoe cover, stepping over the room threshold into the hallway with that foot.
- Remove the shoe cover from the other foot as it is brought into the hallway but before stepping into the hallway with the second foot
- Remove gown from the shoulders, turning it inside out.
- Discard disposable face protection, hair cover, mask, gown and gloves in the red biohazard trash receptacle in the hallway outside ABSL2 room.
  - After leaving ABSL2 room and discarding PPE, hands should be washed using the alcohol hand sprayer located on the wall immediately to the left of the doors to each ABSL2 room

Reference: Biosafety in Microbiological and Biomedical Laboratories (6th edition, 2020)

Appendix N
Verification of Attenuated Biosafety Level 3 (BSL3) Pathogens Policy

I. Purpose

The purpose of this policy is to set forth the procedures for verification of attenuated BSL3 pathogens before they may be safely handled at the lower biosafety level (BSL) designated for the attenuated pathogen.

II. Covered Parties

This policy applies to all individuals engaged in research at or under the auspices of Boston University (BU) and covers all attenuated pathogens that meet all of the following criteria:

i. The attenuated agent is derived from a known and virulent pathogen that requires BSL3 containment;

ii. Attenuation results in decreased virulence of the pathogen; and

iii. Attenuation results in a reduction in the BSL containment in which the attenuated pathogen can be handled compared with the BSL required for the safe handling of the non-attenuated counterpart.

This policy does not apply to BSL3 agents that have been inactivated by a process that meets established and accepted scientific and safety standards approved by the Institutional Biosafety Committee (IBC). The requirements for working with inactivated BSL3 pathogens are covered in the Inactivated Biological Sample Use policy.

Food and Drug Administration (FDA) approved vaccines that contain attenuated agents derived from pathogens may be excluded from this policy if the formulated vaccines are obtained directly from the vaccine manufacturer. Requests for use of such vaccines and the manufacturer's documentation must be submitted as a new IBC protocol or an amendment to an approved IBC protocol. The IBC, in consultation with Environmental Health and Safety (EHS), will determine whether exclusion from the BU policy is allowable.

III. Policy

Attenuation of any BSL3 pathogen must be verified before it may be handled at the lower BSL designated for the attenuated agent. Verification of attenuation must be performed at the BSL designated for the virulent wild-type strain. A verification plan with detailed methods for the particular attenuated pathogen must be approved by the IBC before shipments of the attenuated BSL3 pathogen can be received at BU and before work with the attenuated agent may be initiated. Confirmation of the attenuation must be submitted to the IBC for final approval before the attenuated agent can be moved out of the BSL3 laboratory into lower containment.

If the identity of an attenuated agent cannot be verified, it must be handled at the BSL designated for the non-attenuated wild-type pathogen.

IV. Procedures

The Principal Investigator (PI) must have an IBC approved protocol in place prior to submitting a

verification plan for an attenuated BSL3 agent.

The PI must submit a verification of attenuation plan to the IBC and the IBC must grant the verification plan full approval before shipments of attenuated BSL3 materials can be received and before work with the attenuated agent may begin. EHS must be notified of all incoming shipments. Upon receipt, the package(s) must be transferred to the BSL3 laboratory for verification of attenuation.

Verification must be performed using an approved method to distinguish between the attenuated and wild type strain (e.g., polymerase chain reaction (PCR) or reverse transcription (RT-PCR)). The verification plan may also include an individualized verification protocol to experimentally distinguish the non-attenuated wild-type pathogen and the attenuated pathogen. A good verification plan will include multiple approaches that provide consistent data to support a conclusion that the strain is attenuated.

Each verification plan must include samples from both the inactivated wild-type and the attenuated strain such as genomic DNA or RNA samples, or plasmid DNA containing the original and attenuated virulence factor(s). These samples may be obtained from other investigators. Verification must be conducted on the received stock which is designated the Master Stock. Whenever possible, verification should be carried out on an individual clone (e.g., single colony or plaque) that has been isolated from the Master Stock. Only material from the verified colony/plaque can be studied at the lower BSL.

Confirmation of the attenuation must be submitted to the IBC for final approval before the pathogen can be moved out of the BSL3 laboratory into lower containment.

If attenuation cannot be confirmed, the pathogen must be handled at BSL3.

III. Definitions

Attenuated Strain*:* A debilitated, weakened or less virulent virus, bacteria or other pathogen

Biosafety Level 3 (BSL3): *C*lassification of clinical, diagnostic, teaching, research, or production facilities where work is performed with indigenous or exotic agents that may cause serious or potentially lethal disease through the inhalation route of exposure. Laboratory personnel must receive specific training in handling pathogenic and potentially lethal agents and must be supervised by scientists competent in handling infectious agents and associated procedures.

Inactivation: A process which documents the absence of infectious particles.

Wild Type Strain*:* A strain found in nature or a standard strain.

IV. Related Documents

Policy: Laboratory Safety Training

Policy: Disease Surveillance Reporting

Policy: Inactivated Biological Sample Use policy

V. History

Original Date Approved: 2010
Revised: 11/19/14, 11/13/15, 4/19/16

Appendix O
Boston Public Health Commission Requirements

The Biological Laboratory Regulations adopted by the Boston Public Health Commission (BPHC) as amended in October 2019 requires laboratories working with rDNA and those at Biosafety Level 3 (BSL3) and BSL4 to adhere to local standards, including:

- Obtaining an annual Recombinant DNA permit from the BPHC.
- An IBC that reports to a senior responsible official and that has at least two community members without a connection to the organization.
- Submitting an annual report to the BPHC on minutes and members for the IBC and holding an annual public meeting of the IBC.
- Following the highest safety standards outlined in the NIH Guidelines, *Biosafety in Microbiological and Biomedical Laboratories* 6th edition, BPHC permitting process or other such guidance.
- Reporting laboratory related incidents or illness, and inspections.
- Prohibiting weaponization and classified research in Boston.
- Reporting intended decommissioning of a laboratory facility.
- Establishing a Community Benefits Program to support local health and safety needs as a mandate for BSL4 laboratories.

Appendix P
ROHP Medical Surveillance Program

BU provides medical monitoring to all employees who face workplace risks. The program is designed to monitor potential health hazards associated with research and development activity with recombinant DNA, bloodborne pathogens, other etiologic agents, zoonotic diseases associated with laboratory animals, and hazardous chemicals. The details of the program are provided below:

Objectives and Scope

The Medical Surveillance Program developed and implemented by the ROHP has the following objectives:

a. Determine the initial and periodic medical surveillance requirements for those personnel that perform research and those groups that support research such as animal care workers, EHS, Public Safety, and Facilities (**Table 1**)
b. Define the surveillance requirements based on the work environment, occupational exposure and risk, and access requirements for each position.
c. Determine whether the employee or applicant is able to safely perform the essential functions of the job for which employment has been offered.
d. Determine accommodations, if necessary, for an employee or applicant to perform the functions of the job in a safe and effective manner.
e. Establish a baseline for comparison with future periodic evaluations and termination evaluations.
f. Establish a procedure for performing additional medical surveillance in support of the IBC when new protocols are reviewed and changes in the job function or role, exposure to hazardous materials and access requirements for researchers arises.

The clinical services provided as part of the Initial and Periodic medical surveillance profiles include questionnaires, physical examinations, laboratory testing, and screenings dictated by the job title, exposure type and access/location requirements for each position. Exposure type includes agents, animal types, lasers, chemical or other hazardous materials, bloods, tissues, cells or fluids, or patient care. Access/Location includes Research Laboratory and Biosafety Level, National Emerging Infectious Diseases Laboratory (NEIDL), and Animal Care Facilities.

In addition to the clinical services identified above, biological agent immunization requirements are also defined based on the specific agent the individuals work with or are potentially exposed to. The Initial and Periodic Biological Agent Specific Immunizations are identified in Table 1:

i. These clinical services will be provided to the employees or applicants who perform research, support research, or require access to research facilities.
ii. For the NEIDL facility, Public Safety will determine whether these individuals have escorted or unescorted access. If unescorted NEIDL access is required, medical surveillance will be performed based on minimum NEIDL requirements plus occupational exposure and risk, and access level required. No medical surveillance is required for escorted NEIDL visitors.

All transfers into the NEIDL require mental health and drug screens along with a pre-placement baseline examination, testing and immunizations in accordance with **Table 1**.

Certain testing and immunizations may be avoided if documentation of previous baseline examinations and testing is available and within current guidelines.

a Employees returning to Boston University Research:

i. From leaves of absence of more than one year or previous employment at BU more than one year ago, a complete medical surveillance is required.

ii. From leaves of absence of less than one year or previous employment at BU less than one year ago, completion of an abbreviated health questionnaire is required. No other examinations are needed unless health risks are indicated in the abbreviated questionnaire.

b. Employees returning to BU Research that require access to the NEIDL:

i. From leaves of absence of more than one year or previous employment at BU more than one year ago, a complete medical surveillance is required.

ii. From leaves of absence of less than one year or previous employment at BU less than one year are required to complete an abbreviated health questionnaire and undergo mental health and drug screens. No other examinations are required unless health risks are indicated in the abbreviated questionnaire.

Procedures

The procedures followed by ROHP medical personnel in the determination and performance of medical surveillance are as follows (**Table 1**)

a) Researchers and research support staff will complete a Health Questionnaire and job risk assessment with guidance from the PI or manager;
b) The healthcare provider in ROHP reviews the Health and Job Risk Questionnaires for occupational exposure and risk assessment, immunizations and medical limitations to essential job functions;
c) ROHP contacts the applicant/employee to discuss additional documentation and testing needed for medical clearance;
d) ROHP schedules an appointment in ROHP for required examination components as needed;
e) If no additional information is needed, the healthcare provider in ROHP completes a Medical Clearance Form and clears the Researcher to begin work. A copy of the Medical Clearance Form is provided to the applicant/employee;
f) If a physical examination is required, ROHP schedules the exam with an ROHP Healthcare Provider;
g) The Healthcare Provider reviews all testing results, completes a physical examination as needed, and, is available to confidentially discuss any health issues with the applicant/employee;
h) If a laboratory staff member is working with an infectious agent, the Healthcare Provider will review information about "warning symptoms" that might occur following an unprotected exposure to that agent. The laboratory worker should be given instructions regarding next steps in case of suspected infection, which should be shared with household members;

i) For people requiring NEIDL access, a mental health screen and drug screen are required for medical clearance. The Healthcare Provider reviews the results and is available to confidentially discuss any health issues with the applicant/employee. The Healthcare Provider completes a Medical Clearance Form, files the form in the individual's Medical Record and gives a copy to the applicant/employee;
j) The ROHP notifies the appropriate department when a Researcher is medically cleared;
k) Researchers may be asked to complete additional questionnaires depending on their job function, i.e. OSHA Respirator Users Questionnaire for respirator users, Animal Allergy Questionnaire for Researchers with animal allergies and working with animals;
l) Annual Health Questionnaire is completed by all personnel. The annual questionnaire is used to review any new medical conditions, medications, work exposures or processes that may require additional medical surveillance so that early preventive strategies can be recommended;
m) Respiratory Questionnaire will be completed by personnel whose position requires the use of any type of respirator other than a cloth surgical mask.
n) Tuberculosis Symptom screen surveys will be completed by Researchers every 6 (six) months if their research involves *Mycobacterium tuberculosis*, or every year if they work with or have air exposure to non-human primates. This survey discovers symptoms or conditions that increase the possibility of early tuberculosis infection. Health and Job Risk Questionnaires healthcare provided as needed.

