HARVARD
Campus Services
ENVIRONMENTAL HEALTH & SAFETY

Harvard University Biosafety Manual

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Introduction

Harvard University's Biosafety Manual provides safety guidance, policies, and procedures for using and manipulating biological materials across the institution. This manual serves as an integral part of the Biosafety and Biosecurity Program.

Handling and manipulating biological materials require various biosafety and biosecurity control measures. These controls are determined based on the nature of the materials involved and the procedures being performed.

This manual assists in biological risk assessment and risk management. However, rapid advances in scientific technologies make it impossible to fully anticipate each use of a biological agent and effectively plan for every risk of an operation that involves such materials.

Successfully implementing biosafety and biosecurity practices at Harvard depends on continuous assessment, recognition of potential hazards, and coordination between the Institutional Biosafety Committee (IBC), Biosafety Officers (BSO), Principal Investigators (PIs), and research staff to control identified risks.

Harvard's Lab Safety Program is based on the premise that every member of the research community shares the responsibility for safety.

Scope

This document serves as the Biosafety Manual for all Harvard schools and the Wyss Institute and encompasses research conducted at Biosafety Levels (BSL) BSL1, BSL2, and BSL2+ containment.

Lab-specific policies, procedures, and controls for BSL3 labs are independently described in separate manuals.

Harvard doesn't conduct BSL4 research.

The regulations governing these requirements and guidelines are described in Appendix I. Regulations, Guidelines, and Policies.

Roles and Responsibilities

Harvard University

The institution must provide for the safe conduct of research involving the use of biological materials.

Harvard is responsible for:[1]

- Forming an IBC to review biological research as required by local, state, and federal guidelines.
- Determining the necessity for health surveillance of personnel involved in biological research projects; and if appropriate, conducting a health surveillance program for such projects.

[1] As required by the National Institutes of Health (NIH) Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines) and local biosafety agencies.

Committee on Microbiological Safety

The Committee on Microbiological Safety (COMS) serves as the IBC for Harvard and its affiliated institutions. COMS oversees review of recombinant and synthetic nucleic acids research,[2] along with other types of biological research conducted at Harvard.

COMS is comprised of Harvard faculty, local community members, BSOs, and subject matter experts for topics like animal biosafety, plant containment, and occupational health.

The COMS Office oversees the administration of the committee and acts as non-voting members.

Primary responsibilities of COMS as a committee include:

- Appointing members as required by the types of research conducted within the institution.
- Offering appropriate training for committee members on assessing biological research.
- Reviewing biological research as required by local, state, and federal guidelines, specifically projects involving COMS-regulated materials (CRM).
- Generating and implementing policies that ensure compliance with applicable regulations and safe conduct of biological research.

Environmental Health and Safety Department

The EHS Department manages environmental and occupational safety compliance programs at Harvard and provides technical support and guidance to lab personnel.

[2] As mandated by the NIH Guidelines, the Boston Public Health Commission (BPHC), and the Cambridge Public Health Department.

EHS includes a team of BSOs who serve as biosafety subject matter experts and liaisons between regulatory agencies, COMS, and Harvard labs.

Biosafety Officers

The NIH Guidelines and local biosafety agency regulations require the appointment of a BSO to advise in the safe conduct of biological research at the institution.

BSO responsibilities include:

- Acting as biosafety subject matter expert members of COMS.
- Performing risk assessments for biological research conducted at Harvard.
- Providing regulatory and technical advice to PIs and COMS on research safety procedures.
- Conducting periodic lab inspections to ensure biosafety practices are followed.
- Developing biosafety training modules and providing training on biosafety concepts, as appropriate.
- Reporting any significant problems, regulatory violations, and significant research-related accidents and illnesses to COMS and external agencies.
- Developing and disseminating emergency plans for handling accidental spills and potential exposures.
- Helping to investigate lab exposures and incidents involving biological materials.
- Advising on lab biosecurity.

Environmental and Safety Compliance Officers

Under the authority delegated by the Dean of each School or Faculty, Environmental and Safety Compliance Officers (ESCO) are responsible for promoting and maintaining a safe, healthy, and environmentally responsible workplace on campus.

Department Administrators

A primary responsibility of the Department Administrators (DA) is to:

- Facilitating their department's compliance management program.
- Helping labs remediate department-wide issues.

A Research Operations Manager (ROM) may assist the DA.

The DA, either directly or through a ROM, is responsible for notifying EHS when:

- A new PI who will supervise a lab is accepted into their department.
- Major changes occur to the research infrastructure, like construction projects.

Research Operations Managers

ROMs are responsible for:

- Communicating EHS programs to the labs, PIs, and their appointed Safety Coordinators or Lab Safety Officers (LSO).
- Serving as the primary liaison between EHS and their basic science department.
- Monitoring compliance and safety issues within their department.

Some Harvard schools may not have ROMS. In this case, ROM's responsibilities can be assigned by the DA to the Lab Manager, LSO, Safety Coordinator, or PI.

Principal Investigators, Lab Directors, or Research Supervisors

The PI or equivalent individual is primarily responsible for health and safety in the lab or comparable research space (such as core facility or animal facility). This includes compliance with all applicable regulations and the criteria established in this manual.

Before receiving and beginning any research with biological materials or recombinant or synthetic nucleic acids, PIs must contact their BSO for assistance in:

- Assessing the work.
- Setting up appropriate safety controls.
- Registering applicable research with COMS.

PIs are responsible for:

- Modeling and reinforcing safe practices and ensuring that the lab complies with applicable regulations.
- Registering biological research with COMS as required.
- Identifying and communicating lab hazards to lab personnel.
- Being appropriately trained and ensuring staff receive lab-specific and general training on hazards, protective procedures, and equipment.
- Developing lab-specific standard operating procedures (SOP) that cover the hazards and activities relevant to the lab, including routine activities and unusual events.
- Maintaining availability of engineering controls, such as biosafety cabinets (BSC), that are in good working order and using them appropriately to minimize exposure to biohazardous agents.
- Providing proper personal protective equipment (PPE) and ensuring lab personnel use it appropriately.
- Ensuring that periodic inspections of the lab are conducted with EHS and a lab representative.
- Offering consultation with occupational health, immunizations, and medical surveillance in accordance with current regulations and COMS recommendations.
- Notifying the BSO of spills or other incidents involving biological agents that may result in exposure or release to the environment. PIs notify the BSO though the Operations Center and by emailing biosafety@harvard.edu as appropriate.

- Decontaminating and disposing of biological materials in accordance with the regulations.
- Transporting, shipping, and permitting biological materials as required by regulations.

Safety Coordinator, Lab Manager, or Lab Safety Officer

A qualified lab employee may assist the PI. However, assigning duties to such an employee doesn't diminish the PI's responsibility within the lab. The PI is required to complete these tasks that aren't otherwise assigned.

With the support of the PI, this employee is responsible for:

- Serving as a liaison for environmental, safety, and compliance communications within the lab and coordinating follow-up for identified compliance concerns.
- Adding study staff to COMS registrations as required.
- Conducting joint safety assessments with either or both the department ROM and an EHS representative.
- Ensuring that all personnel have completed the required training classes.
- Completing PPE assessment forms for all activities within the lab and monitoring PPE compliance.
- Ensuring lab personnel properly use all required safety equipment and required documentation is maintained and accessible to lab personnel.
- Coordinating lab participation in periodic safety activities.
- Notifying ROMs or DAs of matters requiring the research department's attention.
- Advising the PI of any areas of non-compliance in the lab.

Lab Personnel

Each individual assumes personal responsibility for their safety, as well as the actions taken affecting the safety of others within the lab space. Individuals should bring safety concerns to their PI or BSO.

Anyone working with biohazards is responsible for:

- Following all safety rules that apply to the work area and completing all necessary safety trainings before starting work.
- Planning and conducting each operation in accordance with institutional processes and lab-specific SOPs.
- Reviewing all new procedures with their PI or Lab Supervisor.
- Promoting good housekeeping practices in the lab work area.
- Using engineering controls and PPE as appropriate for each procedure involving biohazards.
- Reporting all workplace injuries, exposures, incidents, near misses, or unsafe conditions to either or both the PI or equivalent and BSO as soon as possible.
- Contacting the PI, Lab Supervisor, or BSO with any biological safety questions.

