



HARVARD
Campus Services
ENVIRONMENTAL HEALTH & SAFETY

Harvard University

Biosafety Manual

Table of Contents

1. <u>Introduction and Roles of Key University Personnel</u>	Pg. 1
2. <u>Principal Investigator Responsibilities</u>	Pg. 5
3. <u>Committee on Microbiological Safety (COMS)</u>	Pg. 6
4. <u>Incidents and Reporting</u>	Pg. 8
5. <u>Laboratory Training</u>	Pg. 10
6. <u>Occupational Health & Medical Surveillance</u>	Pg. 12
7. <u>Personal Protective Equipment</u>	Pg. 13
8. <u>Standard Microbiological Practices</u>	Pg. 14
9. <u>Laboratory Aerosols</u>	Pg. 15
10. <u>Biological Safety Cabinet Use</u>	Pg. 18
11. <u>Types of Biological Safety Cabinets</u>	Pg. 19
12. <u>Safe Sharps Handling</u>	Pg. 25
13. <u>Biological Waste Management</u>	Pg. 26
14. <u>Biological Spill Procedures</u>	Pg. 28
15. <u>Biological Risk Assessment</u>	Pg. 29
16. <u>Tissue and Cell Culture</u>	Pg. 30
17. <u>Select Agents and Exempted Quantities of Select Agent Toxins</u>	Pg. 31
18. <u>Shipping Biological Materials</u>	Pg. 34
19. <u>Import Permits</u>	Pg. 35
20. <u>List of Regulations and Guidelines</u>	Pg. 38



Introduction and Roles of Key University Personnel

This Biosafety Manual provides a summary of pertinent federal and local government regulations, information about safe work practices, safety equipment and personal protective equipment, and guidance for researchers on Institutional Biosafety Committee registration.

The Campus' Laboratory Safety Program is based on the premise that every member of the research community shares the responsibility for safety.

This document serves as the Biosafety Manual for the following:

- Harvard Departments and Schools: FAS, SEAS, Arnold Arboretum, Concord Field Station, HMS, HSDM, and HSPH.
- The Wyss Institute.

Harvard University laboratories support research utilizing BSL1, BSL2 and BSL3 containment and work practices. There are no BSL4 labs at Harvard.

Roles of Key Personnel:

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

Department Administrator (DA): The primary responsibility of the Department Administrator is to facilitate the compliance management program within his or her department and assist labs in remediating department-wide issues. The Department administrator will typically be assisted by a Research Operations Manager (ROM). It is the responsibility of the DA either directly or through a ROM to notify the EHS Office when a new Principal Investigator (PI) that will be supervising a laboratory has been accepted to their Department.

Research Operations Manager (ROM): These managers communicate EHS programs to the labs, PIs, and their appointed Safety Coordinators. They serve as the primary liaison between the EHS Department and their basic science department, and they monitor compliance and safety issues within their department. Note: some Harvard University schools may not have ROMS. In this case, the ROM's responsibility falls to the Laboratory Manager, Safety Coordinator, or PI.

Principal Investigator (PI): The PI is principally responsible for safety and environmental health in the laboratory and is responsible for identifying hazards associated with the job. S/he is responsible for modeling and reinforcing safe practices; ensuring that staff receives lab-specific and general training on hazards, protective procedures, and equipment; and ensuring that the lab follows pertinent regulations and prudent practices.



Safety Coordinator: A qualified laboratory employee (a “Safety Coordinator”) may assist the PI. The PI’s assignment of duties to such an assistant will not diminish the PI’s responsibility for environmental compliance in the laboratory. With the support of the PI, the Safety Coordinator’s responsibilities are to:

- Serve as a liaison for environmental, safety, and compliance communications within the laboratory, and coordinate follow-up to identified compliance concerns.
- Conduct joint safety assessments with the Department Research Operations Manager and/or EHS Department.
- Ensure that all personnel have completed the Training and Risk Assessment Form and have attended the required training classes.
- Complete Personal Protective Equipment (PPE) assessment forms for all activities within the laboratory and monitor PPE compliance.
- Ensure that all required safety equipment is used properly, and required documentation is maintained and accessible to laboratory personnel.
- Coordinate laboratory participation in periodic safety activities.
- Notify ROMs or Department Administrators of matters requiring the research department’s attention.
- Advise the PI, in writing, if appropriate, of any areas of non-compliance in the lab.

Environmental Health and Safety Department: The primary responsibility of the EHS Department is to provide technical support and guidance to laboratory personnel for the management of environmental and occupational safety compliance programs.

Evacuation Monitor: Walks through to verify that the area has been vacated or to identify persons needing assistance during building evacuation alarms.



Principal Investigator Responsibilities

Principal Investigators (PIs) or the Laboratory Director are responsible for the health and safety of all personnel and compliance with all applicable regulations and the criteria established in this manual in their laboratories.

Before beginning any research with biological materials, recombinant/synthetic nucleic acids, or any genetic manipulations of organisms, please contact biosafety@harvard.edu to begin an assessment of your work, assistance in setting up the appropriate safety controls, and the COMS biological research project registration.

Responsibilities of the PI include:

- Ensuring that specific laboratory hazards are effectively communicated to laboratory personnel;
- Ensuring that personnel have received appropriate training and are competent to perform procedures used in the laboratory
- Developing laboratory-specific standard operating procedures (SOPs) that cover the hazards and activities (both routine activities and unusual events) relevant to the laboratory.
- Ensuring that engineering controls are available, in good working order, and are used appropriately to minimize exposure to biohazardous agents.
- Ensuring that appropriate personal protective equipment is available and used by laboratory personnel.
- Ensuring that laboratory workers are provided immunizations and medical surveillance prior to, and in the event of, exposure to biohazardous agents as appropriate (based on current CDC and COMS recommendations).
 - Immunizations are available through Harvard University Health Services in both [Longwood and Cambridge campus locations](#).
- Notifying the Harvard Operations Center at (617) 495-5560 of any spills, incidents, involving biological agents that may result in exposure to laboratory personnel, the public, or release to the environment. The Operations Center will notify the EHS Biosafety Officer.
- Ensuring that biological agents are disposed of according to regulations, as outlined in this manual.
- Ensuring that any transportation or shipping of biohazardous materials to are packaged and documented in accordance with regulations.
- Ensuring that periodic inspections of the laboratory are conducted with EHS and a laboratory representative.