Responsibilities

The responsibilities for the functional groups involved at any level of the ROHP Medical Surveillance Program are as follows:

Principal Investigator (PI) or hiring manager

i. Requests a job requisition posting from human resources for a new position
ii. Completes job specific information required by human resources to post the position:
    - PS-1 forms
    - Job Specific Risk Assessment Form identifying the specific occupational exposure and risks of the work environment for the position

Human Resources

i. Notifies ROHP to schedule a medical evaluation for employees or applicants seeking positions in research or supporting research

ii. Provides the candidate with the Job Specific Risk Assessment Form completed by the PI or hiring manager for this specific position.

iii. Directs the candidate to the ROHP website to complete the Initial Health Questionnaire (IHQ).

iv. For NEIDL job applicants, performs background check (criminal and credit) in addition to the above for Notifies NEIDL Public Safety whether cleared or not.

v. For NEIDL job applicants, includes information about NEIDL medical clearance procedures in conditional offer of employment including drug testing process, testing locations, and Chain of Custody forms needed to complete the process.

vi. Coordinates ROHP medical clearance notifications with employee or applicant, hiring manager and Public Safety.

Candidate

i. Goes to the ROHP website (www.bu.edu/rohp/forms) for access to the ROHP Health Questionnaire which requests the candidate's medical history information and consent for examination and authorization for disclosure .

ii. The ROHP Job Risk Assessment is completed by the candidate with guidance of the PI or manager and assistance from safety as needed to identify the work environment. The job risk assessment guides medical surveillance.

ROHP

i. Contacts the candidate (via email, phone);

ii. Request completion and return of ROHP Health Questionnaire and Job Risk Assessment;

iii. Reviews the candidate's ROHP Health Questionnaire and Job Risk Assessment to:

- Define the medical surveillance required based on occupational exposure and risk of the work environment for the candidate's position.
- Establish a baseline medical history for the candidate for ongoing medical surveillance, and
- Assess the candidate's ability to safely perform the functions of the position.

iv. Determines additional medical documentation needed, i.e. immunization records, tuberculosis screens, etc.;

v. Schedules physical examination, additional testing (labs, pulmonary function test, electrocardiogram, as needed according to exposure potential to agents, risk, contact;

vi. Schedules mental health and drug screening for personnel requiring NEIDL access;

vii. Reviews results of all testing, screenings and examinations;

viii. Notifies appropriate personnel of examination outcome

- Medically cleared to perform essential functions of the job
- Medically cleared to perform essential function of the job with the following restrictions:_____
- Examination incomplete due to _____
- Medically not cleared to perform essential functions of the job

ix. Issues a medical surveillance wallet card to personnel who may be exposed to hazardous materials while working in a research or animal care facility. The card contains ROHP contact information and is used to facilitate prompt medical attention and appropriate medical care in the event the card holder should experience symptoms or illness while away from Boston University that may be related to activities or exposures in a laboratory research environment.

Environmental, Health and Safety (EHS)

i. EHS will identify those personnel with potential exposure risks that warrant baseline and/or additional monitoring, (e.g. Respiratory Protection, Noise, Laser, baseline for 3b or 4 laser users only), and Emergency Responders

ii. EHS will communicate similar exposure group data (names, exposure type) annually to ROHP after discussion with Principal Investigators and Laboratory Managers, (e.g., noise, laser).

iii. EHS will coordinate training (biosafety level and agent specific) and potential risk exposure with PI and ROHP

iv. EHS will conduct Annual Respirator Fit Testing and Respiratory Protection Safety Training.

v. EHS will conduct safety training appropriate to emergency protocols and general laboratory safety issues, such as lock out/ tag out, fire safety, etc.

vi. Issue Agent Specific Identification Cards to all laboratory personnel approved by the IBC to work with biological agents with the potential to cause LAI (Appendix G). This card contains ROHP contact information and is provided to facilitate prompt medical attention and appropriate medical care in the event the card holder should experience symptoms or illness while away from Boston University that may be related to activities or exposures in a laboratory research environment.

Public Safety

i. Notifies ROHP when an employee or applicant has been approved to enter the NEIDL medical surveillance process and provides ROHP with access level required

ii. Provides employee or applicant with NEIDL security access after all clearance conditions have been met including medical clearance from ROHP. Updates clearances annually from security and safety perspective

Recordkeeping

Refer to the Recordkeeping Guidelines. Medical records will be maintained in the ROHP offices. Electronic medical records will also be maintained for all personnel seen in ROHP.

Questionnaires are available at the ROHP website:

- ROHP Health Questionnaire
- Animal Allergy Screening Form
- OSHA Respiratory Medical Evaluation Questionnaire
- Tuberculosis Screening and Education
- Boston Public Health Department Tuberculosis Clinic Referral Form for Positive TB Testing Result
- Immunization Consent Forms
- Vaccine Information Sheets

TABLE 1. COMPONENTS OF THE PRE-PLACEMENT MEDICAL SURVEILLANCE PROGRAM.

Panels	Orders	Initial	Annual	Description
IBC protocol	Job Risk Assessment Questionnaire	Initial	Annual	
	Health Questionnaire	Initial	Annual	
IACUC protocol	Job Risk Assessment Questionnaire	Initial	Annual	
	Health Questionnaire	Initial	Annual	
Animal access other than NHP's on the Medical Campus	Pneumococcal Vaccine	Initial		If work with chinchillas. Pneumonia vaccination is offered or need signed declination on file. Live streptococcal pneum. NOT USED with Chinchillas on CRC so vaccine not offered.
	Pneumococcal Vaccine Declination	Initial	Annual	If work with chinchillas. Pneumonia vaccination is offered or need signed declination on file. Live streptococcal pneum. NOT USED with Chinchillas on CRC so vaccine not offered.
	Toxoplasmosis Antibody Titer	Initial	Annual	Females only if working with cats
	Influenza Vaccine	Initial	Annual	Influenza vaccine offered if working with ferrets but not required
	Job Risk Assessment Questionnaire	Initial	Annual	
	Health Questionnaire	Initial	Annual	
NHP work with or have space access	Job Risk Assessment Questionnaire	Initial	Annual	
	Health Questionnaire	Initial	Annual	
	Tuberculosis Screening and Education	Initial	Annual	
	OSHA Respirator Questionnaire	Initial		
	TB Skin Test	Initial	Annual	
	IGRA Test	Initial	Annual	
	Measles Titer	Initial		Requires positive measles titer or documentation of two MMR vaccinations
	2 Doses of Measles Vaccine	Initial		Requires positive measles titer or documentation of two MMR vaccinations
	Influenza Vaccine	Initial	Annual	Vaccine recommended but not required
Animal access on the Charles River Campus	Job Risk Assessment Questionnaire	Initial	Annual	
	Health Questionnaire	Initial	Annual	Animal allergen screening is part of the questionnaire
Animal Care Technicians (Medical Campus) working with NHP's or accessing NHP areas	Job Risk Assessment Questionnaire	Initial	Annual	
	Health Questionnaire	Initial	Annual	Animal allergen screening is part of the questionnaire
	TB Skin Test	Initial	Annual	
	IGRA Test	Initial	Annual	
	Measles Titer	Initial		Requires positive measles titer or documentation of two

	2 Doses of Measles Vaccine	Initial		MMR vaccinations if working with non-human primates Requires positive measles titer or documentation of two MMR vaccinations
	OSHA Respirator Questionnaire	Initial		If there is a change in your medical status or condition (including significant weight gain, weight loss, or change in facial configuration) that may affect your ability to use a respirator or a change in your work environment that may result in a substantial increase in physiological burden, please reach out to ROHP for reevaluation
	Td or TDAP Vaccine	Initial		
	Functional Capacity Exam	Initial	Every 10 years	
	Influenza Vaccine	Initial		Vaccine recommended but not required
			Annual	
Animal Care Technicians (Medical Campus) NOT working with NHP's or accessing NHP areas	Job Risk Assessment Questionnaire	Initial	Annual	
	Health Questionnaire	Initial	Annual	
	Tuberculosis Screening and Education	Initial	Annual	
	TB Skin Test	Initial		
	IGRA Test	Initial		
	OSHA Respirator Questionnaire	Initial		If there is a change in your medical status or condition (including significant weight gain, weight loss, or change in facial configuration) that may affect your ability to use a respirator or a change in your work environment that may result in a substantial increase in physiological burden, please reach out to ROHP for reevaluation
	Audiogram	Initial	Annual	
	Td or TDAP Vaccine	Initial	Every 10 years	
	Functional Capacity Exam	Initial		
Animal Care Technicians (Charles River Campus)	Job Risk Assessment Questionnaire	Initial	Annual	
	Health Questionnaire	Annual	Annual	
	Functional Capacity Exam	Initial		
	Td or TDAP	Initial	Every 10 years	
	OSHA Respirator Questionnaire	Initial		If there is a change in your medical status or condition (including significant weight gain, weight loss, or change in

				facial configuration) that may affect your ability to use a respirator or a change in your work environment that may result in a substantial increase in physiological burden, please reach out to ROHP for reevaluation
Animal Science Center staff (Assistant Directors (Ops), Managers, Supervisors, ASC Trainer, Vet Techs, Vet Manager, Supervisors, Veterinarians, W7 floor staff) - administrative staff exempt from this requirement	Job Risk Assessment Questionnaire Health Questionnaire Tuberculosis Screening and Education TB Skin Test IGRA Test Measles Titer 2 Doses Measles Vaccine Influenza Vaccine	Initial Initial Initial Initial Initial Initial Initial Initial	Annual Annual Annual Annual Annual Annual	 Requires positive measles titer or documentation of two MMR vaccinations Requires positive measles titer or documentation of two MMR vaccinations Vaccine recommended but not required
NEIDL Administrative Access	Health Questionnaire Mental/Behavioral Health Urine Drug Screen Ishihara Screen PHQ-9 Questionnaire GAD-7 Questionnaire AUDIT Significant Life Changes and Stressors Checklist Influenza Vaccine	Initial Initial Initial Initial Initial Initial Initial Initial Initial	Annual Annual Random Annual Annual Annual Annual Annual	 Vaccine recommended but not required
NEIDL Biosafety Level 2 Access	Job Risk Assessment Questionnaire Health Questionnaire Mental/Behavioral Health Urine Drug Screen Ishihara Screen PHQ-9 Questionnaire GAD-7 Questionnaire AUDIT Significant Life Changes and Stressors Checklist Influenza Vaccine	Initial Initial Initial Initial Initial Initial Initial Initial Initial Initial	Annual Annual Annual Random Annual Annual Annual Annual Annual Annual	 Vaccine recommended but not required
NEIDL Biosafety Level 3/4 Access	Job Risk Assessment Questionnaire Health Questionnaire	Initial Initial	Annual Annual	

	Mental/Behavioral Health	Initial	Annual	
	Urine Drug Screen	Initial	Random	
	Ishihara Screen	Initial		
	PHQ-9 Questionnaire	Initial	Annual	
	GAD-7 Questionnaire	Initial	Annual	
	Significant Life Changes and Stressors Checklist	Initial	Annual	
	AUDIT	Initial	Annual	
	Physical Exam	Initial		
	Cardiovascular Risk Assessment	Initial		
	Health Intake Form	Initial		
	Urinalysis	Initial		
	Measles Titer	Initial		
	2 Doses of Measles Vaccine	Initial		Requires positive measles titer or documentation of two MMR vaccinations
	Tuberculosis Screening and Education	Initial	Annual	Requires positive measles titer or documentation of two MMR vaccinations
	TB Skin Test	Initial		Annual TB Consent Form and Symptom Screen required if working with any animals.
	IGRA Test	Initial	Annual	Annual TB skin test/IGRA if working with any animals.
	EKG	Initial	Annual	Annual TB skin test/IGRA if working with any animals.
	Spirometry	Initial		
	Audiometry (BSL4 only)	Initial		
	Functional Capacity Exam (BSL4 only)	Initial		
	Snellen	Initial		
	OSHA Respirator Questionnaire	Initial		If there is a change in your medical status or condition (including significant weight gain, weight loss, or change in facial configuration) that may affect your ability to use a respirator or a change in your work environment that may result in a substantial increase in physiological burden, please reach out to ROHP for reevaluation
	CBC w/Diff	Initial		
	Comprehensive Metabolic Panel	Initial		
	Influenza Vaccine	Initial		Vaccine recommended but not required
Human Cells, Blood, or Tissue	Hepatitis B Vaccination	Initial		Requires written documentation of having had 3 doses