Occupational Health

Occupational Health offers preventative health programs and consultations for work-related exposures and illnesses, to align with regulatory or institutionally-mandated programs.

As applicable under such requirements, the roles of Occupational Health include:

- Offering pre-employment screenings, vaccinations, and respirator medical clearances.
- Providing post-exposure screenings and medical examinations.
- Maintaining records of medical examinations, post-exposure health screenings, and immunizations.

Ancillary Personnel

Ancillary personnel don't work directly with biohazardous materials, but may need to enter areas where such materials are present during their work. Ancillary personnel include non-research workers like visitors, vendors, maintenance workers, and administrative personnel.

As the potential for inadvertent exposure still exists, it is imperative for these ancillary personnel to commit to:

- Reading and understanding posted warning notices before entering biological use areas.
- Observing all recommendations and requirements for entry.
- Contacting the PI or EHS Biosafety with any biological safety questions.
- Reporting all workplace injuries, exposures, incidents, near misses, or unsafe conditions as soon as possible.

Biohazards, Risk Assessment, and Risk Management

Definitions

Term	Definition
Biohazard	An agent of biological origin that has the capacity to cause harm or disease in humans, plants, or animals or may produce deleterious effects within the environment, such as microorganisms, toxins, and allergens.
Blood	Human blood, including blood components or products, except where otherwise identified.
Research	Systematic investigation or experimentation for teaching, scientific, or clinical advancement.
Risk	The function of adverse impacts of a hazard and probability of occurrence.
Risk management	Established measures to reduce either or both the impact and likelihood of a risk.

Term	Definition
Virulence	Capacity of a microorganism to establish itself within a host and produce disease; degree of pathogenicity.

Biological Agent-Specific Risks

Risk Groups

Risk groups (RG) rank biological agents predominantly based on their pathogenicity (ability to cause disease) in humans and the availability of effective preventative measures or treatments. Factors used to classify agents into risk groups also include virulence, infectious dose, environmental stability, transmission route of spread,[3] origin, host range, and communicability.

Risk group assignments only apply to wild-type organisms.

The Biosafety in Microbiological and Biomedical Laboratories (BMBL) and NIH Guidelines help define risk group.

Risk Group	Definition[4]	Examples
Risk Group 1 (RG1)	RG1 agents have the lowest risk. They aren't associated with disease in healthy adult humans.	*Bacillus subtilis, S. cerevisiae*

[3] Route by which a microorganism enters a host, like through parenteral, inhalation, ingestion, and eye or mucous membrane contact. This route is generally considered based on the ability to establish infection or route of spread.

[4] As defined by NIH Guidelines Appendix B - Table 1. Basis for the Classification of Biohazardous Agents by Risk Group.

Risk Group	Definition[4]	Examples
Risk Group 2 (RG2)	Agents associated with human disease which is rarely serious and for which preventive or therapeutic interventions are often available.	Adenovirus, rhinovirus, hepatitis B virus (HBV)
Risk Group 3 (RG3)	Agents associated with serious or lethal human disease for which preventive or therapeutic interventions may be available (high individual risk, low community risk).	Human immunodeficiency virus (HIV), *Mycobacterium tuberculosis*, prions
Risk Group 4 (RG4) (not permitted at Harvard)	Agents with the highest risk. They could lead to serious or life-threatening infections, with little to no chance of effective medical intervention (high individual risk, high community risk).	Ebola virus, Lassa virus, tick-borne encephalitis viruses

Recombinant and Synthetic Nucleic Acids

The risks of recombinant organisms depend on the modification method and the nature of the gene insert or modification. Modifications potentially increase or decrease risk depending upon the resultant phenotypic change. If an inserted gene is just a marker or tag, it may not affect risk. Evaluate genetic modifications on a case-by-case basis.

Give special consideration to risks of gene drive modified organisms (GDMO).

NIH-funded institutions must ensure that research involving recombinant or synthetic nucleic acids complies with the NIH Guidelines, including applying described risk assessment and risk mitigation principles.

Recombinant and synthetic nucleic acids are:[5]

[5] As defined in NIH Guidelines (Section I-B. Definition of Recombinant and Synthetic Nucleic Acid Molecules).

- Molecules constructed by joining nucleic acid molecules and that can replicate in a living cell (that is, recombinant nucleic acids).
- Nucleic acid molecules synthesized or amplified chemically or by other means, including those that are chemically or otherwise modified but can base pair with naturally occurring nucleic acid molecules (that is, synthetic nucleic acids).
- Molecules that result from the replication of other recombinant and synthetic nucleic acids as defined by NIH.

Framework for Nucleic Acids Synthesis Screening

To meet federal funding agency requirements, synthetic nucleic acids and benchtop nucleic acid synthesis equipment purchased with federal life sciences funding must be procured from nucleic acid providers and equipment manufacturers that comply with the Office of Science and Technology Policy Framework for Nucleic Acid Synthesis Screening framework.

Framework Definitions

Providers include commercial distributors of synthetic nucleic acid sequences, such as:

- Biofoundries.
- Cloud labs.
- Fee-for-service core facilities.
- Contract research organizations or labs with integrated nucleic acid synthesis capabilities related to sequences of concern (SOC).

Equipment manufacturers produce equipment capable of generating SOCs.

The current framework defines a SOC as a nucleotide sequence of 200 bases or more or a corresponding amino acid sequence that is a Best Match to a sequence of a federally-regulated agent on the Biological Select

Agents and Toxins List or the Commerce Control List (except when the sequence is also found in an unregulated organism or toxin).

In October 2026, the framework's definition of a SOC will:

- Reduce the minimum nucleotide sequence length to 50 bases.
- Include sequences of increased pathogenicity, virulence, or toxicity (even when not derived from regulated agents).

Framework Responsibilities

Nucleic acid providers and synthesis equipment manufacturers must:

- Attest that they're following the framework.
- Provide their attestation to the customer either using a public facing website or in writing by request.

If applicable, labs should discuss framework requirements with their procurement teams and Material Transfer Agreement offices.

Unless an attestation is publicly posted, labs should request an attestation from the vendor and retain a record of the attestation for any relevant materials and equipment.

The framework excludes standard collaborations, for example a Harvard lab providing something to another Harvard lab.

Cores that plan to generate nucleic acids regulated by the framework must:

- Integrate the requirements into their work practices.
- Make an attestation available either on their website or at the request of the customer.

Framework Updates

The framework will be revised or replaced 90 days after the publication of this Executive Order.

EHS will update this information based on the new framework .

Dual Use Research of Concern and Pathogens with Enhanced Pandemic Potential

The federal government oversees research on biological agents and toxins that pose risks to public health, agriculture, food security, economic security, or national security. This includes regulation of dual use research of concern (DURC) and pathogens with enhanced pandemic potential (PEPP).

The United States Government Policy for Oversight of Dual Use Research of Concern and Pathogens with Enhanced Pandemic Potential outlines these requirements.

Research under the policy is grouped into Category 1 (DURC) or Category 2 (PEPP) based on the characteristics of the agents used and the potential research outcomes. Each experimental category has specific review and mitigation processes.

PIs are responsible for:

- Identifying research subject to this policy.
- Registering the research with COMS.
- Following all risk mitigation measures prescribed.

If research is determined to initially fall outside the scope of the policy, but through experimentation, it is determined that the work may be in a regulated category, PIs must:

1. Immediately stop all related research.
2. Secure the agents.
3. Report observations to COMS for further review and evaluation.

COMS must reapprove the research before it can continue.

This Executive Order's policies, actions, and definitions supersede implementing the DURC and PEPP Policy, which will be replaced or revised by September 2025.

Research defined as "dangerous gain-of-function research" is paused. EHS will update this information when a new policy is published.