The responsibilities summarized here based on the requirements provided by the NIH rDNA Guidelines, OSHA Laboratory Standard, CDC Biosafety in Microbiological and Biomedical Laboratories (BMBL) 5th Edition, City of Cambridge and Boston Public Health Department Laboratory regulations as well as other applicable regulatory agencies.



Committee on Microbiological Safety (COMS)

Institutions that receive any research funding from the National Institutes of Health (NIH) are required to abide by the “[NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules](#)” (rDNA Guidelines). Harvard is required by the rDNA Guidelines to establish an institutional biosafety committee (IBC) to review research projects involving recombinant or synthetic nucleic acid molecules.

The IBC for Harvard is called the Committee on Microbiological Safety (COMS). COMS is responsible for reviewing these projects and also reviews and approves any biological research projects including the use of any microbial agents, potentially infectious materials, and any human studies.

COMS review includes projects involving the use of:

- Recombinant DNA (including creation of transgenic organisms)
- Synthetic Nucleic Acids
- Viral Pathogens
- Bacterial Pathogens
- Prions
- Biological Toxins
- Unfixed Human Blood and Tissues
- Unfixed Non-Human Primate Blood and Tissues
- Clinical Gene Transfer
- Clinical xeno-transplantation

COMS review process

Please contact biosafety@harvard.edu to initiate project registration for COMS approval. A brief overview of the process is described below:

1. Projects are submitted online via the [eCOMS](#) web based registration system. eCOMS requires an HUID and Pin to login.
2. The deadline for submittal is typically the first of the month for review by the committee at the end of the month.
3. Projects are initially reviewed by the Harvard Biosafety staff and assigned an appropriate biological safety level and work practices following a thorough risk assessment.
4. Review by the COMS committee
5. Communication of COMS decision to the PI via email or system notification.

Any of these may lead to a request for the PI to take further action, such as providing clarifications or modifying the project.



Additional COMS requirements:

- COMS requires annual laboratory inspections of both BL2 and BL3 laboratories and biennial inspections of BL1 laboratories.
- All PI's with COMS registrations must complete NIH rDNA training and a refresher at least once every 3 years. This training is accessed and completed online via the [Harvard EHS Training Management System](#).

Levels of Review:

Levels of external federal review required for rDNA experiments:

Review by	Experiment	Section
COMS, RAC, NIH OBA	Transfer of drug resistance that affects disease control	III-A
COMS, NIH OBA	Cloning toxin molecules with LD50 <100 ng/Kg body weight	III-B
COMS, RAC, IRB	Transfer of rDNA into human subjects	III-C

Levels of COMS review required for rDNA experiments:

Review by	Experiment	Section
COMS approval prior to initiation	Many experiments involving whole animals; cloning or host-vector experiments using rDNA or organisms in risk group 2, 3, 4 or restricted agents	III-D
COMS notice at same time as initiation	Creation of transgenic rodents (genome altered by rDNA introduced into germline) that require BL1 containment	III-E
Exempt from Guidelines but COMS requires registration	rDNA not in organisms or viruses; purchase of transgenic rodents that require BL1 containment; E. coli K12 host-vector system (COMS requires registration of all host-vector systems)	III-F

To determine whether your research is subject to Section III-A, B, C, D or E, please refer to the summary of [NIH rDNA Guidelines-Covered Experiments](#).



Incidents and Reporting

An [Emergency Response Guide Flipchart](#) should be posted in each laboratory. The guide contains procedures for spills, exposures, incidents, reporting instructions, contact numbers, and the location of emergency equipment. Principal Investigators or a designated lab safety coordinator must review the guide with new personnel.

Report all injuries, accidents, animal bites, and exposures to your supervisor, and complete the Harvard Accident Report Form.

Tenants in Harvard buildings should complete their Institution's accident report form(s).

Exposures and incidents involving genetically modified or infectious materials should be reported immediately to your PI and the Harvard Biosafety Office, which will notify the appropriate regulatory agencies and COMS as necessary.

Medical Emergency

For serious medical emergencies, call 911 or go to the nearest emergency room.

Cambridge: Mt. Auburn Hospital

Longwood: Brigham and Women's Hospital

HUPD personnel (43)2-1212 are trained in first aid and CPR/AED, and can transport uncontaminated, ambulatory patients to local area hospitals.

Non-Emergency Medical Treatment

- During work hours: Harvard employees/students go to Harvard University Health Services (HUHS).

Cambridge Campus: Richard A. and Susan F. Smith Campus Center, 75 Mt. Auburn Street, (43) 5-5711 (M-F 8:00 am – 5:30 pm)

Longwood Campus: 275 Longwood Avenue, Vanderbilt Hall, (43)2-1370 (M/Th 9:00 am–6:30 pm; T/W/F 9:00 am–5:00 pm).

Tenants in Harvard buildings should go to their Institution's health care provider.

- After work hours, Harvard employees/students go to UHS :
Richard A. and Susan F. Smith Campus Center,
75 Mt. Auburn Street, Cambridge, MA
PH: (43) 5-5711 (24 hour Urgent Care).

Tenants in Harvard buildings should contact their Institution's health care center for instructions related to after work hour emergencies.



Incidents - What to Do?

Report any incident or exposure to your supervisor and the Harvard Biosafety office as soon as possible.

Biological Materials Exposure

- Remove contaminated clothing, shoes, jewelry, etc.
- Immediately flood exposed areas with lukewarm water from safety shower, eyewash, or faucet for at least 15 minutes (use soap on skin for biological/blood exposure). Hold eyes open to ensure effective rinsing behind both eyelids.

Needlestick or Cut with Contaminated Sharp Item

- Immediately wash the area with soap and water for at least 15 minutes.
- If the injury warrants seek medical attention.