	Hepatitis B Vaccine Declination	Initial		(dates must include month/day/year and be signed by healthcare provider) of this vaccination If not accepting the Hepatitis B vaccine, read the Centers for Disease Control and Prevention's Vaccine Information Statement and sign a Hepatitis B vaccination declination form
	Hepatitis B Quantitative Titer	Initial		Obtain, once written documentation of 3 Hepatitis B vaccinations has been obtained
Dengue Virus Work	Dengue Titer	Initial		Obtain Dengue IGG prior to working with if checked off on risk assessment
Human subject/ patient care access only if on IBC protocol	Job Risk Assessment Questionnaire	Initial	Annual	
	Health Questionnaire	Initial		
	Tuberculosis Screening and Education	Initial		
	TB Skin Test	Initial		
	IGRA Test	Initial		
	Td or TDAP	Initial		
	Measles Titer	Initial	Every 10 years	
	2 Doses of Measles Vaccine	Initial		Requires positive measles titer or documentation of two MMR vaccinations
	Mumps	Initial		Requires positive measles titer or documentation of two MMR vaccinations
	Rubella	Initial		Requires positive mumps titer or documentation of two MMR vaccinations Requires positive rubella titer or documentation of two MMR vaccinations
	Varicella	Initial		Requires positive varicella titer or documentation of two varicella vaccinations
	2 Doses Varicella Vaccine	Initial		Requires positive varicella titer or documentation of two varicella vaccinations
	Influenza Vaccine	Initial		Vaccine recommended but not required
	Hepatitis B Vaccination	Initial		Requires written documentation of having had 3 doses (dates must include month/day/year and be signed by healthcare provider) of this vaccination
	Hepatitis B Vaccination Declination	Initial		If not accepting the Hepatitis B vaccine, read the Centers for Disease Control and Prevention's Vaccine Information Statement and sign a Hepatitis B vaccination declination

	Hepatitis B Quantitative Titer OSHA Respirator Questionnaire	Initial Initial		form Obtain, once written documentation of 3 Hepatitis B vaccinations has been obtained If there is a change in your medical status or condition (including significant weight gain, weight loss, or change in facial configuration) that may affect your ability to use a respirator or a change in your work environment that may result in a substantial increase in physiological burden, please reach out to ROHP for reevaluation
Influenza Virus Work	Influenza Vaccine	Initial	Annual	Vaccine recommended but not required
MRI Work Space	MRI Screening Form	Initial	Annual	
Mycobacterium tuberculosis Work	Tuberculosis Screening and Education TB Skin Test IGRA Test	Initial Initial Initial	Annual Bi-annual Bi-Annual	
Non-human Primate Access	Job Risk Assessment Questionnaire Health Questionnaire Tuberculosis Screening and Education TB Skin Test IGRA Test Influenza Vaccine Measles Titer 2 Doses of Measles Vaccine	Initial Initial Initial Initial Initial Initial Initial Initial	Annual Annual Annual Annual Annual Annual	Vaccine recommended but not required Requires positive measles titer or documentation of two MMR vaccinations Requires positive measles titer or documentation of two MMR vaccinations
Neisseria meningitidis Work	Meningococcal vaccine	Initial		Offered appropriate meningococcal ACWY or B vaccination as appropriate
Reproductive Counseling	Reproductive Counseling			Provided if requested on Health Questionnaire submitted annually or if office contacted directly for counseling request
Streptococcal pneumoniae	Pneumococcal Vaccine Pneumococcal Vaccine Declination	Initial Initial		Offer vaccination or have signed declination on file Offer vaccination or have signed declination on file
Toxoplasma or work with cats	Toxoplasma Titer	Initial	Annual	If no history of positive titer, working with toxoplasma or cats
Vaccinia virus work	Vaccinia Vaccine Vaccinia Vaccine Declination	Initial Initial		
Yellow Fever Virus Work	Yellow Fever Vaccine	Initial	10-year booster	Should be completed 10-14 days before potential exposure to YF virus

	Yellow Fever Vaccine Declination	Initial		
Japanese Encephalitis Work	Japanese Encephalitis Vaccine Japanese Encephalitis Vaccine Declination	Initial Initial		Two doses administered on day 0 and day 7-28 and booster in greater than or equal to 1 year (2 dose series should be completed at least 1 week before potential exposure to JE virus) If older than 65 years old two doses administered on day 0 and 28 and booster in greater than or equal to 1 year
Rabies Virus Work	Rabies Titer Rabies Vaccine	Initial Initial	Annual	Titer screening or vaccination offered as appropriate Offered if negative Rabies titer
Work with Bats	Rabies Titer Rabies Vaccine	Initial	Every 2 years	Titer screening or vaccination offered as appropriate Offered if negative Rabies titer
Polio Virus Work	Polio Titer Polio Vaccine	Initial Initial		Titer screening prior to working with virus and vaccination offered as appropriate
Complete Freund's Adjuvent	Tuberculosis Screening and Education TB Skin Test IGRA Test	Initial Initial Initial		Baseline Tuberculosis Screening and Education prior to work with CFA Baseline TB Skin Test prior to work with CFA Baseline IGRA Test prior to work with CFA
SARS-CoV-2 virus work	Covid Vaccine	Initial		Encouraged if working with the virus
Diphtheria toxin work	Td or TDAP Vaccine	Initial	Every 10 years	Encouraged if working with the toxin
Ebola Virus Work	Ebola Vaccine Ebola Vaccine Declination	Initial Initial		
Scientific diving	Job Risk Assessment Questionnaire Health Questionnaire	Initial Initial	Annual Annual	Completed by researcher
Facilities Mechanics accessing Animal Science Center	Job Risk Assessment Questionnaire Health Questionnaire TB Skin Test IGRA Test Tuberculosis Screening and Education Influenza Vaccine Measles Titer 2 Doses of Measles Vaccine	Initial Initial Initial Initial Initial Initial Initial Initial	Annual Annual Annual Annual	Vaccine recommended but not required Requires positive measles titer or documentation of two MMR vaccinations Requires positive measles titer or documentation of two MMR vaccinations

NEIDL Public Safety	Job Risk Assessment Questionnaire	Initial	Annual	
	Health Questionnaire	Initial	Annual	
	Mental/Behavioral Health	Initial	Annual	
	Urine Drug Screen	Initial	Random	
	Ishihara Screen	Initial		
	Health Questionnaire	Initial	Annual	
	PHQ-9 Questionnaire	Initial	Annual	
	GAD-7 Questionnaire	Initial	Annual	
	Significant Life Changes and Stressors Checklist	Initial	Annual	
	AUDIT	Initial	Annual	
	Physical Exam	Initial		
	Cardiovascular Risk Assessment	Initial		
	Health Intake Form	Initial		
	Urinalysis	Initial		
	Measles Titer	Initial		
	2 Doses of Measles Vaccine	Initial		Requires positive measles titer or documentation of two MMR vaccinations
	Tuberculosis Screening and Education	Initial		Requires positive measles titer or documentation of two MMR vaccinations
	TB Skin Test	Initial	Annual	
	IGRA Test	Initial		
	EKG	Initial		
	Spirometry	Initial		
	Audiometry	Initial		
	Functional Capacity Exam	Initial		
	Urinalysis	Initial		
	Snellen	Initial		
	OSHA Respirator Questionnaire	Initial		
		Initial		If there is a change in your medical status or condition (including significant weight gain, weight loss, or change in facial configuration) that may affect your ability to use a respirator or a change in your work environment that may result in a substantial increase in physiological burden, please reach out to ROHP for reevaluation
	CBC with diff	Initial		
	Comprehensive Metabolic Panel	Initial		
	Td or TDAP	Initial		
	Mumps	Initial		
		Initial	Every 10 years	

	Rubella	Initial		Requires positive mumps titer or documentation of two MMR vaccinations
	Hepatitis B Vaccination	Initial		Requires positive rubella titer or documentation of two MMR vaccinations
	Hepatitis B Vaccination Declination	Initial		Requires written documentation of having had 3 doses (dates must include month/day/year and be signed by healthcare provider) of this vaccination If not accepting the Hepatitis B vaccine, read the Centers for Disease Control and Prevention's Vaccine Information Statement and sign a Hepatitis B vaccination declination form
	Hepatitis B Quantitative Titer	Initial		Obtain, once written documentation of 3 Hepatitis B vaccinations has been obtained
	Varicella Titer	Initial		Requires positive varicella titer or documentation of two varicella vaccinations
	2 Doses of Varicella Vaccine	Initial		Requires positive varicella titer or documentation of two varicella vaccinations
	Influenza Vaccine	Initial		Vaccine recommended but not required
	Vital Signs	Initial		
	Height and Weight	Initial		
	External Chandler Psychological Exam			
NEIDL IT	Job Risk Assessment Questionnaire	Initial	Annual	
	Health Questionnaire	Initial	Annual	
	Mental/Behavioral Health	Initial	Annual	
	PHQ-9 Questionnaire	Initial	Annual	
	GAD-7 Questionnaire	Initial	Annual	
	AUDIT	Initial	Annual	
	Significant Life Changes and Stressors Checklist	Initial	Annual	
	Measles Titer	Initial		
	2 Doses of Measles Vaccine	Initial		Requires positive measles titer or documentation of two MMR vaccinations
	Ishihara	Initial		Requires positive measles titer or documentation of two MMR vaccinations
	Influenza Vaccine	Initial	Annual	Vaccine recommended but not required
	Tuberculosis Screening and Education	Initial	Annual	
	TB Skin Test	Initial		
	IGRA Test	Initial		
EHS	Job Risk Assessment Questionnaire	Initial	Annual	
	Health Questionnaire	Initial	Annual	

	Mental/Behavioral Health	Initial	Annual	
	PHQ-9 Questionnaire	Initial	Annual	
	GAD-7 Questionnaire	Initial	Annual	
	AUDIT	Initial	Annual	
	Significant Life Changes and Stressors Checklist	Initial	Annual	
	OSHA Respirator Questionnaire	Initial		
				If there is a change in your medical status or condition (including significant weight gain, weight loss, or change in facial configuration) that may affect your ability to use a respirator or a change in your work environment that may result in a substantial increase in physiological burden, please reach out to ROHP for reevaluation
	Tuberculosis Screening and Education	Initial	Annual	
	TB Skin Test	Initial		
	IGRA Test	Initial		
	Hepatitis B Vaccination	Initial		
				Requires written documentation of having had 3 doses (dates must include month/day/year and be signed by healthcare provider) of this vaccination
	Hepatitis B Vaccination Declination	Initial		If not accepting the Hepatitis B vaccine, read the Centers for Disease Control and Prevention's Vaccine Information Statement and sign a Hepatitis B vaccination declination form
	Hepatitis B Quantitative Titer	Initial		Obtain, once written documentation of 3 Hepatitis B vaccinations has been obtained
	Measles Titer	Initial		Requires positive measles titer or documentation of two MMR vaccinations
	2 Doses Measles Vaccine	Initial		Requires positive measles titer or documentation of two MMR vaccinations
	Mumps	Initial		Requires positive mumps titer or documentation of two MMR vaccinations
	Ishihara	Initial		
	Rubella	Initial		Requires positive rubella titer or documentation of two MMR vaccinations
	Varicella Titer	Initial		Requires positive varicella titer or documentation of two varicella vaccinations
	2 Doses Varicella Vaccine	Initial		Requires positive varicella titer or documentation of two varicella vaccinations