Select Agents and Toxins

Select agents and toxins pose a severe threat to public, animal, or plant health and have the potential to be exploited for bioterrorism or biological warfare. The Federal Select Agent Program oversees the possession, use, and transfer of select agents and toxins.[6] Due to the seriousness of the risks associated with these agents, their use is heavily restricted with significant civil and criminal penalties for non-compliance.

Only excluded forms of select agents and unregulated quantities of toxins are permitted at Harvard.

Some genetic elements, recombinant nucleic acids, and recombinant organisms may also be regulated as select agents:

- Nucleic acids (synthetic or naturally derived, contiguous or fragmented, or in host chromosomes or in expression vectors) that can encode infectious or replication-competent forms of select agent viruses.
- Nucleic acids (synthetic or naturally derived) that encode for the functional form or forms of any toxins listed, if the nucleic acids are in a vector or host chromosome or can be expressed *in vivo* or *in vitro*.
- Recombinant forms of regulated agents.

Select Agents or Toxins	**Use at Harvard**
Regulated select agents	Harvard prohibits possession and use of regulated select agents and toxins.

[6] Under the joint purview of the Centers for Disease Control and Prevention (CDC) and the United States Department of Agriculture (USDA)/Animal and Plant Health Inspection Service (APHIS) (7 C.F.R. Part 331: Agriculture; 9 C.F.R. Part 121: Animals and Animal Products; 42 C.F.R. Part 73: Public Health).

Select Agents or Toxins	Use at Harvard
Excluded select agents	Before receiving excluded select agents, labs must register with and receive approval from COMS. When receiving and using excluded select agents, labs must follow the COMS Validation and Use of Attenuated Organisms Policy.
Permissible amounts of select toxins	Labs must follow specific requirements for select toxin inventory management, transfer, storage, handling, and destruction.

If a select agent or toxin is isolated from mixed microbial samples or otherwise discovered within a lab, the lab must:

1. Stop all related activities and secure the materials until EHS Biosafety can advise on handling and disposal.
2. Immediately contact EHS Biosafety.

Bloodborne Pathogens

Human blood and other potentially infectious materials (OPIM) may harbor bloodborne pathogens such as HIV, HBV, and hepatitis C virus (HCV).[7] OPIM also includes established human cell lines, like HeLa and HEK293.[8]

The OSHA Occupational Exposure to Bloodborne Pathogens Standard requires a combination of:

- Using engineering and work practice controls.

[7] OPIM are defined in the Occupational Safety and Health Administration (OSHA) Occupational Exposure to Bloodborne Pathogens Standard (29 CFR 1910.1030 1910.1030(b)).

[8] Under an OSHA Bloodborne Pathogens Standard letter of interpretation.

- Creating a lab-specific Exposure Control Plan (ECP).
- Annual training.
- Offering HBV vaccination (offered or declined in writing).
- Other provisions to help identify and control health risks from occupational exposure to blood and OPIM.

To learn more, visit Bloodborne Pathogens.

Poliovirus and Potentially Infectious Materials

Between 2019 and 2023, EHS inventoried poliovirus-containing infectious materials and potentially infectious materials held at Harvard.[9]

Infectious materials are samples or cultures known to contain poliovirus (wild or oral vaccine strains). Potentially infectious materials may include:

- Permissible cell cultures.
- Respiratory and enteric virus stocks where poliovirus contamination is possible.
- Respiratory secretions, fecal samples, or untreated environmental surface water samples collected for any purpose in a time and geographic area of wild poliovirus circulation or oral poliovirus vaccine use.

To align with poliovirus containment practices required by CDC, labs that discover infectious or potentially infectious materials as defined by CDC must:

1. Immediately contact EHS Biosafety.
2. Stop all related activities and secure the materials until EHS Biosafety can advise on next steps.

[9] Using the CDC National Inventory for Poliovirus Containment Survey and following guidance from the CDC, Center for Preparedness and Response, and U.S. National Authority for Containment of Poliovirus (U.S. NAC).

Risk Assessments

Risk identification is the first step in assigning appropriate mitigation measures. It requires carefully considering biological agent and procedural hazards. A risk assessment involves identifying hazards, characterizing them, assessing exposure or release and its likelihood, and determining an acceptable level of risk.

The PI performs the initial risk assessment of the planned work:

1. Determine the initial risk group using the NIH Guidelines and BMBL.

   If risk groups aren't otherwise assigned, consult the American Biological Safety Association (ABSA) Risk Group Database, Public Health Agency of Canada (PHAC) Pathogen Safety Data Sheets (PSDS), and literature references.

2. For all human, animal, or plant source material, determine if infectious agents are reasonably anticipated to be present and their approximate level of associated risk.

   When assessing risk, consider using this manual, consulting your BSO, and reviewing regulatory requirements.

3. Address hazards applicable to the planned work:

   - Procedural hazards contribute to the possibility of exposure. Perhaps the greatest hazards are processes that create infectious aerosols, including centrifugation, pipetting, sonication, shaking, homogenization, and animal inoculation. Aerosols increase exposure risks for agents infectious by inhalation or contact with contaminated surfaces.
   - Sharps, such as needles, scalpels, or cryostat blades, increase the likelihood of exposure through percutaneous injury. Whenever feasible, substitute plasticware for glass and consider alternatives to sharps.

- Large scale cultures increase risks of splashes, spills, and whole-body exposures. Use higher containment conditions to handle even RG1 agents in single containers greater than 10L.
- Research animals increase risks of bites, scratches, splashes and aerosolization of infectious body fluids and waste, and exposure to zoonotic agents.

Biosafety Levels

BSLs describe facility design requirements, engineering controls, work practices, PPE, and occupational health considerations to manage risks associated with handling biological agents. Such controls are described in other sections of this manual. An agent's risk group correlates with, but doesn't necessarily equate to, the BSL.

The BMBL and the NIH Guidelines also include general containment requirements and safe work practices for research using animals, plants, and arthropods. GDMOs under the NIH Guidelines have a minimum containment level of BSL2 (or equivalent).

PIs are responsible for initially proposing the appropriate BSL for their planned work. However, COMS assigns BSLs to COMS-regulated materials (CRM) during their review and approval process.

COMS Oversight

Before purchasing, receiving, storing, or handling CRM at Harvard, labs must receive approval from COMS.

CRM subject to COMS oversight:

- Recombinant or synthetic nucleic acids as defined in the NIH Guidelines, including GDMOs.
- Human or non-human primate blood, cells, tissues, fluids, and secretions.
- Biological toxins subject to the National Select Agent Program.
- Bacteria, virus, fungi, yeast, parasitic protozoa, and prions.

Harvard Core Facilities that receive, store, or process materials should determine an intake process for:

- Properly identifying biohazards.
- Determining safety requirements.
- Ensuring appropriate COMS registration.

COMS Review Process

PIs and their designees login to eCOMS with their HarvardKey.

PIs or their designees can create a new COMS protocol to register their lab's research. Only PIs can submit new projects and scientific amendments in eCOMS.

1. The PI submits a project in eCOMS.
2. EHS Biosafety performs an initial risk assessment.
3. During the approval process, COMS reviews the registration and formally assigns BSLs and stipulations for the work. The review and approval depends on the lab's responsiveness to any questions about the registration.
4. COMS communicates their decision to the PI by email or system notification. An approval letter outlining the requirements is provided within the online system.

Any of these steps may require the PI to take further action, such as providing clarifications or modifying the project. To help plan research timelines, review COMS meeting and submission schedules.

Recombinant or Synthetic Nucleic Acids Experiments Levels of Review

The NIH Guidelines generally determine the level of review required for recombinant or synthetic nucleic acids experiments.

NIH Guidelines Section	Minimum Review and Approval by
III-A	COMS, NIH Director

NIH Guidelines Section	Minimum Review and Approval by
III-B	COMS, NIH Office of Science Policy (OSP)
III-C	COMS, Institutional Review Board (IRB)
III-D	COMS
III-E	COMS
III-F	COMS (NIH Guidelines exempt)

Refer directly to the NIH Guidelines to determine the sections that apply to your lab's research. All research falling under NIH Guidelines (Sections III-A through III-F) requires a minimum of COMS approval before it can commence.