Injury Involving Research Animal (excluding Non-human primates)

- Immediately stop what you are doing and secure the animal in its cage.
- Wash the area with soap and water for at least 15 minutes.
- **CALL: 1-866-360-8100** 24 Hrs, 7 days/week Exposure Response Call Center

Tell the operator:

- Exposure/Injury with; hazardous, infectious, or toxic substance
- Your PI/Supervisor's phone number
- your return phone number

The on-call physician will return your call and direct you as to where to go for immediate treatment.

Injury Involving Non-Human Primate (NHP)

- Immediately stop what you are doing and secure the animal in its cage.
- Eye Splash: Rinse eyes with water for 15 minutes. Hold eyes open to ensure effective rinsing behind both eyelids.
- Bite/Scratch/Cut: Go to nearest Bite Kit:
 - Wash the wound with the antiseptic scrub brush for 15 minutes.
- Rinse the wound with sterile saline solution and bandage with sterile gauze.
- **CALL: 1-866-360-8100** 24 Hrs, 7 days/week Exposure Response Call Center

Tell the operator:

- Exposure/Injury with; hazardous, infectious, or toxic substance
- Your PI/Supervisor's phone number
- your return phone number

The on-call physician will return your call and direct you as to where to go for immediate treatment.



Laboratory Training

Initial training for all new laboratory personnel is provided online through the [Harvard Environmental Health and Safety Training Management System](#) (TMS). Trainings required will vary depending on the type of research conducted, COMS approval, and any lab or individual specific requirements. EHS provides generic environmental and occupational health and safety training covering regulations and guidelines, safe work practices, and exposure controls.

Regulatory agencies require Principal Investigators or their designee to provide training on laboratory specific hazards and safety controls to supplement EHS safety training.

L a b o r a t o r y - specific training must include review of procedures and hazards inherent in the type of experiments being conducted. This training should be documented and training records kept by the lab.

1. TMS user roles:

a. Training Director

- i. Individuals who oversee distinct groups of trainees for compliance oversight and require an overview of departmental or group training status.
- ii. This includes, but is not limited to: Directors, Deans, Research Operations Managers, and Department Administrators.

b. Training Manager (PI or designee)

- i. Individuals who directly manage or oversee a group of people in need of training.
- ii. Training managers create and manage a training roster of the laboratory personnel.
- iii. Training managers will oversee and assign relevant trainings to laboratory personnel.

c. Trainee

- i. Laboratory personnel listed on a roster who are required to take laboratory safety training.

2. EHS provided Laboratory Trainings

The table below lists the most common safety trainings required for laboratory personnel but is not exhaustive. Any personnel actively working with biological materials must complete Laboratory Biosafety and its refresher at least annually.



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
Recombinant DNA for the PI (LAB 110)	Recombinant DNA for the PI (LAB 110)	Every Three Years
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
Shipping Dry Ice (LAB 114)	Shipping Dry Ice (LAB 114)	Every Two Years
Radioactive Materials Safety (RPO 101)	Radioactive Materials Safety Refresher (RPO 201)	Every Two Years
Laser Safety (RPO 102)	Laser Safety Refresher (RPO 202)	Every Two Years
Respiratory Protection (IHS 107)	Respiratory Protection Refresher (IHS207)	Annual



Occupational Health & Medical Surveillance

Harvard University provides occupational health evaluations, medical surveillance, and treatment for personnel with the potential for occupational exposure to work place hazards. The following outlines the available resources and administrative controls which must be in place based on potential exposures.

1. General Medical Surveillance and Treatment

[Harvard University Health Services \(UHS\)](#) provides medical treatment and post-exposure evaluation to students and employees working in BL1 and BL2 laboratories.

2. Working with Research Animals

Medical surveillance for personnel that have direct contact with research animals is provided at through the managing Institutional Animal Care and Use Committee (IACUC) on Cambridge, Longwood, and other University campus. The program includes pre-screening questionnaires, animal and job-specific occupational health evaluations and training, vaccination and PPE requirements, as well as post-exposure medical treatment and evaluation. Contact the appropriate IACUC program administrator for your campus.

Cambridge: iacuc@fas.harvard.edu

Longwood: iacuc@hms.harvard.edu

3. Working in BL3 Laboratories

A detailed Occupational Health Response Program has been developed for each BL3 laboratory. The medical surveillance program and post-exposure evaluations for BL3 laboratory personnel is provided through the Occupational and Environmental Health Network and managed with the BL3 laboratory operations manager.



Personal Protective Equipment

Personal protective equipment (PPE) is used to directly protect personnel from contact with infectious agents. Supervisors are responsible for conducting laboratory PPE assessments, providing PPE, and training personnel in the use of proper use.

PPE must not be taken home or worn outside the laboratory. For assistance in selecting PPE for work with biological materials, contact biosafety@harvard.edu.

1. Recommended Laboratory PPE

- a. Laboratory outer garments
 - i. Dedicated long sleeved outer garments, i.e. lab coats, which are used to prevent contamination of the skin and street clothes.
- b. Gloves
 - i. Gloves must be worn when working with infectious and potentially infectious materials. Gloves are recommended for all manipulations of biological materials to avoid cross contamination of experiments.
 - ii. If personnel develop or have latex allergies, then a suitable alternative should be available for use.
 - iii. Double-gloving adds further protection when applied appropriately.
- c. Face protection
 - i. Safety glasses are recommended for all laboratory procedures.
 - ii. Goggles, face shields, or other splatter guards should be used for anticipated splashes or sprays of infectious material when procedures are conducted outside of containment.
- d. Respiratory protection
 - i. May be necessary in some cases depending on the materials being used or procedures performed.
 - ii. Personnel who are required to wear respiratory protection must be evaluated by a physician and trained in respirator selection and usage. Contact the EH&S office for more information.

PPE should be provided for visitors, maintenance and cleaning personnel.



Standard Microbiological Practices

The following provide a basis of proper work practices which must be used to protect you and others from exposure to hazardous materials. These basic work practices also aide in the reduction of cross-contamination and improve the quality of the work performed.