	Influenza Vaccine	Initial		Vaccine recommended but not required
NEIDL Facilities	Job Risk Assessment Questionnaire	Initial	Annual	
	Health Questionnaire	Initial	Annual	
	Mental/Behavioral Health	Initial	Annual	
	Health Intake Form	Initial		
	PHQ-9 Questionnaire	Initial	Annual	
	GAD-7 Questionnaire	Initial	Annual	
	AUDIT	Initial	Annual	
	Significant Life Changes and Stressor Checklist	Initial	Annual	
	Physical Exam	Initial		
	Ishihara	Initial		
	Urine Drug Screen	Initial	Random	
	CBC with diff	Initial		
	Comprehensive Metabolic Panel	Initial		
	Urinalysis	Initial		
	Measles Titer	Initial		
	2 Doses Measles Vaccine	Initial		Requires positive measles titer or documentation of two MMR vaccinations
	Hepatitis B Vaccination	Initial		Requires positive measles titer or documentation of two MMR vaccinations
	Hepatitis B Vaccination Declination	Initial		Requires written documentation of having had 3 doses (dates must include month/day/year and be signed by healthcare provider) of this vaccination
	Hepatitis B Quantitative Titer	Initial		If not accepting the Hepatitis B vaccine, read the Centers for Disease Control and Prevention's Vaccine Information Statement and sign a Hepatitis B vaccination declination form
	Tuberculosis Screening and Education	Initial		Obtain, once written documentation of 3 Hepatitis B vaccinations has been obtained
	TB Skin Test	Initial	Annual	
	IGRA Test	Initial		
	Td or TDAP	Initial		
	Influenza Vaccine	Initial		
	Vital Signs	Initial	Every 10 years	
	Height and Weight	Initial	Annual	
	EKG	Initial		Vaccine recommended but not required
	Spirometry	Initial		
	Audiometry	Initial		

	Snellen Functional Capacity Exam	Initial Initial		

WORK GROUPS AND HAZARDS		EXPOSURE TYPES	Initial Health Questionnaire	Respirator Questionnaire	Physical Exam or Assessment	Functional Capacity Exam	EKG	Spirometry	Audiometry	Vision Exam	CBC with differential	Comprehensive Metabolic Panel	Urine Dip Stick	Mental Health Screen	Drug Screen
ANIMAL CARE															
LASC and LACF STAFF	ANIMALS	Rats, mice, hamsters and rodents	✓	Y		F								NDL	NDL
		Bats	✓	Y		F								NDL	NDL
		Non-human primates	✓	Y		F								NDL	NDL
		Cats, pigs, rabbits	✓	Y		F								NDL	NDL
		Chickens, ferrets	✓	Y		F								NDL	NDL
		Fish, birds, fruit flies	✓	Y		F								NDL	NDL

	AGENTS	**Any work involving F. tularensis, S. pneumoniae, M. Tb, Hep B, or Yellow Fever**	✓	**Y**										**NDL**	**NDL**
Animal Care Technicians		**Works with all species**	✓	**Y**		**F**			**✓LASC**						
IACUC		**Works with all species**	✓	**Y**					**✓LASC**						
LABORATORY RESEARCH															
Minimum Surveillance by BSL		**Work with non-specific hazards in a BSL 1 laboratory**	✓												
		Work with non-specific hazards in a BSL 2 laboratory	✓											**NDL**	**NDL**
		Work with non-specific hazards in a BSL 3 laboratory	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	**NDL**	**NDL**
RESEARCHERS WORKING WITH SPECIFIC HAZARDS															
ANIMALS		**Rats, mice,**	✓	**Y**											

	hamsters, or rodents													
	Bats	✓	**Y**											
	Non-human primates	✓	**Y**											
	Cats, pigs, rabbits	✓	**Y**											
	Chickens, ferrets	✓	**Y**											
	Fish, birds, fruit flies	✓	**Y**											
LASER	**Work with Class 3b or 4 lasers**	✓							**V**					
PATIENT CARE	**Work involves patient contact**	✓												
HUMAN MATERIAL	**Works with human blood, fluid, cells, and tissues**	✓												
SPECIFIC HAZARDOUS MATERIALS	**Works with F. tularensis**	✓	**Y**											
	Works with Hepatitis B	✓												
	Works with Influenza	✓												

	Works with J. encephalitis	✓												
	Works with M. tuberculosis	✓	**Y**											
	Works with N. meningitidis	✓												
	Works with Polio virus	✓												
	Works with Rabies virus	✓												
	Works with S. pneumoniae	✓												
	Works with Vaccinia	✓												
	Works with Yellow Fever	✓												
RESEARCH SUPPORT														
EHS[1]	**All Areas**	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	**NDL**	**NDL**
PUBLIC SAFETY	**POLICE**	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	**10p**
	Medical Campus	✓	✓	✓										

	NEIDL	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	**6p**
ADMIN[2]	**All Areas**	✓											**NDL**	**NDL**
FACILITIES & OPERATIONS[3]	**Charles River Campus**	✓												
	Medical Campus	✓												
	NEIDL Limited Access	✓											✓	**6p**
	NEIDL BSL 2 Access	✓											✓	**6p**
	NEIDL Full Access	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	**6p**

✓	Required
6P	6 panel drug screen required
10P	10 panel drug screen required
A	Annual Tb Screen
B	Bi-Annual Tb Screen
C	Recommended for females of child-bearing age working with Cats
F	Optional based on job requirements and medical history
M	Measles only
NDL	Mandatory for access to the NEIDL
r	Recommended
sr	Strongly recommended
T	Tdap initially, Tetanus required every 10 years
V	Voluntary vision exam program for Class 3b or 4 laser users
Y	Mandatory for jobs requiring respirator rated N95 and above
1	EHS personnel trained and cleared to provide Emergency Response

2 Includes admin for RC, NEIDL, EHS, LASC/LACF, and Research
3 Includes facilities, IT, Telecom, and housekeeping

TABLE 2. COMPONENTS OF THE PERIODIC HEALTH EVALUATION.

WORK GROUPS AND HAZARDS		EXPOSURE TYPES	Annual Health Questionnaire	Annual Respirator Questionnaire	TB Surveillance	Annual Influenza	* Annual Rabies Test	Annual Hearing Conservation	Annual Mental Health Screen	Annual Drug Screen
ANIMAL CARE										
LASC and LACF STAFF	ANIMALS	Rats, mice, hamsters and rodents	✓	Y		r				
		Bats	✓	Y		r	✓			
		Non-human primates	✓	Y	✓B	sr				
		Cats, pigs, rabbits	✓	Y		r				
		Chickens, ferrets	✓	Y		r				
		Fish, birds, fruit flies	✓	Y		r				
	AGENTS	Works with any species involved with F. tularensis, S. pneumoniae, M. Tb, Hep B, or Yellow Fever	✓	Y	✓B	sr				

Animal Care Technicians	**Works with all species**	✓	**Y**	**✓B**	**sr**		**✓LASC**		
IACUC	**Works with all species**	✓	**Y**	**✓A**	**r**				
LABORATORY RESEARCH									
Minimum Surveillance by BSL	**Work with non-specific hazards in a BSL 1 laboratory**	✓			**r**				
	Work with non-specific hazards in a BSL 2 laboratory	✓			**r**				
	Work with non-specific hazards in a BSL 3 laboratory	✓	✓		**sr**				
RESEARCHERS WORKING WITH SPECIFIC HAZARDS									
ANIMALS	**Rats, mice, hamsters, or rodents**	✓	✓						
	Bats	✓	✓			✓			
	Non-human primates	✓	✓	**✓B**					
	Cats, pigs, rabbits	✓	✓						
	Chickens, ferrets	✓	✓						
	Fish, birds, fruit flies	✓	✓						
LASER	**Work with Class 3b or 4 lasers**	✓			**r**				
PATIENT CARE	**Work involves patient contact**	✓		**✓A**	**r**				

HUMAN MAT'L	**Works with human blood, fluid, cells, and tissues**	✓			r				
SPECIFIC HAZARDOUS MATERIALS	**Works with F. tularensis**	✓	Y						
	Works with Hepatitis B	✓							
	Works with Influenza	✓	Y		✓				
	Works with J. encephalitis	✓							
	Works with M. tuberculosis	✓	Y	✓B					
	Works with N. meningitidis	✓	Y						
	Works with Polio virus	✓							
	Works with Rabies virus	✓				✓			
	Works with S. pneumoniae	✓	Y						
	Works with Vaccinia	✓							
	Works with Yellow Fever	✓	Y						
RESEARCH SUPPORT									
EHS[1]	**All Areas**	✓	✓	✓A	sr			**NDL**	**NDL**
PUBLIC SAFETY	**POLICE**				r				

	Medical Campus			**✓A**	**r**				
	NEIDL	**✓**	**✓**	**✓A**	**r**			**✓**	**6p**
ADMIN[2]	**All Areas**	**✓**			**r**			**NDL**	**NDL**
FACILITIES & OPERATIONS[3]	**Charles River Campus**	**✓**			**r**				
	Medical Campus	**✓**		**✓A**	**r**				
	NEIDL Limited Access	**✓**			**r**			**✓**	**6p**
	NEIDL BSL 2 Access	**✓**		**✓A**	**r**			**✓**	**6p**
	NEIDL Full Access	**✓**	**✓**	**✓A**	**sr**			**✓**	**6p**

✓	Required
6P	6 panel drug screen required
10P	10 panel drug screen required
A	Annual Tb Screen
B	Bi-Annual Tb Screen
C	Recommended for females of child-bearing age working with Cats
F	Optional based on job requirements and medical history
M	Measles only
NDL	Mandatory for access to the NEIDL
r	Recommended
sr	Strongly recommended
T	Tdap initially, Tetanus required every 10 years
V	Voluntary vision exam program for Class 3b or 4 laser users
Y	Mandatory for jobs requiring respirator rated N95 and above
1	EHS personnel trained and cleared to provide Emergency Response
2	Includes admin for ORC, NEIDL, EHS, LASC/LACF, and Research
3	Includes facilities, IT, Telecom, and housekeeping
*****	Written declination required

TABLE 3. SPECIAL IMMUNIZATIONS OR SURVEILLANCE

WORK GROUPS AND HAZARDS	EXPOSURE TYPES	* Anthrax	* Hepatitis B	Influenza	* Japanese Encephalitis	* Measles, Mumps,	* Meningococcal	* Pneumococcal	* Polio	* Rabies Series (3)	Tetanus or Tdap	Toxoplasmosis	Tuberculosis	* Tularemia	* Vaccinia	* Yellow Fever
ANIMAL CARE																
LASC and LACF STAFF	ANIMALS	Rats, mice, hamsters and rodents			r							✓T					
		Bats			r						✓	✓T					
		Non-human primates			sr		✓M					✓T		✓			
		Cats, pigs, rabbits			r							✓T	C				
		Chickens, ferrets			r							✓T					
		Fish, birds, fruit flies			r							✓T					