Timelines for COMS approval depend on when the protocol is submitted in the review cycle, the required level of review, the BSL of the work, and if the work has precedent with COMS.

Some protocols may qualify for administrative approval before full review at the next COMS meeting. Others need full COMS review and approval before starting work.

BSL3 work also requires review and approval by the applicable city public health department before work may commence.

COMS Requirements for Lab Personnel

All persons working on a COMS protocol must be listed on the project and review the protocol before performing work. COMS requires approval letters be available and accessible to everyone working in the lab at BSL2 and above and recommends this practice at BSL1.

COMS Policies

COMS policies clarify expectations about BSL assignments, standard biological work practices, inspections, training, and incident reporting. PIs and lab members should review COMS policies for the most current requirements.

Hierarchy of Controls for Biosafety and Biosecurity

A primary goal of biosafety is to prevent unintentional exposure to or release of biohazards. This is done through the implementation of a multi-layered containment approach.

1. The lab's biological risk assessment and determination of BSL dictate the specific set of controls.
2. Ideally, risks are minimized by using lower risk biological agents and processes. Where this can't happen, steps are taken to design facilities to eliminate or mitigate hazards and use primary containment to control hazards at the point of use. Work practices and PPE are then applied to alleviate any remaining hazards.

Biosecurity focuses on preventing misuse of biohazards through loss, theft, or intentional release.

Control measures applied for biosafety purposes may align or conflict with those needed to maintain biosecurity. When determining how to apply controls to ensure an appropriate balance, consider both biosafety and biosecurity and consult EHS Biosafety.

Biological Lab Facility Design

Biological lab construction and functional layout must provide for biohazard containment. This includes considering ventilation, capacity for room and surface (floors, walls, casework, and furniture) decontamination, and installing and using emergency systems and equipment.

General lab design considerations and requirements for different BSLs are described in:

- The BMBL

- EHS Lab Design Guidelines
- NIH Design Requirements Manual (DRM)

EHS Biosafety should review construction projects for biological labs in collaboration with the lab team and construction and design team.

Biosafety Cabinets

BSCs are the primary containment for working safely with infectious materials. When BSC users follow good microbiological practices and procedures, BSCs provide personnel and environmental protection.

BSCs use high efficiency particulate air (HEPA) filtration to control airborne particulates. Laminar airflow pulls contaminants away from the user and environment.

HEPA filters efficiently remove microscopic contaminants from the air. A BSC HEPA filter removes particles equal to and greater than 0.3 µm (essentially removing all bacteria, spores, and viruses) with an efficiency of 99.99%.

BSC Classifications

The three main types of BSCs are designed for different research and clinical needs.

The BMBL (Appendix A - Primary Containment for Biohazards) includes functional aspects for each BSC class and the BSC selection process based on biosafety containment and planned use.

BSC Type	Air Flow and Filtration	Air Curtain
Class I and II	Takes room air and air within the BSC, and pulls it down through the grates on the work surface, up through the back of the BSC, and then either recirculates or exhausts the air through HEPA filters.	Recirculated HEPA-filtered air creates an air curtain between the user and their work inside the BSC. For Class II BSCs, the air curtain also creates a sterile work surface to protect the materials the BSC user is using.
Class III	Encloses the work in a glove-box style setup with fully exhausted HEPA-filtered air.	

BSC Selection Through Risk Assessment

Suitable For Work At	BSC Class	Personnel Protection Provided?	Product Protection Provided?	Environment Protection Provided?
BSL 1-3	I	Yes	No	Yes
BSL 1-3, BSL 4 (suit lab)	II (A1, A2, B1, B2)	Yes	Yes	Yes
BSL 4 (none at Harvard)	III	Yes	Yes	Yes

BSC Characteristics Comparison

BSC Class	Face Velocity (ft/min)	Airflow Pattern	Nonvolatile Toxic Chemical and Radionuclides	Volatile Toxic Chemicals and Radionuclides[10]
I	75	Air is pulled in at front, through HEPA to the outside or into the room through HEPA.	Yes	Yes (when exhausted outside)
II, A1	75	70% recirculated to the BSC work area through HEPA. 30% balance can be exhausted through HEPA back into the room or to outside through a canopy hood.	Yes	Yes (when exhausted outside)
II, B1	100	30% recirculated, 70% exhausted. Exhaust BSC air must pass through a dedicated, internal BSC duct to the outside through a HEPA filter.	Yes	Yes (determined by risk assessment)
II, B2	100	Total exhaust to the outside through hard-duct and a HEPA filter. Affected by building exhaust system status.	Yes	Yes (determined by risk assessment)

[10] BSCs aren't designed for using large volumes of hazardous chemicals, particularly volatile compounds. Contact EHS for a risk assessment before working with chemicals in a BSC.

BSC Class	Face Velocity (ft/min)	Airflow Pattern	Nonvolatile Toxic Chemical and Radionuclides	Volatile Toxic Chemicals and Radionuclides[10]
II, A2	100	Like II, A1, but higher intake air velocity. Exhausted through HEPA back into the room or to outside through a canopy hood.	Yes	Yes (when exhausted outside)
III	N/A	Supply air is HEPA-filtered. Exhaust air passes through two HEPA filters in series and is exhausted to the outside via a hard connection.	Yes	Yes (determined by risk assessment)

BSC Installation

The air curtain at the front of the BSC is fragile, creating a downward and inward air velocity of only 1 mph or less than 80 ft/min. This air curtain is easily disrupted.

Locate BSCs away from air supply registers, entrances and exits, high traffic areas, and lab equipment (such as fume hoods or centrifuges) which can disrupt airflow.

BSC Certification

The National Sanitation Foundation (NSF) International Standard 49 for Class II Biohazard Cabinetry establishes performance criteria and minimum requirements for design, manufacture, and testing.

- BSCs used to contain biological materials must be professionally certified after installation, annually, and after they are moved or serviced.
- BSCs must be professionally decontaminated before disposal, removal, or relocation from a lab space.

- BSCs that don't pass certification or were relocated must be posted as not to be used for worker protection (BSL2 and above) until they are recertified. Labs can use the Non-Certified BSC Sign template.

BSC Safe and Effective Use

Before Beginning BSC Work

- Make sure the BSC certification is unexpired, within 12 months of the last certification.
- Monitor alarms, pressure gauges, or flow indicators for any changes.
- Turn on the blower and let it run for 3 to 5 minutes.
- Wipe the work surface, interior BSC walls, and sash with an appropriate disinfectant.
- Plan your work and place everything you need for the procedure inside the BSC.
- Before placing items in the BSC, wipe them with an appropriate disinfectant.
- Setup to work from clean to dirty.

During BSC Work

- To avoid airflow disruption that could affect the level of protection provided by the BSC:
  - Minimize movement in and out of the BSC and abrupt side to side motions.
  - Move your arms slowly when removing or introducing items.
- Only place what is necessary for the experiment inside the BSC to keep the cabinet free of clutter.
- Keep all materials at least 4 inches inside the front sash.
- Don't place objects over the front or rear intake grilles.
- Limit traffic in the area when the BSC is in use.
- Keep nearby lab doors closed and avoid opening and closing the door located near the BSC.

- Segregate contaminated and clean items. Work from clean to dirty, left to right or right to left.
- To minimize the potential for cross contamination, keep clean materials at least 1 foot away from any aerosol-generating activities.
- Place any equipment that creates air turbulence in the back third of the BSC and stop other work while the equipment is running.
- Avoid using Bunsen burners or other open flames in the BSC, which can disrupt air flow and damage the HEPA filter.
- When working with infectious materials, change gloves when moving in and out of the BSC.
- Clean up all spills in the BSC. Let the BSC run for 3 to 5 minutes before resuming work.