1. Use good aseptic technique for all procedures whether they involve infectious material use or not.
2. Personnel must wash their hands after work materials and before leaving the laboratory.
3. Gloves, laboratory coats, eye protection and other relevant personal protective equipment must be worn and dedicated for research use.
4. Eating, drinking, smoking, handling contact lenses, applying cosmetics, and storing food for human consumption must not be permitted in laboratory areas.
5. Mouth pipetting is prohibited; mechanical pipetting devices must be used.
6. Whenever practical, laboratory supervisors should adopt improved engineering and work practice controls that reduce risk of sharps injuries.
7. Precautions must always be taken with sharp items. These include:
 - a. Careful management, transportation and use of needles and other sharps are of primary importance.
 - b. Needles must not be bent, sheared, broken, recapped, removed from disposable syringes, or otherwise manipulated by hand before disposal.
 - c. Used disposable needles and syringes must be carefully placed in conveniently located puncture-resistant containers used for sharps disposal.
 - d. Non-disposable sharps must be placed in a hard walled container for transport to a processing area for decontamination, preferably by autoclaving.
 - e. Broken glassware must not be handled directly. Instead, it must be removed using a brush and dustpan, tongs, or forceps.
 - f. Plasticware should be substituted for glassware whenever possible.
8. Perform all procedures to minimize the creation of splashes and/or aerosols.
9. Decontaminate work surfaces after completion of work and after any spill or splash using an appropriate disinfectant for the material.
10. Decontaminate all cultures, stocks, and other liquid cultures before disposal.
11. Transportation of any viable cultures, stocks and other liquid cultures should be carried in durable, leak proof container, where the outer surface is easily decontaminated and secured for transport.
12. Laboratory personnel must have proper training in procedures and methods being performed in the laboratory by a qualified and experienced person.
 - a. Personnel must receive annual updates or additional training when procedural or policy changes occur.
13. Personal health status may impact an individual's susceptibility to infection, ability to receive immunizations or prophylactic interventions. All laboratory personnel and particularly women of childbearing age should be provided with information regarding immune competence and conditions that may predispose them to infection. Individuals having these conditions are encouraged to self-identify to the institution's healthcare provider for appropriate counseling and guidance.



Laboratory Aerosols

A significant amount of laboratory procedures have the ability to create biological aerosols that can be potentially hazardous to the personnel and the surrounding environment. Standard microbiological practices provide aerosol minimization techniques, but some special precautions can help increase the level of prevention.

- **Standard Precautions**
 - When working with infectious or potentially infectious materials, aerosol generating procedures should be performed in a biological safety cabinet.
 - Utilize respiratory protection whenever required.
 - When spills occur, leave the area and allow any aerosols to settle before addressing the spill.
- **Specific precautions for laboratory procedures with aerosol potential**
 - **Pipetting**
 - Dispense liquids as close to the reservoir as possible.
 - Make sure to rinse with the appropriate disinfectant before disposing pipettes or pipette tips
 - Take caution when removing pipette or pipette tips.
 - **Syringe usage**
 - Make sure to avoid air bubbles in liquid being discharged.
 - **Inoculation loops**
 - Try to use pre-sterilized, disposable loops when possible.
 - When heat sterilizing reusable loops, allow loop to cool before introducing it to any potentially infectious materials.
 - **Liquid decanting**
 - Pour carefully and as close to the vessel receiving as possible.
 - **Animal inoculation**
 - Remove syringe needles from animals slowly, with a smooth and steady motion.
 - **Vortexing**
 - Make sure all substances being vortexed are in a durable container with a tight fitting lid.
 - **Blending**
 - Use a laboratory grade blender with a tight fitting lid.
 - Operate the blender in a biosafety cabinet if infectious material is being used.
 - Allow aerosols to settle before opening the lid.
 - **Sonication**
 - Operate the sonicator in a biosafety cabinet or aerosol containment if infectious material is being used
 - **Centrifuging**
 - Use aerosol-proof rotors or safety buckets with caps that seal with O-rings.



- Before use inspect O-rings and safety caps for cracks, chips, and erosion.
- Use tubes with threaded caps.
- Avoid overfilling the tube and getting caps/closures wet.
- Wipe tubes down with disinfectant after filling.
- Load and unload rotors and buckets inside the BSC
- 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**
 - House vacuum lines and vacuum pumps must be protected by using a hydrophobic filter installed between the collection flask and vacuum source.
 - In some cases a HEPA filter may be required to protect against infectious aerosols



Biological Safety Cabinet Use

Biological safety cabinets (BSC) are the primary means of containment for working safely with infectious materials. Biosafety cabinets operate by controlling airborne contaminants during work through the use of laminar airflow and high efficiency particulate air (HEPA) filtration.

BSC location in the laboratory

The air curtain created at the front of the cabinet is fragile creating at downward and inward air velocity of only 1 mph . Since the air curtain created at the front of the cabinet can be easily disrupted, a BSC should be located away from air supply registers, entrances/exits, high traffic areas, and laboratory equipment.

Safe and effective BSC use

- Before beginning work:
 - Monitor alarms, pressure gauges, or flow indicators for any changes.
 - Shut off the UV light.
 - Turn the cabinet on and let it run for 3-5 minutes.
 - Wipe work surface with an appropriate disinfectant such as 70% ethanol.
 - Plan your work and place everything needed for the procedure inside the BSC.
 - Wipe items with disinfectant before placing in BSC.
- During work:
 - Avoid airflow disruption that could affect the level of protection provided by the BSC.
 - Keep the BSC free of clutter.
 - Don't place objects over the front air intake grille.
 - Don't block the rear air intake grille.
 - Limit traffic in the area when the BSC is in use.
 - Make sure lab door is closed and avoid opening/closing door if located near the BSC.
 - Move arms slowly when removing or introducing items. Avoid sweeping arm motions.
 - When working with infectious materials, change gloves when moving in and out of the cabinet.
 - Keep all materials at least 4 inches inside the front sash.
 - Keep clean materials at least one foot away from any aerosol generating activities to minimize the potential for cross contamination.
 - Place any equipment that creates air turbulence in the back 1/3 of the cabinet and stop other work while the equipment is running.
 - Don't operate a Bunsen burner in the cabinet as this can disrupt air flows within the cabinet.
 - Segregate contaminated and clean items. Work from "clean to dirty."
 - Clean up all spills in the cabinet immediately. Allow the cabinet to run for 3-5 minutes before resuming work.