	AGENTS	**Works with any species involved with F. tularensis, S. pneumoniae, M. Tb, Hep B, or Yellow Fever**		✓	**sr**				✓		✓	**✓T**		✓	✓	✓	✓
Animal Care Technicians		**Works with all species**			**sr**		**✓M**					**✓T**	**C**	✓			
IACUC		**Works with all species**			**r**		**✓M**					**✓T**		✓			
LABORATORY RESEARCH																	
Minimum Surveillance by BSL		**Work with non-specific hazards in a BSL 1 lab**			**r**							**✓T**					
		Work with non-specific hazards in a BSL 2 lab			**r**							**✓T**					
		Work with non-specific			**sr**							**✓T**					

	hazards in a BSL 3 lab															
RESEARCHERS WORKING WITH SPECIFIC HAZARDS																
ANIMALS	**Rats, mice, hamsters, or rodents**															
	Bats									✓						
	Non-human primates					✓M							✓			
	Cats, pigs, rabbits											C				
	Chickens, ferrets															
	Fish, birds, fruit flies															
LASER	**Work with Class 3b or 4 lasers**			r									✓			
PATIENT CARE	**Work involves patient contact**		✓	r		✓							✓			
HUMAN MATERIAL	**Works with human blood, fluid, cells, and tissues**		✓	r												

SPECIFIC HAZARDOUS MATERIALS	**Works with F. tularensis**													✓		
	Works with Hepatitis B		✓													
	Works with Influenza			✓												
	Works with J. encephalitis				✓											
	Works with M. tuberculosis												✓			
	Works with N. meningitidis						✓									
	Works with Polio virus								✓							
	Works with Rabies virus									✓						
	Works with S. pneumoniae							✓								
	Works with Vaccinia														✓	

	Works with Yellow Fever															✓
RESEARCH SUPPORT																
EHS[1]	**All Areas**		✓	sr		✓					✓T		✓			
PUBLIC SAFETY	**POLICE**		✓	r		✓					✓T		✓			
	Medical Campus		✓	r		✓					✓T		✓			
	NEIDL		✓	r		✓					✓T		✓			
ADMIN[2]	**All Areas**			r												
FACILITIES & OPERATIONS[3]	**Charles River Campus**		✓	r							✓T					
	Medical Campus		✓	r		✓					✓T		✓			
	NEIDL Limited Access			r		✓										
	NEIDL BSL 2 Access		✓	r		✓					✓T		✓			
	NEIDL Full Access		✓	sr		✓					✓T		✓			

✓ Required

6P 6 panel drug screen required

10P 10 panel drug screen required

A	Annual Tb Screen

B Bi-Annual Tb Screen

C Recommended for females of child-bearing age working with Cats

F	Optional based on job requirements and medical history
M	Measles only
NDL	Mandatory for access to the NEIDL
r	Recommended
sr	Strongly recommended
T	Tdap initially, Tetanus required every 10 years
V	Voluntary vision exam program for Class 3b or 4 laser users
Y	Mandatory for jobs requiring respirator rated N95 and above
1	EHS personnel trained and cleared to provide Emergency Response
2	Includes admin for ORC, NEIDL, EHS, LASC/LACF, and Research
3	Includes facilities, IT, Telecom, and housekeeping
*****	Written declination required

Appendix Q
Laboratory and Equipment Decontamination Procedures

Decontamination of Lab Space and Equipment Punch List

1. Assigning a designate a Move Coordinator. The coordinator will work with EHS and other stakeholders to facilitate and coordinate the move.

2. Contact an outside vendor for the decontamination of biological safety cabinets (tissue culture hoods).

3. Have appropriate personal protective equipment available (lab coat, gloves, eye protection).

4. Dispose of old chemicals and all other chemical waste as hazardous waste. Notify the Environmental Manager at (617) 358-7840 at BUMC or (617) 353-4094 at CRC upon termination of a hazardous waste accumulation area or with any questions on this issue.

5. Decontaminate all equipment that is either to be moved or left behind.

6. Contact EHS regarding the discarding of equipment.

7. On the decontamination certificate, list all decontaminated equipment by room (one sheet per room).

8. Small pieces of equipment can be deconned and boxed by lab personnel.

9. Any working equipment to be left behind without a new owner must be reported to Facilities Management and EHS.

10. Contact the Radiation Safety for the guidance on decontamination and moving of radiological materials and work spaces.

11. Decontaminate all labs, including fume hoods, the outside of tissue culture hoods, cold/warm rooms, darkrooms, etc.

12. If perchloric acid was used in a fume hood contact EHS at (617) 358-7840 at BUMC or (617) 353-4094 at CRC. This will require a special procedure.

13. Fill out one decontamination sheet for each room, tape one copy to the outside of the lab door (if it is a section of a lab, tape to bench), sendone copy to the Biosafety Office, and keep one copy for the records.

14. Disinfectants: the most common are 10% freshly diluted bleach (leave on for 20-30 minutes, then wash off), 70% ethanol, or isopropanol. Phenolic agents are not recommended.

15. If refrigerators, freezers, incubators, etc., are to be moved with content inside, make sure the content is well protected from sliding, breaking, etc.

16. The Move Coordinator must ensure the following emergency procedures are covered:
    - Chemical spills
    - Biological spills
    - Fire
    - Personal injuries, such as slips, falls, cuts, etc.

17. Protective clothing and spill absorbent materials must be on hand.

18. Follow and complete the Laboratory or Equipment Decontamination certification form. EHS will inspect the laboratory space or equipment to ensure they have been appropriate cleaned and decontaminated.

19. EHS will affix a decontamination sticker on equipment that had been properly cleaned and disinfected. The equipment will be moved out within 15 days that the sticker is issued. The equipment will not be moved if the 15 days issuance lapses. EHS will inspect the equipment again and issue a new sticker.

20. Biohazard sticker will be removed once the equipment has been properly decontaminated.

The Environmental Health and Safety Laboratory or Equipment Decontamination Certification form can be found here.

Appendix R
Laboratory Decommissioning and Relocation Procedures

Purpose and Applicability

It is the policy of Boston University that laboratory decommissioning take place prior to the relocation of any laboratory space or upon vacating laboratory space or leaving either institution. In addition, safe-moving practices must be adhered to at all times.

This policy is intended to minimize research and clinical lab downtime due to moving of a laboratory, and to protect contractors, laboratory personnel, and any other personnel involved in the process from laboratory hazards.

This policy applies to all Boston University employees and tenants occupying laboratory space within Boston University buildings.

Definitions

Abandoned Laboratory: A clinical or research laboratory that is left vacant by a Principal Investigator or Laboratory Director and his or her laboratory staff, and has laboratory materials (biological, surplus chemical, radioactive), equipment or waste that has not been disposed of.

Biological Materials: All human, plant, and animal pathogens; all human blood, blood components and products, tissues and body fluids; all human and animal cultured cells; all infected animals and animal tissues; all cultures/stocks of biological agents, including recombinant DNA materials; and all biological toxins. Also includes biomedical waste and physically dangerous (sharp) waste.

Decommissioning: The process whereby a Principal Investigator or Laboratory Director and his or her laboratory staff decontaminate existing laboratory space and make a clinical or research laboratory safe prior to vacating the space.

Decontamination: The process whereby the Principal Investigator or Laboratory Director and his or her laboratory staff clean and disinfect laboratory surfaces and equipment so they are safe to handle.

Roles and Responsibilities

The Principal Investigator or Laboratory Director is responsible for the complete decommissioning of the laboratory space prior to vacating the laboratory. In cases where an abandoned lab is identified, the department that the PI or Laboratory Supervisor reported to will be responsible for the decommissioning and all costs associated with the process.

EHS will distribute this policy and attachments and advise Principal Investigators, Laboratory Directors, and laboratory personnel on how to implement the various aspects of the policy. They will also verify that a lab has been appropriately decommissioned before a Principal Investigator or Laboratory Director may leave or move his or her laboratory.

The Move Coordinator for the laboratory is appointed by the Principal Investigator or Laboratory Director and is responsible for coordinating the laboratory decommissioning and move. The Move Coordinator is the primary contact with EHS.

Other personnel (Facilities, moving personnel, and contractors) should be aware of this policy and should not handle laboratory materials, equipment, or waste unless instructed to do so by their supervisor and/or EHS.

Procedures: Preparation

Prior planning is key to a successful laboratory decommissioning and move. Preparation and communication with EHS will be a major factor in minimizing delays, protecting property against damage and loss, and most importantly, reducing the potential for personal injury. Contact EHS at (617) 358-7840 with any questions or for assistance.

Procedures: Waste Disposal

All biological waste and hazardous waste must be disposed of according to current EHS policies and procedures as outlined in the EHS *Policy Manual*. All radioactive waste must be disposed of according to Radiation Safety policies and procedures. Boxes and trash must not be left in corridors. Prior arrangements for regular trash must be made with Custodial or Environmental Services.

Chemical waste must be labeled with hazardous waste stickers regardless of whether or not they are labeled from the manufacturer.

Unwanted, unopened, or uncontaminated chemicals should be offered to other labs that may be able to use them before the chemicals are considered for disposal.

Any unknown chemical must be identified and labeled as hazardous waste. For chemical unknowns that cannot be identified by the Principal Investigator, Laboratory Director or laboratory personnel, the laboratory may be assessed a service fee for hazardous waste analysis prior to disposal.

Darkroom tanks must be drained and the contents disposed of as hazardous waste. Empty compressed gas tanks must be returned to the distributor prior to the move. Mercury thermometers must be disposed of as hazardous waste, and vacuum pumps must be drained of oil and the oil disposed of as hazardous waste.

Procedures: Decontamination

All laboratory bench-top surfaces must be decontaminated prior to vacating the laboratory, and all laboratory equipment that is either remaining in the laboratory or being moved to a new laboratory must be decontaminated if potentially contaminated with biological, chemical, or radioactive materials.

Lab equipment requiring decontamination includes, but is not limited to, animal cages, centrifuges, fermenters, fish tanks, incubators, water baths, refrigerators, and freezers (if not moving intact).

Fume hoods must be decontaminated. Contact the Industrial Hygienist at (617) 358-7840 for decontamination and certification advice. Notify the Industrial Hygienist if there is any current or past practices that may reveal potential problems. Certain chemicals such as perchloric acid and mercury may remain on surfaces or equipment or in building systems.

Biological safety cabinets and glove boxes that have been used with potentially infectious materials must be decontaminated using paraformaldehyde gas before moving. This must be done by a qualified outside contractor. If BSCs are either being moved to new laboratory areas or being left behind, contact the Biological Safety Officer at (617) 638-8830 to discuss decontamination well in advance of the move. BSCs that are moved must be re-certified after installation. Contact B&V Testing at (781) 891-9081 to arrange for re-certification.

An appropriate disinfectant must be utilized in cases where biological materials were in use. A disinfectant is deemed appropriate if it targets the biological materials that were in use in the laboratory. In most cases, 70% alcohol, bleach solution (1:10 made fresh), or a phenolic disinfectant should be adequate for disinfection of lab furniture and equipment potentially contaminated with biological materials. Call the Biological Safety Officer at (617) 358-7840 with questions or concerns.

A *BU Equipment Decontamination Record* sticker must be affixed to all equipment that has been decontaminated. This will allow moving personnel to safely move the equipment to the new laboratory space. Only equipment with this sticker will be moved. Stickers may be obtained from EHS at (617) 358-7840.

The Principal Investigator or Laboratory Director must complete the "Laboratory Decontamination Certification Form" and submit the form to EHS (M-470) when decontamination and decommissioning activities are completed. This will allow EHS personnel to review the decommissioning activities, visit the decommissioned laboratory, and alert the appropriate administrative personnel that the decommissioning has been performed. Upon receipt of the completed form, EHS will contact the Principal Investigator or Laboratory Director to schedule a tour of the laboratory to confirm the decommissioning activities.