After Completing BSC Work

- Don a new pair of gloves.
- Wipe down all items with an appropriate disinfectant before removing them.
- Remove all materials and wipe all surfaces inside the BSC with an appropriate disinfectant.
- After completing work and removing your gloves, wash your hands.
- Periodically decontaminate and clean under work grilles. Once every 3 to 6 months is recommended and immediately after any known spills.

Horizontal and Vertical Laminar-Flow Clean Benches

Horizontal and vertical laminar-flow “clean benches” aren’t BSCs. They discharge HEPA-filtered air across the work surface and toward the user. These benches only provide product protection.

- Don’t use these benches when handling biohazardous materials or drug formulations. They can expose workers to the materials being manipulated on the clean bench and lead to hypersensitivity.

- Don’t use these benches instead of a BSC for biological applications requiring containment of or protection from the materials being used.

Standard Microbiological Practices

Standard microbiological practices are proper work practices to prevent exposure to biohazardous materials and protect the environment. These basic work practices also help reduce the risk of cross-contamination and improve the quality of work.

Practices include:

- Use aseptic techniques for all procedures, even if they don’t involve infectious materials.
- Wash hands after working with biological materials and before leaving the lab.
- Wear gloves, lab coats, eye protection, and other relevant PPE.

  Don’t reuse disposable PPE.

  Don’t take reusable PPE home. Reusable PPE must be laundered by a vendor or decontaminated onsite.
- When in lab areas, don’t eat, drink, smoke, handle contact lenses, apply cosmetics (such as hand lotion and lip balm), or store food for human consumption.
- Don’t handle, store, or charge personal cell phones in lab work areas (including at benches and BSCs).
- When pipetting, use mechanical pipetting devices. Don’t perform mouth pipetting.
- For rooms where infectious agents are used, ensure rooms are appropriately signed to show infectious agents are present and any additional precautions required for entry.
- For lab equipment used with materials requiring BSL2 containment or higher, label equipment with the universal biohazard symbol.
- Whenever practical, lab supervisors should adopt improved engineering and work practice controls that reduce the risk of sharps injuries.

Always take precautions with sharp items, including:

- Securely store sharps in a manner to prevent injury.
- Ensure needles aren't ever bent, sheared, broken, recapped, removed from disposable syringes, or otherwise manipulated by hand before disposal.
- Carefully place used disposable needles and syringes in conveniently located, puncture-resistant containers used for sharps disposal.
- Place non-disposable sharps in a hard-walled container for transport to a processing area for decontamination, such as by autoclaving.
- Don't handle broken glassware directly. Instead, remove it using a brush and dustpan, tongs, or forceps.
- Substitute plasticware for glassware whenever possible.
- Perform all procedures to minimize creating splashes and aerosols.

- Follow aspiration guidelines for culture work.
- Decontaminate work surfaces after completing work and after any spill or splash using an appropriate disinfectant for the material.
- Carry any viable cultures, stocks, and other biohazardous materials in a durable, leak-proof container. Decontaminate the outer surface and secure the container for transport.
- Lab personnel must receive proper safety training in lab-specific procedures and methods by a qualified and experienced person. Personnel must receive annual updates or additional training when procedures or policies change.
- All lab personnel should receive information about immunocompetence and conditions that may predispose them to infection, like reproductive risks. Those with these conditions are encouraged to self-identify to the institution's healthcare provider for appropriate counseling and guidance.

Personal health status may impact a person's susceptibility to infection or ability to receive immunizations, prophylactic interventions, or treatments.

- After performing work with animal pathogens in the laboratory, personnel must avoid vivarium spaces on campus or shower and change clothes prior to entry. A shower and clothes change should be performed before interactions with pets or livestock.

Lab Training

Harvard uses the Harvard Training Portal (HTP) to administer initial training required for all new lab personnel. Additional training depends on the type of research conducted, applicable regulations and institutional policies, and any lab or individual specific requirements.

PIs and lab managers should review the COMS Training Policy to establish necessary training for their staff.

- EHS provides general environmental health and safety training about regulations and guidelines, safe work practices, and emergency response procedures. BSOs can help provide agent-specific training as required.
- PIs or their designee must provide training about lab-specific hazards and safety controls to supplement EHS safety training.
- Lab-specific training must include reviewing procedures and hazards inherent in the type of experiments conducted. Labs should document this training and keep training records. For help with this process, follow the Lab Safety Orientation Checklist.

Training Roles

Role	Description and Responsibilities
Training manager (PI or their designee)	Individuals who directly manage or oversee a group of people who need training: • Create and manage a training roster or audience of lab personnel. • Oversee and assign relevant trainings to lab personnel.
Trainee	Lab personnel listed on a PI's or lab director's roster or audience who must complete lab safety training.

EHS-Provided Trainings

These are the most common safety trainings required for lab personnel who work with biohazards.

- Lab personnel actively working with biological materials must complete Laboratory Biosafety (LAB 103) initially and its refresher (LAB 203) at least annually as long as they continue working with biological materials.
- PIs who must register their work with COMS must complete NIH Guidelines Training for the PI (LAB 110).
- Other training courses may depend on job functions or tasks.

Initial Course	Refresher Course	Refresher Frequency
General Laboratory Safety (LAB 100)	General Laboratory Safety Refresher (LAB 200)	Annual
Laboratory Biosafety (LAB 103)	Laboratory Biosafety Refresher (LAB 203)	Annual

Initial Course	Refresher Course	Refresher Frequency
Shipping Regulated Biological Materials and Dry Ice (LAB 104)	Shipping Regulated Biological Materials and Dry Ice (LAB 104)	Every two years
Shipping Excepted Quantities: Flammables, Corrosives, and Common Fixatives (LAB 109)	Shipping Excepted Quantities: Flammables, Corrosives, and Common Fixatives (LAB 109)	Every Two Years
Biosafety and Biosecurity Compliance for the PI (LAB 110)	Biosafety and Biosecurity Compliance for the PI (LAB 110)	Every three years
Shipping Dry Ice (LAB 114)	Shipping Dry Ice (LAB 114)	Every two years
Respiratory Protection (IHS 107)	Respiratory Protection Refresher (IHS 207)	Annual
Biological Import/Transport Permits (EHS-0000066003)	Not applicable	Not applicable

Decontamination

Decontamination is a process that reduces microbial contamination to a level unlikely to produce disease in healthy people, plants, or animals. Sterilization, disinfection, and sanitization provide different levels of contamination reduction and inactivation of viable microorganisms, with sterilization being the most stringent.

Selecting a Decontamination Method

Decontamination methods include chemical (liquid, vapor, or gas), heat (wet or dry), or radiation. The appropriate method depends on the agents used and what is being decontaminated.

EHS doesn't endorse radiation, including ultraviolet (UV) light, as a decontamination method at Harvard. To learn more, review Culture Contamination Follow-up and Decontamination.

Disinfectants

Wherever feasible, consider consulting the Environmental Protection Agency (EPA)-registered disinfectants list when selecting chemical disinfectants or sterilants. This list includes products validated to inactivate specific agents or materials.

Labs performing work under the OSHA Bloodborne Pathogens Standard must consult and use a disinfectant from the EPA's Registered Antimicrobial Products Effective Against Bloodborne Pathogens: HIV, Hepatitis B and Hepatitis C [List S].[11]

Autoclave Sterilization

Autoclaves are available across campus for heat-sterilization of glassware and media.

Autoclaves used to fully inactivate biological materials, like biological waste, must be periodically validated to ensure they meet temperature and pressure requirements. The lab or facility must maintain validation test results, use logs, and disposal logs for at least 3 years.

Consult EHS Biosafety for guidance before using autoclaving as an inactivation method for biologicals.

Contaminated Surface Decontamination

The most common form of decontamination in labs is liquid chemical disinfection of surfaces.

- At minimum, decontaminate surfaces after work and immediately after spills. Consider also disinfecting surfaces before work to reduce any remaining contamination.

[11] The EPA used to separate these disinfectants under EPA List C, List D, List E, and List F.

- To help select chemical disinfectants, follow the Disinfection Guide in conjunction with applicable EPA-registered disinfectant lists.
- When using any disinfectant, always follow the manufacturer's instructions for disinfection.
- Date all disinfectants with the date received.