- After completion of work:
 - Don a new pair of gloves, and wipe down all items with an appropriate disinfectant before removing.
 - Remove all materials and wipe all interior surfaces of the BSC with an appropriate disinfectant.
 - Wash hands after completion of work.
 - Periodically decontaminate and clean under work grilles.

Certification

The National Sanitation Foundation (NSF) International Standard no. 49 for Class II biohazard cabinetry establishes performance criteria as well as minimum requirements for design, manufacture, and testing.

- A BSC in a BL1 and BL2 laboratory must be professionally certified after installation, annually, and after being moved or serviced.
- A BSC must be professionally decontaminated before disposal or removal/relocation from a lab space.

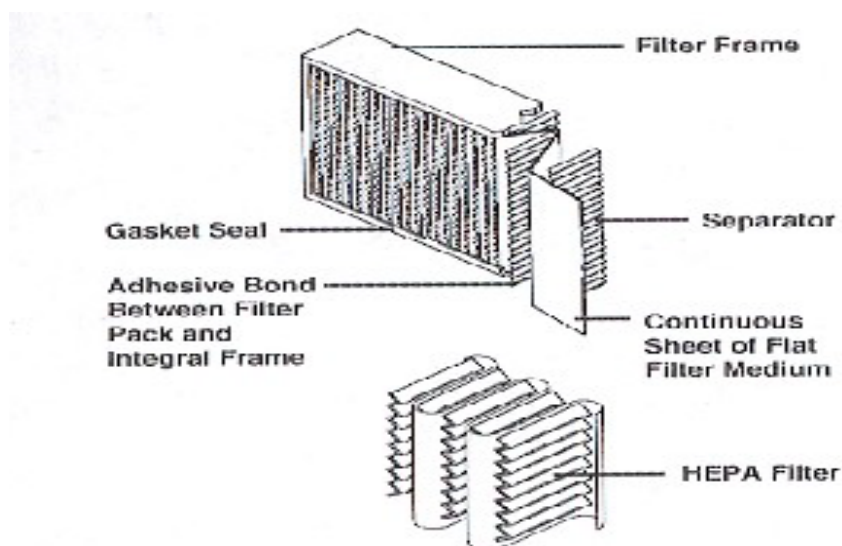


Types of Biological Safety Cabinets

Biological Safety Cabinets (BSCs) are the primary means of containment for working safely with biological materials. BSCs are designed to provide personnel, environmental, and product protection when good microbiological practices and procedures are followed. Three types of BSCs, designated as Class I, II, and III, have been developed to meet varying research and clinical needs.

High Efficiency Particulate Air (HEPA) Filters

Control of airborne particulate materials is achieved with high-efficiency particulate filters that efficiently remove microscopic contaminants from the air. The HEPA filter removes particles equal to and greater than $0.3\ \mu\text{m}$ (which essentially includes all bacteria, spores, and viruses) with an efficiency of 99.99%.



Types of Biological Safety Cabinets

Tables 1 and 2 (below) compare and contrast the level of protection offered by the different classes of BSCs.

Table 1. Selection of a BSC Through Risk Assessment

Biological risk	Protection provided			BSC
	Personnel	Product	Environment	Class
BSL-1-3	YES	NO	YES	I
BSL-1-3	YES	YES	YES	II (A1, A2, B1, B2)
BSL 4	YES	YES	YES	III



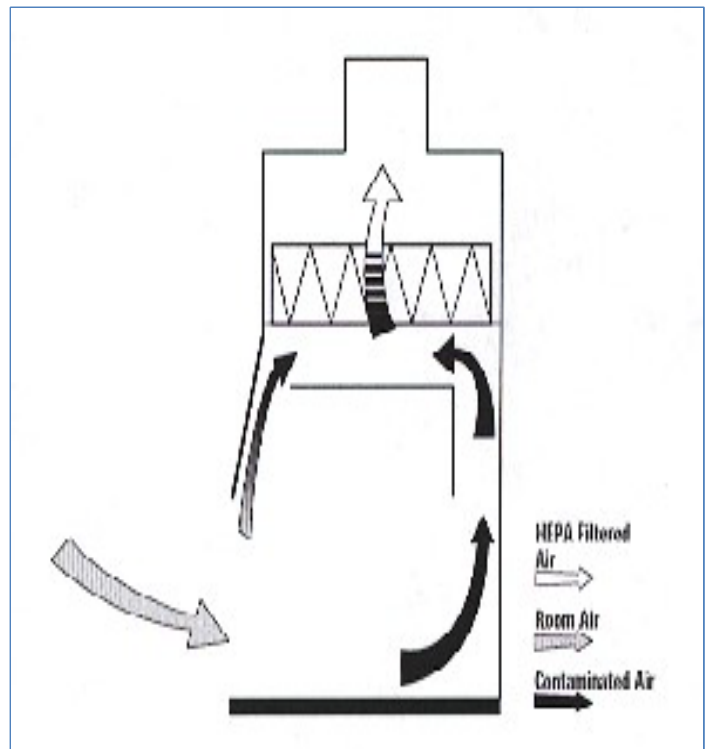
Table 2. Comparison of BSC Characteristics

BSC class	Face velocity	Airflow pattern	Nonvolatile toxic chemical and radionuclides	Volatile toxic chemicals and radionuclides
I	75	In at front; exhausted through HEPA to the outside.	Yes	Yes
II, A1	75	70% recirculated to the cabinet work area through HEPA; 30% balance can be exhausted through HEPA back into the room or to the outside through a thimble unit.	No	No
II, B1	100	Exhaust cabinet air must pass through a dedicated duct to the outside through a HEPA filter.	Yes	Yes (minute amounts)
II, B2	100	No recirculation; total exhaust to the outside through hard-duct and a HEPA filter.	Yes	Yes (small amounts)
II, A2	100	Same as II, A, but plenums are under negative pressure to room; exhausted air is thimble-ducted to the outside through a HEPA filter.	Yes	Yes (minute amounts)
III	N/A	Supply air inlets and hard-duct exhausted to outside through two HEPA filter in series.	Yes	Yes (small amounts)

Diagrams showing the cabinet types and air flow are provided on the following pages.