For more information regarding proper disinfection or decontamination procedures, contact EHS at (617) 358-7840 or the Radiation Safety at (617) 358-7688.

Procedures: Designation of New Laboratory Space

The Principal Investigator or Laboratory Director must inform EHS of any new laboratory space, so that the appropriate safety signage may be provided.

The Principal Investigator is responsible for notifying all applicable Boston University research committees and outside agencies, as necessary, of the move to new laboratory space. Research projects approved by the IBC must have updated laboratory location information. USDA Veterinary Service or Plant Service permits are laboratory site specific, as are CDC Select Agent registration permits. Contact the Biological Safety Officer at (617) 358-7840 for assistance.

Procedures: Packing and Moving Laboratory Materials

Laboratory personnel are responsible for collecting all packaging items needed before the move date. Carts, plastic bags, toweling, or other cushioning, absorbent materials, sealable plastic or plastic-lined boxes, labels (e.g. Fragile, Universal Biohazard, ID, Location, Caution, Radioactive Material), sturdy tape, and spill kits should be readily accessible. Each container or piece of equipment must be labeled. Labels must identify the agent, hazard, and necessary precautions.

The Principal Investigator or Laboratory Director is responsible for establishing safety and emergency procedures for all phases of the move. Potential emergencies include material spills, fires, slips and falls, and cuts. Protective clothing and spill absorbent materials must be available during packing, moving, and unpacking.

Procedures: Packing and Moving Laboratory Chemicals

In order to minimize the amount of chemicals that need to be packed and moved, new chemicals should be ordered only as necessary and in small quantities. Laboratory personnel should plan in advance to minimize the inventory of liquid volume and weight of materials being moved. In addition, reduction of active materials should be planned the week prior to the move. Laboratory chemicals must be packed and moved by an outside contractor approved by EHS. Prior to the packing and moving, laboratory personnel are responsible for labeling each chemical container with the chemical identity.

Compressed gas tanks that are to be moved must have regulators removed and caps secured prior to moving. If possible, have old tanks collected prior to a move and arrange for future tanks to be delivered to the new location.

Thermometers must be removed from refrigerators, water baths, and incubators prior to equipment moving.

Vacuum pump oil must be drained from pumps prior to equipment moving.

Procedures: Packing and Moving Biological Materials

Biological materials must be appropriately packed and moved by the laboratory personnel. Regulated materials and biological materials include all human, plant, and animal pathogens; all human blood, blood components and products, tissues and body fluids; all human and animal cultured cells; all animal carcasses and unfixed animal tissues; all cultures/stocks of biological agents including recombinant DNA materials; and all biological toxins.

Proper packaging consists of a primary sealed container placed within a secondary sealed, unbreakable container, with enough absorbent material in between to contain and absorb any spill. ***Some examples of proper packaging include*** petri dishes in a plastic sleeve within a plastic-lined box using paper towel spacers; stabs in a sealed Tupperware container with paper towels to cushion vials; sealed tubes in a rack placed into plastic sealable container with enough paper towels to absorb any spilled contents; tissue culture dishes placed into a plastic-lined dishpan or a sealable cardboard box with an absorbent. Freezers can be moved intact, provided all contents are in sealed, unbreakable containers and the freezer remains closed. Because shifting of contents may occur, enclose loose items in boxes, or fix in some other way to

avoid breakage and spills when the freezer is reopened. Other equipment, such as fermenters, refrigerators, incubators, and biological safety cabinets must be empty and decontaminated prior to the move.

Labeling: Once packaged, all biological materials must be properly labeled. ***Labels must include*** the name, Principal Investigator (PI), new location, ID of agent, biosafety level, telephone number for assistance in the event of any breakage, and a FRAGILE notice if applicable. Also the **universal biohazard label** should be used whenever packaging a BSL2 or higher agent. Questions concerning the biosafety level of biological materials or requests for biohazard labels should be directed to the Biosafety Safety Officer at (617) 358-7840.

Procedures: Laboratory Furniture and Equipment

Furniture: The Move Coordinator must be informed if there is any furniture of particular concern (fragile, valuable, requires dismantling) not already mentioned. Different moving companies may have different requirements that should be ascertained in advance of the move.

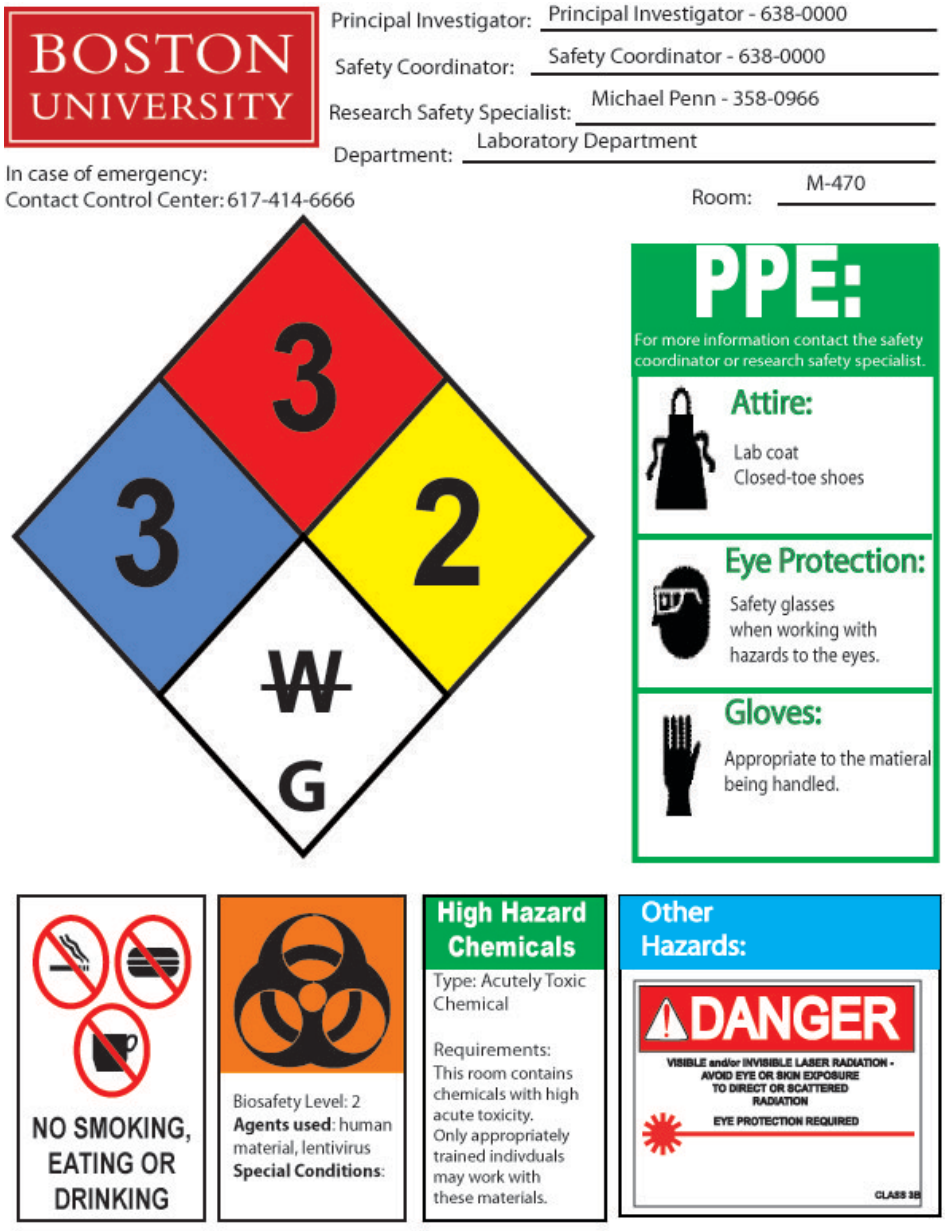
Special Requirements: The Move Coordinator must be informed in advance of any equipment under service contract, as well as equipment not under contract but requiring servicing and/or special handling.

Alarms: Laboratory personnel must disconnect alarms on freezers (if moving intact) and any other sensor alarms on or before the day of the move.

Keys and Combinations: Laboratory personnel must keep keys and combinations to locks readily accessible.

Appendix S
Laboratory Door Signage

Boston University Door Sign Sample: This is completed in accordance with the NFPA 704 Hazard Identification ratings system (the NFPA "hazard diamond") for health, flammability, and instability



Appendix T
Boston University Research Compliance Policy on Disease Surveillance and Reporting for High-Risk Agents

Purpose and Applicability

This policy implements BPHC's *Guidelines for Implementation and Enforcement of Boston Public Health Commission's Disease Surveillance and Reporting Regulation.* The BPHC's guidelines require laboratory registration and a medical surveillance program for research laboratories working with high-risk agents. The guidelines are designed to ensure that BPHC receives timely access to information regarding incidence of disease syndromes, any outbreak or cluster of a disease, and potential exposures to reportable diseases deemed harmful to the public health.

This policy sets forth the roles and responsibilities of researchers and compliance staff, as mandated by the BPHC guidelines.

This policy supplements, but does not replace or supersede, any other existing BU policies or procedures. For example, additional procedures relating to laboratory safety are set forth by EHS in the *EHS Manual*, aand other subsidiary EHS documents.

Definitions

The **Associate Vice President, Research Compliance** (AVPRC) is the individual responsible for overall research compliance oversight at BU.

The **Biological Safety Officer** is the individual responsible for overall leadership of the biosafety program.

Expose or Exposure is any situation arising from, or related to, the work operation where an employee or community resident may ingest, inhale, absorb through the skin or eyes, or otherwise come into contact with any high-risk agent.

EHS Director is the Director of Research Safety in the EHS of Boston University.

Occupational Health Officer (OHO) is the physician(s) who is the Occupational Health Officer of ROHP at Boston University. The Occupational Health Officer may also name a designee to perform occupational health assessments or evaluations, provided that the designee is also a licensed physician experienced in occupational medicine or a registered nurse experienced in occupational health nursing.

High–Risk Agent is a select agent, defined as:

- Agents in Risk Group (RG) 4 as specified in the National Institute of Health's *Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules* and *Biosafety in Microbiological and Biomedical Laboratories 6th edition*, published by the Centers for Disease Control and Prevention and the National Institutes of Health and the amendments and rulings made relative thereto from time to time.
- Highly pathogenic avian influenza
- SARS Co–V
- Any other agent identified by the director of BPHC on a list to be posted on the BPHC's website or

appearing on reporting forms. See details for applicable regulations.

Select Agent means microbial and toxic agents listed at 42 CFR 73.4, 42 CFR 73.5, and 9 CFR 121.2 and the rulings made by the CDC and U.S. Department of Agriculture relative thereto as amended from time to time.

Research Laboratory is a workplace or a work area of a workplace that is used primarily for research, development, non–routine testing, or experimentation activity in which any high-risk agent is used by or under the direct supervision of a technically qualified individual.

Work Area is a defined space, or a room or rooms, or other area where infectious agents or substances are produced, stored, or used, and where employees are present in the course of their employment. A work area may include an entire workplace.

Workplace is an establishment or business of an employer at one geographic location at which work is performed and containing one or more work areas.

Registration of Research Laboratories

The office of the AVPRC will be responsible for registering with BPHC all research laboratories possessing, producing, storing, or otherwise working with any high–risk agent.