When selecting a disinfectant, consider:

Disinfectant Characteristic	**Considerations**
Efficacy	Select a disinfectant that's effective against the organisms you plan to handle. Different chemical disinfectants have different active ingredients that impact efficacy. Some organisms, like spore-producing bacteria or prions require specific types of disinfectants or disinfection protocols. Non-enveloped viruses and bacteria with cell walls are more resistant to certain disinfectants. Enveloped viruses are susceptible to a broader range of disinfectants. High organic loads can reduce a disinfectant's efficacy, even disinfectants effective against the specific organisms in use.

Disinfectant Characteristic	Considerations
Contact time	Follow the product label for how long the disinfectant must remain in contact with the surface to disinfect the material. Different materials or organisms may require different contact times. For general disinfection of contaminated surfaces, use the longest contact time listed. Consider the feasibility of the required contact time when selecting a disinfectant. Disinfectants like activated hydrogen peroxide products have very short contact times for many organisms. Ensure the disinfectant keeps the surface wet for the entire contact time.
Shelf life	Dispose of and replace disinfectants after their expiration date. The shelf life of concentrated bleach is 12 months. Use 10% bleach solutions for surface disinfection within 7 days, ideally making fresh dilutions daily. Store disinfectants in opaque bottles to reduce the decomposition rate.
Formulation	Ready-to-use formulations save time and prevent dilution errors. Concentrated disinfectants that must be diluted to a working concentration have a much shorter shelf life.
Toxicity	Disinfectants with toxic ingredients require additional PPE. Check the manufacturer's instructions and safety data sheet (SDS) for appropriate control measures.

Disinfectant Characteristic	Considerations
Compatibility	Consider chemical compatibility with surfaces and other materials that may come in contact with the disinfectant. For example, bleach can be corrosive to surfaces if not rinsed after use. Keep bleach separate from ammonia-containing disinfectants.
Cost	Ready-to-use formulations may cost more initially but save time spent diluting concentrated disinfectants.
Odor	Some disinfectants have an unpleasant odor.
Residue and staining	Some disinfectants leave a residue or discolor clothing or surfaces (like iodine-based products).

Equipment Decontamination

Decontaminating equipment follows the same basic principles as surface decontamination. However, consider reading the equipment manuals and consulting EHS Biosafety to ensure that the disinfectant is compatible with the biological agents in use and the equipment being decontaminated.

Decontaminate all equipment used with biological materials before it is serviced, relocated, or disposed of. Labs must perform and document the decontamination using the Laboratory Equipment Decontamination Form.

A third-party vendor must perform full decontamination of BSCs, incubators, and more complex equipment using vapor or gas decontamination. Contact EHS Biosafety for assistance.

Room Decontamination

Large-scale room or facility decontamination requires vapor or gas decontamination and must be performed through a third-party vendor. Contact EHS Biosafety for assistance.

Biological Waste Decontamination

See Biological Waste Management.

Aerosol Reduction Work Practices

A significant number of lab procedures can create biological aerosols that can be hazardous to personnel and the environment. Standard microbiological practices minimize aerosols, but specific precautions contain or reduce aerosol generation even further.

Standard Work Practices

- When working with infectious or potentially infectious materials, perform aerosol-generating procedures in a BSC or fume hood if feasible.
- When spills occur, leave the area to let any aerosols settle before addressing the spill.

Lab Procedures with Aerosol Potential

Contact your BSO to determine other requirements or recommendations for additional work practices and equipment, like using cell sorters.

Pipetting

- Dispense liquids as close to the reservoir as possible.
- Be cautious when removing pipettes or pipette tips from infectious liquids and when depositing them in waste containers for later disposal.

Syringe Use

- Avoid air bubbles when discharging liquid.

Inoculation Loops

- Use pre-sterilized, disposable loops when possible.
- When heat-sterilizing reusable loops, let the loop cool before introducing it to any potentially infectious materials.

Liquid Decanting

- Pour liquids carefully and as close to the receiving vessel as possible.

Animal Inoculation

- Remove syringe needles and gavage from animals slowly, with a smooth and steady motion.

Vortexing

- Ensure all substances being vortexed are in a durable primary container with a tight-fitting lid.

Blending or Homogenizing

- Operate the equipment in a BSC or fume hood if using an infectious material.
- Use a lab grade blender with a tight-fitting lid.
- Allow aerosols settle before opening the lid.

Sonication

- If using an infectious material, operate the sonicator in a BSC, fume hood, or aerosol containment device.

Centrifuging

- Use aerosol-proof rotors or safety buckets with caps that seal with O-rings, when required by COMS.
- Before use, inspect O-rings and safety caps for cracks, chips, and erosion.

- Load and unload rotors and buckets inside a BSC or fume hood, when required by COMS.
- Use tubes with threaded caps.
- Avoid overfilling the tube and getting caps and closures wet.
- Wipe tubes down with disinfectant after filling.
- Balance buckets, tubes, and rotors before centrifuging.
- Wait a few minutes after centrifuge completes to allow aerosols to settle.
- Disinfect the centrifuge after use.

Vacuum Flask and Aspiration Set-Ups

- Follow Aspiration/Vacuum Flask Set-Up for aspirating biological materials.
- Protect house vacuum lines and vacuum pumps by using a hydrophobic filter installed between the collection flask and vacuum source.
- If required, you must use a HEPA filter to protect against infectious aerosols.

Safe Sharps Handling

The term “sharps” refers to any instrument that can cause punctures, cuts, or scrapes. Common examples of sharps include:

- Needles
- Syringes
- Scalpels
- Razor blades
- Slides

- Coverslips
- Glass Pasteur pipettes
- Capillary tubes
- Sharp or broken glass
- Lancets
- Microtome or cryostat blades

Sharps Precautions

- Labs should review the COMS Sharps Policy.
- Sharps are regulated medical waste. Don't dispose of sharps in regular trash.
- Restrict the use of sharps to trained personnel and only use sharps when no alternative is available.

  Avoid using needles and other sharps whenever possible. Use blunt tipped needles, safety devices, and plastic alternatives to glass, as feasible.
- Minimize contact with sharps by disposing or storing them immediately after use.
- Ensure needles are not recapped, removed from the syringe, sheared, bent, or broken.
- Use a mechanical device to remove blades from holders. Never use your fingers.
- Follow Cryostat SOP and Safety Guidelines for work with cryostats and microtomes.

Biological Waste Management

Multiple agencies regulate the management of biological waste.[12] Biological or regulated medical waste includes:

- Human blood and materials contaminated with human blood.
- Human parts, tissues, and fluids.
- Infectious agent cultures and all non-decontaminated labware used with cultures generated in research and clinical labs.
- Biotechnology by-product effluents such as cultures and solutions contaminated with microorganisms (including those genetically altered).
- Animal carcasses, body parts, body fluids, blood, and bedding.
- Unused or biologically contaminated sharps.
- Recombinant and synthetic nucleic acids.

Sharps Waste

- Dispose of all sharps into an approved, puncture resistant, and closable sharps container.
- For sharps used with biological materials, collect sharps in red, biohazard sharps containers for disposal.

[12] The Massachusetts Department of Public Health (MADPH): 105 CMR 480.00: State Sanitary Code Title VIII and Massachusetts Department of Environmental Protection (MassDEP): 310 CMR 19.000: Solid Waste Management Regulations regulate the management and disposal of infectious waste. Local Boards of Health, the Massachusetts Department of Telecommunications & Energy, and the U.S. Department of Transportation (DOT) (Hazardous Materials 49 CFR Parts 100–185) regulate transporting infectious waste.

- Only fill sharps containers to the fill line or no more than three-quarters full. Don't overfill sharps containers.
- When a sharps container is three-quarters full, close it and arrange for disposal:
  - For disposable containers, place sealed containers in a biowaste box or bin.
  - For reusable containers, submit a waste vendor pickup request (currently only available in specific campus locations).
- Don't force materials into a sharps container or reach into a sharps container.
- Keep sharps containers upright on the floor or work surface.
- Don't remove the lid from the sharps container.
- Refer to the EHS Lab Waste Guide for instructions on how to dispose of sharps with mixed contamination.