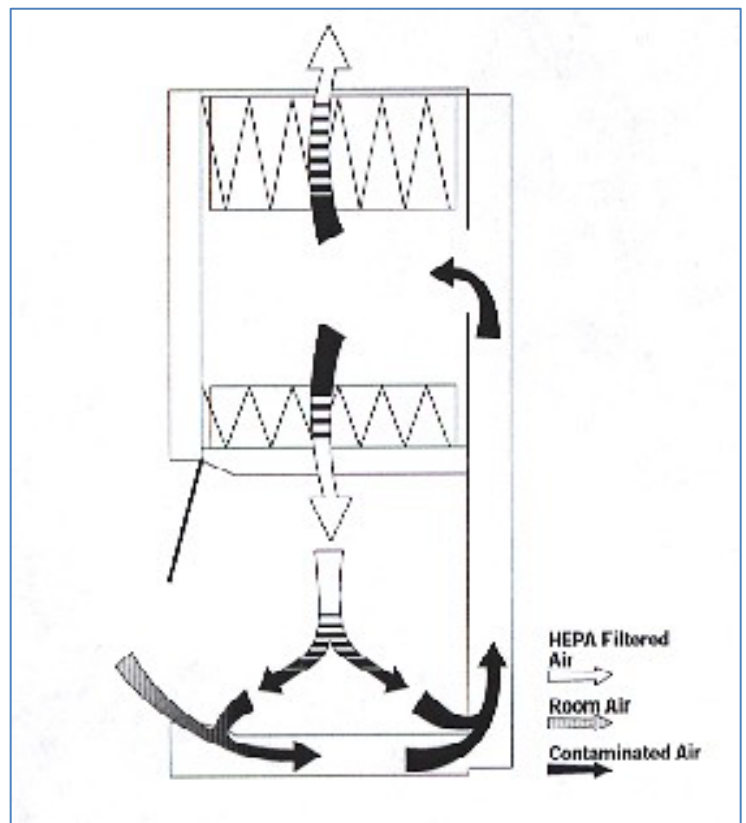


Class I Biological Safety Cabinet provides personnel and environmental protection, but



Class II Biological Safety Cabinet (Types A1, A2, B1, and B2) provide personnel, environmental, and product protection. All Class II cabinets are designed for work involving microorganisms assigned to biosafety levels 1, 2, and 3.

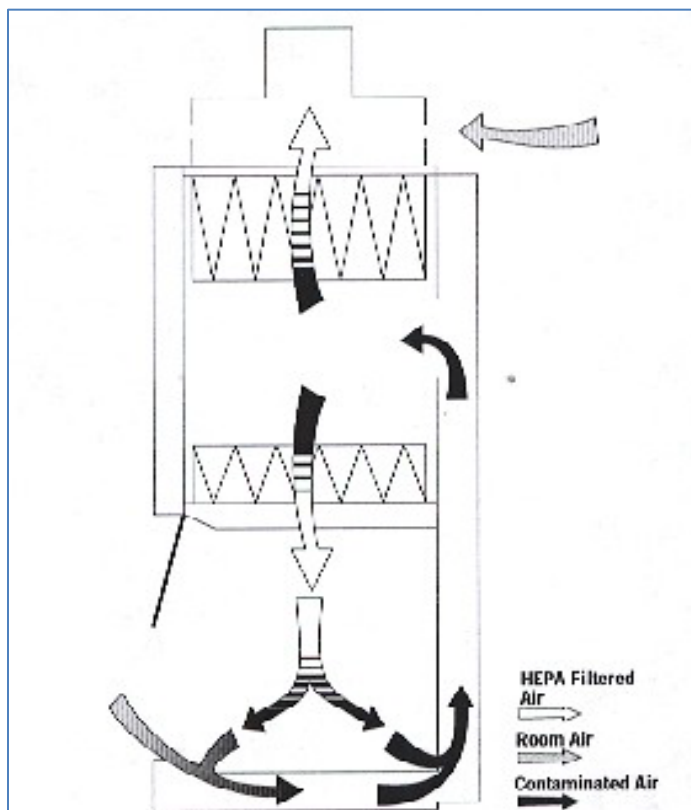
An unducted Class II, Type A, cabinet cannot be used for work involving volatile, toxic, or flammable chemicals. The buildup of chemical vapors or gases in the cabinet by recirculated air and in the laboratory from exhaust air can create health and safety hazards.





Class II Type A Cabinet with Canopy

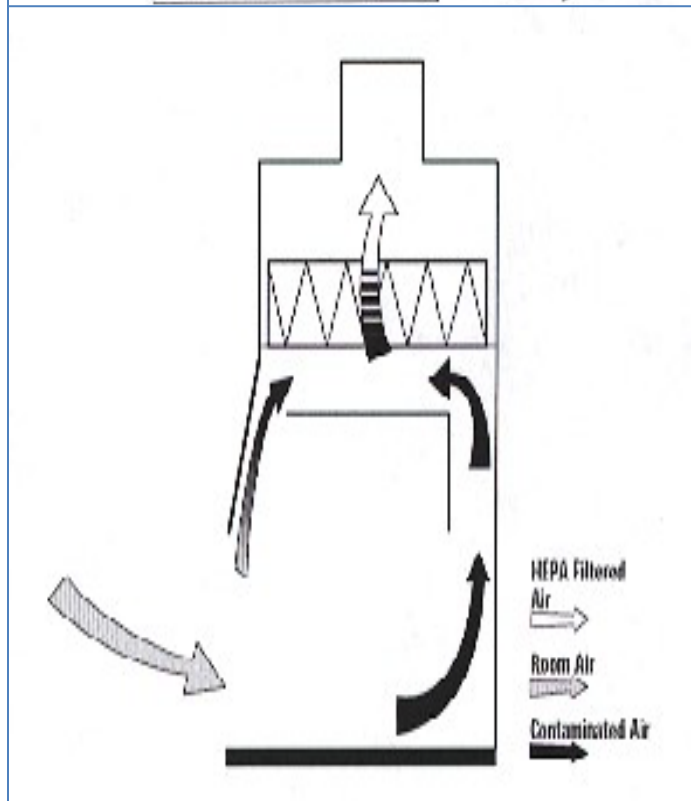
Type A cabinet exhaust can be ducted out of the building through an indirect “thimble” connection to an exhaust system or through a canopy hood. The volume of the exhaust must be sufficient to maintain the flow of room air into the space between the thimble unit and the filter housing. The performance of a cabinet with this exhaust configuration is unaffected by fluctuations in the building exhaust system.