Such registration shall be on a form, or electronic format, provided by the BPHC's Office of Environmental Health, and shall include the following:

- Name of the high-risk agent
- The location of each high-risk agent (but only if such disclosure is consistent with federal, state and institutional security restrictions and policies concerning select agents or high-risk agents).
- Principal Investigator responsible for the high–risk agent(s).
- Title and a brief description of the nature of the project.
- Grant identification number or other unique institutional identifier number for the project.
- Contact information for the IBC.
- Name and contact information for the Occupational Health Officer.

The information in the registration form shall be updated, on a form provided by the BPHC's Office of Environmental Health, twice a year, every July 31st and January 31st (or on the next business day if it falls on a holiday or weekend) following registration.

The AVPRC shall inform the OHO of all high-risk agents as they are identified and shall provide the OHO with a copy of each registration and update, simultaneously with filing.

Responsibilities of Principal Investigators, Supervisors, Laboratory Directors

Ensure Registration Prior to Project Commencement
The Principal Investigator, Supervisor, or Laboratory Director of any research project that proposes to possess, produce, store, or otherwise work with any high–risk agent must first contact the AVPRC, or designee, and ensure that a registration for the research laboratory is properly filed with the BPHC.

Develop Approved Plan Prior to Project Commencement

The Principal Investigator, Supervisor, or Laboratory Director of any research project who proposes to possess, produce, store, or otherwise work with any high–risk agent must:

- Develop a plan jointly with the OHO that will enable the Principal Investigator, Supervisor, or Laboratory Director to determine whether a significant exposure of personnel has occurred in the Research Laboratory and that will set forth a protocol for monitoring significantly exposed employees (for more information, see "Medical Surveillance of Employees Working With High-Risk Agents" under "Responsibilities of the Occupational Health Officer").
- Indicate in writing that the Principal Investigator, Supervisor or Laboratory Director, and OHO have each approved the plan
- The plan must also be approved by the AVPRC and the IBC before researchers on the project will be allowed access to a high-risk agent.

Mandated Reporting to OHO and EHS Director

The IBC, Principal Investigator, Supervisor, and/or Laboratory Director shall promptly report to the OHO:

- Any diagnosis of any disease caused by a high-risk agent; and
- Any laboratory employee or other individual having access to a research laboratory that possesses, produces, stores, or otherwise works with any high-risk agent **who is absent from the workplace due to illness for a period of two or more consecutive work days**.

The IBC, Principal Investigator, Supervisor, and/or Laboratory Director shall report to the AVPRC and the OHO any violation or breach of any laboratory procedures or any other incident that the IBC, Principal Investigator, Supervisor, or Laboratory Director **should reasonably believe resulted in exposure of laboratory personnel to a high-risk agent in the workplace or released any high-risk agent beyond the work area**.

The manner of reporting to ROHP is outlined in the section, "Manner of Reporting to ROHP."

Follow-up on Reporting Requirements of Laboratory Workers

Principal Investigators, Supervisors, and Laboratory Directors who learn of laboratory workers with reporting responsibilities as outlined in "Responsibilities of Laboratory Employees, Trainees, Students, and Others Who Have Access to High-Risk Agents" must confirm that such employees have reported to the ROHP **before returning to work** and that the employees have a written release to return to work provided by the ROHP.

Principal Investigators, Supervisors, and Laboratory Directors should refer any ill employee who has had access to a high-risk Agent to the ROHP for evaluation.

Responsibilities of Laboratory Employees, Trainees, Students, and Others Who Have Access to High-Risk Agents

Mandatory Reporting to OHO, AVPRC, and EHS

Laboratory workers or other individual having access to a research laboratory that possesses, produces, stores, or otherwise works with any high–risk agent and who are exposed to a high-risk agent from a spill or a breach in laboratory practices must immediately contact the OHO, AVPRC, and EHS Director of Research Safety to receive instructions as to appropriate immediate steps to be taken.

Mandatory Medical Evaluations
Any laboratory employee or other individual having access to a research laboratory that possesses, produces, stores, or otherwise works with any high–risk agent ***and*** who has been diagnosed with, is exhibiting symptoms of, or may have been exposed to, any high–risk agent ***or*** who has been absent from the work place due to illness for a period of two or more consecutive work days must report to the OHO prior to returning to work, for medical evaluation **before, and as a condition for**, returning to work.

Laboratory workers are **encouraged** to report **any** illness to the OHO if working with high–risk agents, even if the illness does not result in a two-day workplace absence.

The manner of reporting to ROHP is outlined in the section, "Manner of Reporting to ROHP."

Responsibilities of the Occupational Health Officer

Medical Surveillance of Employees Working With High-Risk Agents

The OHO is responsible for having in place a general plan to determine whether employees working with various high-risk agents have had a significant exposure to a high-risk agent and a plan to monitor significantly exposed employees.

The OHO will work with the Principal Investigator, Supervisor, or Laboratory Director on any research project that proposes to possess, produce, store, or otherwise work with any high–risk agent to:

- Develop the project-specific plan described in "Develop Approved Plan Prior to Project Commencement" as outlined in "Responsibilities of Principal Investigators, Supervisors, Laboratory Directors" which will enable the Principal Investigator, Supervisor, or Laboratory Director to determine whether a significant exposure of personnel has occurred in the research laboratory and which will set forth a protocol for monitoring significantly exposed employees; and
- Ensure that the project-specific plan is approved by EHS and the IBC before researchers have access to a high-risk agent.

The Occupational Health Officer will immediately notify the BPHC of all presumptive Lab Acquired Infections (LAI) followed by a confirmatory report once additional information is available. In the event of any incident the Occupational Health Officer will act as a single point of contact and coordinate all Occupational Health activities and notify other agencies as appropriate.

The OHO is responsible for generating the following reports and reporting to the BPHC as indicated:

Report of Diagnosis, Symptoms, or Exposure
The OHO shall perform an occupational health assessment for any laboratory employee or other individual having access to the laboratory who:

- Has been diagnosed with
- Is exhibiting symptoms of ***or***
- May have been exposed to any high-risk agent.

The findings of the assessment shall be immediately reported to the BPHC, via their Reporting Form, but in any event not later than one business day after completion of the assessment.

The OHO will conduct a follow-up assessment and provide information requested by BPHC regarding isolation and/or quarantine issues. If the determination is made that the illness is caused by a high-risk agent, BPHC will be consulted before an ill worker is allowed to return to work.

The OHO will send BPHC documentation that an exposed person has been cleared to return to work within three business days of clearance.

Report of Workplace Absence Due to Illness
The OHO shall perform an evaluation of any laboratory employee or other individual having access to a research laboratory that possesses, produces, stores, or otherwise works with any high–risk agent **and** who has been absent from the work place due to illness for a period of two or more consecutive work days.

The evaluation shall be completed prior to the employee's return to work.

If the OHO has a reasonable suspicion that the employee's illness may be related to an exposure to any high-risk agent, the OHO shall immediately notify the BPHC.

If Occupational Health determines that the illness was caused by a high-risk agent and may be work related, the BPHC must be consulted at least three business days prior to the employee's expected return to work.

Report of Diagnosis of Disease
The OHO shall report to the BPHC any diagnosis of any disease caused by a high-risk agent.

This report shall be made within one business day of the diagnosis.

Report of Violation of Laboratory Procedures Resulting in Release of High-Risk Agent
The OHO shall report to the BPHC any violation or breach of any laboratory procedures or any other incident which the OHO should reasonably believe released a high-risk agent beyond the work area.

This incident shall be reported to BPHC within one business day of the breach or incident.

EHS Notification
The OHO shall provide the AVPRC and EHS Director of Research Safety with written notification of all reports made to the BPHC.

Manner of Reporting to ROHP

Contact the ROHP 24/7 at (617) 358-7647 (ROHP).

Appendix U
Criteria for Development of Standard Operating Procedures (SOP)

In this manual, there are a number of sections where the laboratory is required to prepare standard operating procedures (SOPs). This appendix is intended to provide guidelines on the development of such documents. It is not mandatory to follow these procedures. The lab may seek the advice of EHS when developing an SOP.

Introduction

What is a Standard Operating Procedure (SOP)?

A standard operating procedure (SOP) document is a comprehensive set of instructions written to provide employees with guidelines to follow to complete a job safely. SOP should be written in a manner that provides the user with a clear set of guidelines that ensure the task is performed as desired by the institution and that meet regulatory compliance standards.

Institutions write SOPs for the following reasons:

- to provide individuals who perform operations with all the safety, health, environmental, and operational information required to perform a job properly;
- to ensure that operations are done consistently to maintain quality control of processes and products;
- to ensure that processes continue and are completed on a prescribed schedule;
- to ensure that no failures occur in manufacturing and other processes that would harm employees or anyone in the surrounding community;
- to ensure that approved procedures are followed in compliance with company and government regulations;
- to serve as a training document for teaching users about a process;
- to serve as a historical record of the how, why, and when of steps in a process for use when modifications are made to that process and when a SOP must be revised;
- to serve as an explanation of steps in a process that can be reviewed in incident investigations that seek to improve safety practices and operating conditions.

Purpose and Scope of this Document

The purpose of this document is to provide guidance and a template for drafting SOPs.

Developing an SOP

Except for the simplest operations, an SOP must be developed for each of the operations for reasons described above. An SOP is best developed by a team that includes the worker, the job supervisor, a safety and health professional, etc. When an SOP has been properly written, the result is satisfactory completion of the work with regard to efficiency, risk, and safety.

The first step in preparing to write an SOP should have the worker demonstrate how he or she will

accomplish a particular procedure. The worker must be someone who is already doing that job or who has done similar work. The supervisor acts as an advisor to monitor the required efficiency and contributes necessary information about the correct use of the equipment involved. The safety person notes the hazards of the job and lists the protective equipment that should be required.

The SOP should include identifying information (e.g., title and/or number) and all the procedure's steps, including associated hazards and precautions. Precautions for the employee's overall health and safety must be addressed, especially in terms of training and personal protective equipment and what to do in emergencies. The SOP also must address the precautions needed to prevent any impacts to the environment, whether it is the immediate workplace environment, the waste disposal system, or the surrounding community.

Note*: Detailed information does not need to be provided on some of the areas where there is already another document describing the procedure. For example, when describing the operation of a particular piece of equipment, a notation could be included that refers to the operating manual for that equipment or another SOP describing the operation. In these instances, it is important to ensure that these referenced documents are readily available*.

SOP Template

No standard SOP templates exist nationally, so each institution develops its own. The template presented at the end of this SOP is compliant with the requirements of Good Laboratory Practices (GLP) and will be used for all SOPs developed by the Office of AVPRC and is strongly recommended for use by others.

General Information

This is the top section of the SOP template and includes information about:

- *Unit*: The unit that develops and owns the SOP.
- *SOP Title*: The full title of the SOP.
- *SOP number*: Based on a standard numbering system.
- *Version*: The version of the SOP with V1.0 as the initial number and each subsequent revision having a new number such as V1.1.
- *Implementation Date*: The date the current version of the SOP went, or will go, into effect.
- *Approval*: The name and title of the individual who is responsible for approving the SOP. The responsible individual must sign or initial this section to indicate approval.
- *Page Number*: Indicates the page number using the notation "Page 1 of X."
- *Expiration date*: If the SOP is for a given operation that is for a specific duration, it should indicate that date; otherwise it should note "*until revoked.*"

Purpose and Scope

There should be brief statement on the purpose and scope of the SOP.

References

This section should list any additional resources that may be useful in performing the procedures. These may include:

- **Regulations**

Regulatory references should be listed here.