Solid Biological Waste

Wear a lab coat, safety glasses, and disposable gloves when handling biological waste.

Certain materials may require inactivation before being placed in the biowaste container for final disposal, including:

- Materials listed as Category A infectious substances by DOT.
- USDA or CDC-permitted materials where the permit requires on-site decontamination.

Contact EHS Biosafety with questions or to ensure proper treatment of solid biological waste. Also review the COMS Solid Waste Policy for more information.

To collect non-sharps, solid biological waste:

1. Collect biological waste in red bag-lined biowaste cardboard boxes or reusable plastic bins for pick-up and off-site treatment.

2. When containers are three-quarters full, tie off the red bag liner with a single knot and tuck bag completely inside the container.
3. If using cardboard boxes, tape the cover or box closed with packaging tape.
4. For plastic reusable containers, snap the cover flaps shut.

Incinerate Only Biological Waste

Pathological wastes (animal carcasses, body parts, tissues, organs, and surgical specimens) and some USDA or CDC-permitted wastes require incineration as the final means of disposal.

- Segregate waste for incineration.
- Collect waste in cardboard biowaste boxes using two red bag liners.
- Check the checkboxes for “Incineration Only” printed on the biowaste box.

  If pathological waste, also check the box “Pathological Waste”.
- To avoid nuisance odors, package and transfer pathological waste from freezers or refrigerators to the cardboard boxes according to the waste vendor’s pick-up schedule. Contact the Operations Center in your location to determine the pickup schedule.

Mixed Biohazardous Waste

Mixed Waste Type	Disposal
Animal or human tissue treated with a chemical fixative	Processed as solid chemical waste. Label the hazardous waste with the appropriate chemical hazard and identify the waste as non-infectious animal or human tissue. **Don’t autoclave materials treated with a chemical fixative.**

Mixed Waste Type	Disposal
Mixed biological, chemical, or radioactive waste	Reference the EHS Lab Waste Guide. Follow special procedures for decontamination and disposal. For guidance, contact EHS. **Don't autoclave materials treated with chemicals or radionuclides.**

Liquid Biological Waste

Treat liquid biological waste with an appropriate decontamination method before sink drain disposal. Review the COMS Liquid Waste Policy for more information.

1. Labs should use a final concentration of 10% bleach (0.525%, sodium hypochlorite solution) to inactivate liquid waste. Add concentrated bleach from the manufacturer's container to the waste to reach 10% of the total volume.
2. Allow a minimum contact time of 20 minutes before drain disposal.
3. Carefully pour the disinfected liquid waste down the sink drain and flush with generous amounts of water.

Some biological agents, select agent toxins, and prions may need an alternative disinfection method. In that case, please refer to the recommendations in the COMS approval letter, your select agent toxin SOP, or contact EHS Biosafety for guidance.

Certain mixed chemical and biological waste generated in the labs may not be compatible for disinfection with bleach and may produce hazardous gases when mixed with bleach. For example, DNA/RNA extraction kits potentially have ingredients that shouldn't be mixed with bleach.

Contact EHS Biosafety to evaluate other liquid waste treatment methods before use.

Personal Protective Equipment

PPE is used to protect personnel from direct contact with infectious agents.

- Supervisors are responsible for conducting lab PPE assessments, providing appropriate PPE, and training personnel in proper PPE use.
- Don't take PPE home or wear it outside the lab.
- Provide PPE for visitors, maintenance personnel, and cleaning personnel, as required.

For COMS-regulated work:

- The level of PPE is dictated by the BSL of the work and the risks of the agents in use.
- In addition to PPE, wear garments that fully cover one's legs and shoes that cover the entire foot.
- COMS-specific PPE requirements can be found in the COMS approval letter and COMS Policies Appendices.
- COMS approval letters may include recommendations for additional PPE stipulations based on risk assessments.

For help selecting PPE for work with biological materials, contact EHS Biosafety.

For general PPE guidance, refer to PPE Selection by Task or Activity Guide and PPE Selection by Type.

Lab Coats or Gowns

Wearing a lab coat or gown prevents workers from contaminating skin and everyday clothing worn outside the lab.

- Always wear lab coats while performing lab work in BSL2 labs.
- Strongly consider wearing lab coats while performing work in BSL1 labs.
- Lab coats may be required for other non-biological hazards present.

Gloves

- Wear disposable lab gloves for work with CRM at BSL1 and above.
- Change your gloves when contaminated or compromised.
- When choosing gloves, consider compatibility with both the biological and non-biological hazards being manipulated.
- Consider wearing gloves for all materials to avoid cross-contaminating experiments.
- Suitable alternatives to latex gloves should be available, as required.
- Double-gloving adds further protection when applied appropriately. You must double-glove under BSL2+ containment.
- Never reuse disposable gloves.

Eye and Face Protection

- Consider wearing eye protection (such as safety glasses or goggles) for all lab procedures.
- Always wear eye protection for procedures likely to result in splashes or sprays on open benches.
- Take extra precautions and consider eye protection if you wear contact lenses, as your eyes can't be as easily flushed following an exposure.
- Use goggles, face shields, or other splatter guards for added protection from anticipated splashes or sprays of infectious material for procedures conducted outside of containment.

Respiratory Protection

Lab personnel who are required to wear respiratory protection must be evaluated by a physician and trained in respirator selection and use. Review Respirator Evaluations and Requests or contact EHS for more information.

Incidents and Reporting

While appropriately implementing engineering, work practices, and PPE controls reduce the chance and severity of accidents and injuries within biological labs, it's still important to prepare for such emergencies.

Emergency Response Guide

- The Emergency Response Guide (ERG) contains procedures for spills, exposures, incidents, and reporting and contact information.
- An Emergency Response Guide (ERG) must be accessible in each lab.
- PIs or their designees must review the ERG with new personnel.

BSL3 lab emergency response procedures are separately described in the lab-specific manuals.

Reporting Incidents

- Immediately report incidents involving CRM to the PI and EHS Biosafety. EHS Biosafety notifies regulatory agencies and COMS as necessary.
- Report all injuries, accidents, animal bites, and exposures through the University-wide incident reporting system.

Medical Emergencies

For serious medical emergencies:

Call 911 or go to the nearest emergency room.

Contact Harvard University Police Department (HUPD) for assistance with transport or to ensure access for emergency medical services (EMS) personnel.

Other Emergencies or Incidents

Follow all procedures in the ERG.

Occupational Health and Medical Surveillance

Following regulatory requirements, Harvard provides occupational health evaluations, medical surveillance, and treatment for personnel who may be occupationally exposed to workplace hazards.

General Medical Surveillance and Treatment

Harvard's Occupational Health provider offers consultations, medical treatment, and post-exposure evaluation to students and employees working in labs.

For emergencies involving potential or confirmed exposure to biological materials, contact the Exposure Response Call Center (ERCC): 1-866-360-8100.

For other occupational health inquiries, contact EHS.

Working with Research Animals

Personnel with direct contact with research animals must receive medical surveillance.[13]

The program includes pre-screening questionnaires, animal and job-specific occupational health evaluations and training, vaccinations as required, PPE assessments, and post-exposure medical treatment and evaluation.

Contact your IACUC program administrator for more information.

[13] This requirement is mandated through the respective Institutional Animal Care and Use Committee (IACUC) on Cambridge, Longwood, and other Harvard campuses.

Working in Biosafety Level 3 Labs

Each BL3 lab has a detailed Occupational Health Management and Response Program.

BL3 manuals include separate procedures for:

- Medical surveillance.
- Respirator medical evaluation.
- Post-exposure care for BSL3 lab personnel.

BL3 lab directors administer these procedures.

Shipping Biological Materials

Shipments of research materials that may be classified as hazardous materials or dangerous goods by the DOT and the International Air Transport Association (IATA) must be managed in accordance with very strict requirements.