Class II, Type B1

Some research requires the use of small quantities of certain hazardous chemicals, such as carcinogens. The powdered form of these carcinogens should be weighed or manipulated in a chemical fume hood. Carcinogens used in cell culture or microbial systems require both biological and chemical containment.

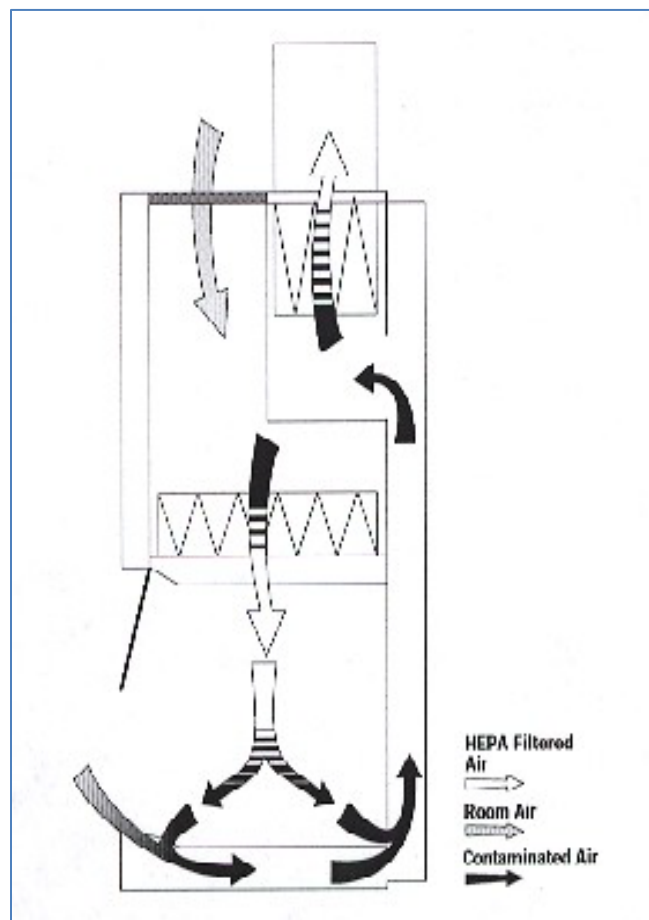
Type B1 cabinets must be hard-ducted to a dedicated exhaust system. A failure in the building exhaust system may not be apparent to the user, as the supply blowers in the cabinet will continue to operate. A pressure-independent monitor should be installed to sound an alarm and shut off the BSC supply fan, should failure in exhaust airflow occur. Because all BSC manufacturers do not supply this feature, it is prudent to install a sensor in the exhaust system, as necessary.





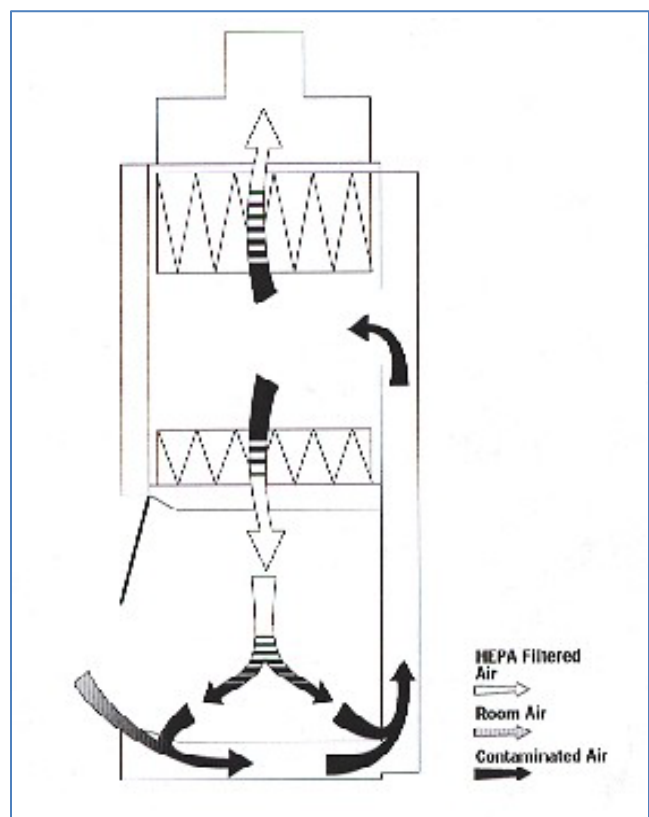
Class II, Type B2—This BSC is a total-exhaust cabinet; no air is recirculated within it. This cabinet provides primary biological and chemical containment. All air entering this cabinet is exhausted and passes through a HEPA filter prior to discharge to the outside.

Should the building or cabinet exhaust fail, the cabinet will be pressurized, resulting in a flow of air from the work area back into the laboratory. Cabinets built since the early 1980s usually have an interlock system installed by the manufacturer to prevent the supply blower from operating whenever the exhaust flow is insufficient. A pressure-independent device should monitor the exhaust air movement.