- **Policies**
  All relevant BU policies should be listed here.
- **Other SOPs**
  SOPs referred to in any other section of this SOP should be listed here
- **Supplementary Documents Policies**

Definitions

Definitions for the major terms used in the SOP should be included to provide the reader a clear understanding. Spell out the acronyms fully and show the abbreviations in (); this format should also be followed each time a new term is introduced in any part of the SOP.

Roles and Responsibilities

If the particular procedures require that individuals from various sections participate, the roles and responsibilities for each should be clearly defined. For example, if a procedure requires a cage washer to deliver clean cages to the rooms before the technicians responsible for changing the cages can do so, define the roles. If EHS must perform hazard evaluation as part of the SOP, EHS's role and responsibility should be defined.

Special Requirements

Equipment and Supplies Required

This section should list all equipment and supplies needed for performing the task or procedures. In a SOP with extensive supply list, it might be more appropriate to include the supplies in the description of each procedure.

Safety Requirements

This section should define all health, safety, and environmental protection measures that must be followed while performing the procedures, including spill and accident response procedures relevant to the particular operation defined in the SOP.

Training

Clearly define all the training requirements (e.g., courses), including the schedule for training (e.g., prior to the start of performing the procedures), re-training frequency, and how to obtain the courses.

Monitoring Requirements

This section should define the need, frequency, and methods of conducting personnel or environmental monitoring.

Personnel Protective Equipment (PPE)

List all the PPE required for performing this task, identifying which are mandatory and which are recommendations for further enhancing employees' health and safety.

Medical Surveillance

Clearly define the medical surveillance requirements for the procedures, if any.

Other Prerequisites

List any other prerequisites that exist for performing the procedures. These could include requirements for being familiar with companion polices, professional or special operating permits, etc.

Applicable Locations
List all locations where this SOP is applicable (e.g. all barrier facilities, all research laboratories, areas where nanoparticles are used, Rooms 111, 222 and 333 only, etc.)

Procedures or Instructions
This is the most important component of the SOP and requires a complete and step-by-step description of how the function should be performed.

When developing this section, consider the possibility of using the document as a training tool for new employees. Therefore, the details included should be such that after reading the document, a new employee could obtain a high level of understanding of how the function is performed.

Include the equipment used as part of this section and reference any SOP or operating manuals required.

Note*: Some SOP might include a listing of all equipment used at the start of this section.*

The title of any manufacturer's manuals, good practices, and professional organization guides, available or used in this procedure, should be listed here. The location of these documents should also be noted.

Note*: To avoid the need for frequent updating of the procedures, each program should designate a permanent location that acts as a reference library*.

Forms
The SOP should include all the forms required by the SOP. It is recommended that:

- All forms are included as attachments to the main SOP with a clear reference in the "Procedures and Instruction" or "Record Management" sections. This will make revisions of the SOP simpler if forms are changed.
- A form numbering system is established that correlates to the SOP numbers.

Record Management
This section incorporates record management practices, including location of active records, archived records, and record retention times.

SOP Revision History
It is extremely important to track the history of the SOP and document all its revisions. This expectation should be integral part of all SOP development and maintenance processes.

The SOP should be reviewed by the team that created when:

- There is a change in regulatory requirements.
- Operating procedures have changed significantly.
- Forms used or the record management system has changed.
- Introduction of new facilities, equipment, risks, hazards, or processes.

- At least annually.

The following provides a template for use:

Unit:	**SOP #:**
	Revision #:
	Current Version Implementation Date:
Page #: Page 177 of 182	**Last Reviewed/Update Date:**
Expiration Date:	**Approval Authority:**
SOP Titles	

1. Purpose and Scope

2. References

2.1. Regulations
2.2. BU Policies
2.3. Other SOP
2.4. Supplementary Documents

3. Definitions

4. Roles & Responsibilities

5. Special Requirements

5.1. Equipment and Supplies Required
5.2. Safety Requirements
5.3. Training
5.4. Monitoring Requirements
5.5. Personnel Protective Equipment (PPE)
5.6. Medical Surveillance
5.7. Other Prerequisites

6. Applicable Locations

7. Procedures and Instructions

8. Forms

9. Records Management

10. SOP Revision History

Version	Section / Paragraph Changed	Changes Made	Effective Date
V.1	N/A	None, Original Version	2016

Appendix V
Boston University Institutional Biosafety Committee Noncompliance Policy

1. Purpose

The Boston University (BU) Institutional Biosafety Committee (IBC) has developed this policy for evaluating issues of noncompliance with IBC protocols, policies, and regulatory guidelines. Although uniform standards can serve as a guide, each individual situation is unique and will be judged on its own merits.

2. Reporting

All personnel involved in research overseen by the BU IBC have an obligation to report concerns of noncompliance to the IBC, Research Compliance, or via the processes outlined for reporting concerns to the University, including the BU Ethics and Compliance Hotline.

3. Applicability

The policy applies to all laboratories conducting IBC-approved activities and the personnel listed on BU IBC-approved protocols.

4. Authority

The BU IBC is charged with ensuring adherence with the National Institutes of Health Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines), OSHA Bloodborne Pathogen Standard (29 C.F.R. part 1910.1030), the Federal Select Agent Program (7 C.F.R. Part 331, 9 C.F.R. Part 21 and 42 C.F.R. part 73), The United States Government Policy for Oversight of Dual Use Research of Concern (DURC) and consistency with the guidance found in the Centers for Disease Control's (CDC) Biosafety in Microbiological and Biomedical Laboratories 6th Edition (BMBL). The IBC, therefore, monitors the conduct of research programs that fall under purview of BU for compliance with all the appropriate regulations, as well as institutional policies and procedures. Noncompliance may also be reported to the IBC as a result of annual/routine lab inspections performed by staff of the Environmental Health and Safety (EHS) program.

5. Definitions

Allegation of noncompliance: An unproven assertion of noncompliance.

Finding of noncompliance: A determination by the IBC that an assertion or allegation of noncompliance has been proven or substantiated. Findings of noncompliance by the IBC may include: violations of University policy, noncompliance with the NIH Guidelines, the BMBL, OSHA Bloodborne Pathogen Standards, and other applicable federal, state and local laws or regulations governing the use of biohazardous materials and/or recombinant or synthetic nucleic acid molecules.

Serious noncompliance means noncompliance that adversely affects the health or welfare of research subjects (human and animal) and/or staff and:

- Harms or poses an increased risk of substantive harm to personnel; or
- Poses a risk of substantive harm to the general public or environment; or
- Compromises the integrity or validity of the research.

Examples of serious noncompliance may include, but are not limited to, the following:

- Failure of the Principal Investigator (PI) to adhere to the responsibilities outlined in Section IV-B-7 of the NIH Guidelines;
- Conducting procedures involving biohazardous materials and/or non-exempt recombinant/synthetic nucleic acid molecules without IBC approval;
- Continuing to conduct procedures involving biohazardous materials and/or non-exempt recombinant/synthetic nucleic acid molecules after an IBC protocol has expired;
- Working with an infectious agent, viral vector, or host system that is not documented in an approved IBC protocol;
- Deviating from approved IBC protocol in a way that could increase the exposure risk of personnel or the environment to biohazardous materials and/or non-exempt recombinant/synthetic nucleic acid molecules;
- Conducting of procedures by personnel not adequately trained but with a signed/approved personnel training form in the lab or on file with the IBC;
- Conducting procedures involving biohazardous materials and/or recombinant/synthetic nucleic acid molecules in a facility not approved for such use.

Continuing noncompliance means noncompliant activity that recurs after a report of the activity has been evaluated by the IBC (which may be either minor or serious) and after corrective action has been communicated in writing (e.g., email) to the PI. Note: determinations of continuing non-compliance that recur after IBC corrective action has been implemented may be reportable to external oversight authorities, as appropriate.

Minor noncompliance means any behavior, action, or omission in the conduct or oversight of research activities that deviates from the IBC-approved research plan, federal regulations, local, or institutional policies, but does not rise to the level of serious noncompliance.

Examples of minor noncompliance may include, but are not limited to, the following**:**

- Failure to respond to requests for revisions to protocols by the IBC in a timely manner;
- Addition of study personnel without notifying the IBC;
- Implementing minor wording or procedural changes in a study without first obtaining IBC approval.

6. Determinations and Corrective Actions

Initial Evaluation and Actions

A concern may be reported through various channels. Depending on the channel, and the nature of the concern, other offices and individuals will be informed, and in consultation with Research Compliance staff, the IBC Chair, EHS, and the Biosafety Officer, when applicable, immediate actions may be taken to address the concern. The PI will be notified in writing of these concerns and any required actions. During an evaluation it may be necessary to review research and other documentation, inspect facilities, and/or hold discussions with pertinent individuals including the PI, lab personnel and/or administrative personnel, as appropriate. In some cases, involvement by the Institutional Official (IO), BU Office of General Counsel (OGC), and other University administration (e.g., Department Chair)

may be required at the outset of an evaluation.

IBC Determination

Following an evaluation, the IBC Chair, in consultation with the above parties, may:

- bring the matter before the full IBC;
- appoint a subcommittee to review the reported concern;
- in the instance of minor non-compliance, may handle the matter or delegate handling of the matter to Research Compliance staff or the Biosafety Officer.

Determinations of Serious or Continuing Non-Compliance

If the IBC chair believes that the allegations may be serious or continuing non-compliance, the results of the evaluation, including all supporting documentation and the PI's corrective action plan, if developed, will be provided to the IBC for review at a convened meeting. Based on the information, the IBC will determine:

1. the nature of the concern as it relates to the *NIH Guidelines*, BMBL, University policies, and other applicable regulations;
2. the need for additional actions, such as further investigation or notification of other University officials as appropriate; and
3. further corrective measures to address the concern and prevent recurrence along with appropriate deadlines for response from the PI.

The IBC has the authority to address noncompliance based on *NIH Guidelines*, the BMBL, University policies, and other regulatory requirements. Findings of noncompliance may result in one or more of the following actions:

- Suspending the use of recombinant/synthetic nucleic acid molecules and/or biohazardous materials pending completion and acceptance by the IBC of a written plan by the PI for the correction and prevention of recurrence;
- Termination of approval for use of recombinant/synthetic nucleic acid molecules and/or biohazardous materials;
- Confiscation and destruction of the recombinant/synthetic nucleic acid molecules and/or biohazardous materials;
- Any other action necessary to protect personnel, the environment, the public and/or University, including restricting access to the laboratory in order to suspend activities.

The PI will be notified of the IBC's decision in writing. If the allegation involves other BU personnel for whom corrective actions may result, those individuals will be included in any appropriate communications.

Reporting to External Agencies

Findings of serious or continuing noncompliance will be reported to the appropriate agency, including, but not limited to, the study sponsor, NIH Office of Biotechnology Activities (NIH/OBA), the BPHC and the CDC. The IBC, in concert with Research Compliance, is responsible for reporting any significant problems (e.g., serious non-compliance) with, or violations of, the *NIH Guidelines* and any significant research-related accidents or illnesses to the NIH/OBA within thirty (30) days of the

incident. These reports are not intended to be punitive toward the individuals involved, but rather are intended to assist the institution in developing new and better policies and practices to prevent future non-compliances from occurring.

References:

- Biosafety in Microbiological and Biomedical Laboratories (BMBL) 6th Edition
- NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules
- Occupational Safety and Health Standards for Bloodborne Pathogens
- Federal Select Agent Program
- United States Government Policy for Oversight of Dual Use Research of Concern (DURC)

Appendix W
BSL-3 and BSL-4 Biosafety Plan

For BSL-3 and BSL-4 Biosafety Plan, please contact NIEDL BSL-3 or NEIDL BSL-4 Biosafety Officer.