All Harvard shipments must follow the requirements of the Research Material Shipment and Transport Manual.

The shipper (individual who packages, labels, and prepares paperwork for a shipment) of any biological material is ultimately responsible for the package throughout its shipment.

Shipper responsibilities include:

- Completing function-specific training every two years and following DOT and IATA regulations.

  Researchers who ship biological research materials can complete HTP trainings to meet these requirements.

- Classifying the material correctly.

- Packaging and securing the material for shipment by using the correct packing instructions as provided in the EHS-provided function-specific shipping training.
- Labeling the outer package appropriately.
- Completing the air waybill and other shipping paperwork.
- Retaining shipping documentation for the required length of time.

Shipping Permits and Licenses

In addition to the DOT and IATA training and packaging requirements for shipments of biologics and other dangerous goods, shipping or receiving research materials may also require import permits, transport permits, and export licenses.

Import and Export

Import and export requirements vary based on the port of entry (import location).

Check with your contact in the receiving institution to make sure they have the required permits in place to receive the research materials being sent.

Enclose a copy of any permits or licenses in the shipment to avoid delays.

If you are receiving the materials, send the shipper any required permits to include in the shipping documentation.

Export Control Licenses

A Harvard Export Control Officer must evaluate all shipments sent from the United States to a foreign country. Contact your Export Control Administrator before shipping materials internationally.

The Department of Commerce (DOC) requires export licenses for a wide variety of disease-causing agents, genetic material from these agents, and other products derived from them. This includes agents that affect humans, plants, and animals.

Limitations may also be placed on who may receive the materials and the intended use of the materials.

Biological Permits

Agencies like the CDC, USDA/APHIS, Food and Drug Administration (FDA), and Fish and Wildlife Service (FWS) regulate import or interstate transport of certain biological materials.

Harvard or Harvard personnel can't receive regulated materials until all permits are issued.

Agencies that issue permits may require an inspection of the recipient's facility and safety validation from EHS.

To help researchers determine when permits are necessary, review Regulated Biological Materials Permits and complete Biological Import and Transport Permits training.

Contact EHS Biosafety with permitting questions or if an agency contacts you for an inspection. EHS Biosafety can also help with the permit application and inspection process.

Lab Move-In and Closeout

A successful lab move requires cooperation and effective communication between lab department contacts, DAs, lab coordinators, move coordinators, space coordinators, lab personnel, EHS, and support vendors.

Depending on the processes and materials the lab will be moving into or out of the spaces, the move may require a lead time of several months.

Departments and PIs should consider contacting their respective EHS Biosafety contact as soon as possible when a lab move is impending.

Follow these checklists for help with the setup and moveout processes:

- Lab Move-In Checklist
- Lab Moveout or Renovation Guidelines

Labs must follow a separate decommissioning process when either:

- Transitioning a lab space to a non-lab space.
- Transitioning to a lab space involving significantly different hazards.

If your lab is considering lab decommissioning, contact EHS for more information and assistance.

Appendix I. Regulations, Guidelines, and Policies

This section contains a summary of federal, state, and local agency regulations and institutional policies that govern biological agents in research at Harvard.

Regulatory Entity	Summary
BMBL	Guidelines for microbiological best practices, safety equipment, and facilities of established BSLs. Generally considered the standard for biosafety in the United States and is the basis for this manual.
NIH Guidelines	Standards for constructing and handling recombinant or synthetic nucleic acids molecules and organisms containing recombinant or synthetic nucleic acids. Institutions that receive NIH funding for recombinant or synthetic nucleic acids research must follow the NIH Guidelines. Each institution must establish an IBC with the authority to approve proposed recombinant or synthetic nucleic acids research.

Regulatory Entity	Summary
OSHA Bloodborne Pathogens Standard (29 CFR 1910.1030)	Standard for occupational exposure to human blood and OPIM, including human tissue and cells. Specifies a combination of engineering controls, work practices, and training to reduce infection risk. Protects those with reasonably anticipated occupational exposure by reducing exposure risks to bloodborne pathogens. Personnel potentially exposed to human blood and OPIM must receive annual training and be offered immunization against HBV. Personnel who work with HIV or HBV in research labs must receive additional training, demonstrate proficiency in working with human pathogens, and follow other requirements specific to HIV and HBV research labs.
BPHC Biological Laboratory Regulations (As of January 16, 2019) BPHC Biological Laboratory Regulations Implementation & Enforcement Guidelines (As of October 15, 2019)	Institutions in Boston working with recombinant or synthetic nucleic acids molecules (BSL2 and above) or operating BSL3 or BSL4 labs must be permitted by BPHC. Requires strictly following the CDC and NIH guidelines and other regulations that the BPHC may reference.

Regulatory Entity	Summary
BPHC Disease Surveillance and Reporting Regulation	All institutions in Boston that do research with select agents, RG4 agents, and other BPHC high-risk agents must maintain disease surveillance and reporting programs to minimize potential exposures to these agents.
Cambridge Public Health Department Cambridge Biosafety Regulation and rDNA Technology Ordinance	Oversight of university and commercial labs that do recombinant or synthetic nucleic acids research within Cambridge. Requirements are based on NIH Guidelines.
MADPH Center for Environmental Health	Regulations for storage and disposal of potentially infectious material and requirements for labeling and recordkeeping. 105 CMR 480.000 oversees proper disposal of regulated medical or biological wastes.

Regulatory Entity	Summary
Select Agent Rule, Department of Health and Human Services (HHS): 42 CFR Parts 42 and 43 Possession, Use, and Transfer of Select Agents and Toxin; Final Rule; and USDA/APHIS: 7 CFR Parts 331 and 9 CFR Parts 121, Agricultural Bioterrorism Protection Act of 2002: Possession, Use, and Transfer of Biological Agents and Toxin; Final Rule	Institutions that possess, use, or transfer biological select agents and toxins in regulated forms must register with and receive approval from either or both HHS and USDA/APHIS.

Regulatory Entity	Summary
United States Government Policy for Oversight of Dual Use Research of Concern (DURC) and Pathogens with Enhanced Pandemic Potential (PEPP)	Unifies the oversight framework for federally funded research on biological agents and toxins that pose risks to public health or national security through a risk-based approach. Classifies research under Category 1 (DURC) or Category 2 (PEPP) through evaluation of the specific agents in conjunction with the anticipated research outcomes.
Framework for Nucleic Acids Synthesis Screening	Federal agency requirements for the procurement and provision of nucleic acid sequences and synthesis equipment.
DOT and IATA	Requirements for shipping and transporting hazardous materials, including biological agents.
CDC: Import Permits U.S. Public Health Service (USPHS) 42 CFR - Part 71 Foreign Quarantine. Part 71.54, 71.54 Import regulations for infectious biological agents, infectious substances, and vectors	Regulates the importation of infectious biological materials that could cause disease in humans. Includes a permit application that must be submitted and approved before importing these agents.

Regulatory Entity	Summary
USDA/APHIS	Import and interstate transport regulations for animals and animal-derived materials, plants and plant products, plant pests, and animal and plant pathogens. Includes a permit application that must be submitted and approved before receiving these agents.
DOC	Strictly follow these agent-specific and country-specific requirements for exporting biological materials.
COMS (IBC)	Institutional policies and procedures for work with biological materials.

Appendix II. Key Contacts

Emergency Phone Numbers

Location-specific emergency phone numbers (view Resources section).

EHS Biosafety

Contact Type	Contact Information
General inquiries	biosafety@harvard.edu
School, unit, or lab	BSOs and biosafety contacts

Occupational Health

Contact Type	Contact	Contact Information
Exposures	Exposure Response Call Center	1-866-360-8100
Other inquiries	EHS	Contact EHS

COMS Office

Contact Type	Email Address
General inquiries	coms@hms.harvard.edu

IACUC Offices

Campus	IACUC Program Administrator Email Address
Cambridge and Allston	iacuc@fas.harvard.edu

Campus	IACUC Program Administrator Email Address
Longwood	iacuc@hms.harvard.edu