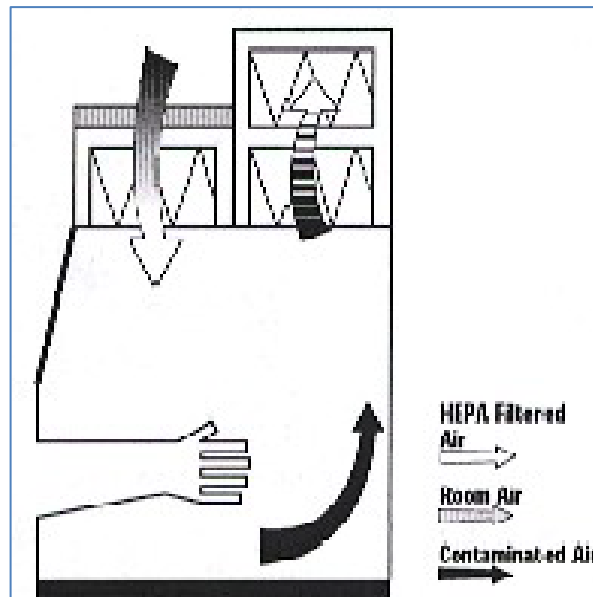
Class II, Type A2—This BSC is a ducted Type A cabinet exhaust can be ducted out of the building through an indirect “thimble” connection to an exhaust system or through a canopy hood with the same requirements for airflow and design.

Special applications—Class II BSCs can be modified to accommodate special tasks. For example, the manufacturer also can modify the front sash to accommodate the eyepieces of a microscope, or the work surface can be designed to accept a carboy, a centrifuge, or other equipment that requires containment.

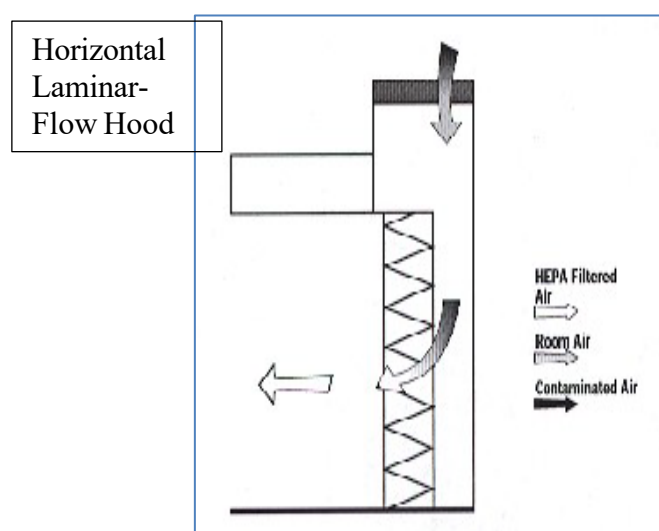
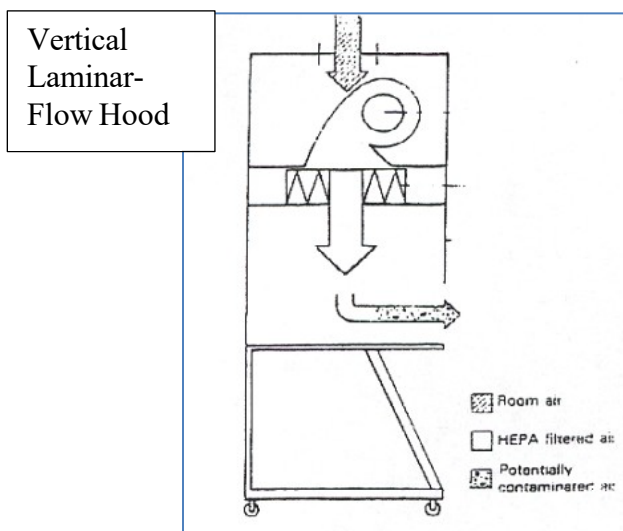




Class III Biological Safety Cabinet is totally enclosed, ventilated cabinet of gas-tight construction. Operations in the cabinet are conducted through attached rubber gloves. The cabinet is maintained under negative air pressure of at least 0.5 inch (12.7 mm) water gauge (w.g.). Supply air is drawn into the cabinet through HEPA filters. The exhaust air is treated by double HEPA filtration, or by HEPA filtration and incineration (Figure 6). Class III cabinets are suitable for work with agents that require Biosafety Level-1, -2, -3 or -4 containment.



Horizontal and Vertical Laminar-Flow “Clean Bench” are *not* BSCs. They discharge HEPA-filtered air across the work surface and toward the user. These devices only provide product protection. These benches should not be used when handling cell culture materials or drug formulations, or when manipulating potentially infectious materials. The worker can be exposed to materials being manipulated on the clean bench, and subsequently develop hypersensitivity. Horizontal and vertical clean-air benches should never be used as a substitute for a BSC in research, biomedical, or veterinary laboratories and/or applications.





Safe Sharps Handling

The term “sharps” refers to any instrument that is capable of causing punctures, cuts, or scrapes to the body. Sharps includes but is not limited to: needles, syringes, scalpels, razor blades, slides, coverslips, Pasteur pipettes, capillary tubes, sharp or broken glass, lancets, suture needles, and microtome blades. Use of sharps should be restricted to trained personnel and instances in which no alternative is available. In addition, sharps are covered under regulatory waste guidelines and **must not be disposed of with regular trash.**

Sharps Precautions

- Avoid the use of needles and other sharps whenever possible. Use plastic alternatives to glass if available.
- Minimize any contact with sharps by disposing or storing them immediately after use.
- Needles must never be recapped, removed from the syringe, sheared, bent or broken.
- Use a mechanical device to remove scalpel blades. Never use your fingers.

Disposal of Laboratory Sharps

- All sharps must be disposed of into an approved, puncture resistant, sharps container.
- Sharps used with genetically modified and biological materials must be collected in red biohazard sharps containers for disposal.
- Do not overfill the sharps container.
- Never force materials into a sharps container.
- Never reach into the sharps container.
- Do not remove the lid from the container.
- When sharps container is $\frac{3}{4}$ full, close it and arrange for disposal.
 - If disposable, place it in a biowaste box/bin.
 - If reusable, waste vendor will pick up filled, closed containers.
- Refer to the [Harvard EHS Waste Guide](#) for instructions on how to dispose of sharps with mixed contamination.



Biological Waste Management

Biological waste includes but is not limited to the following: potentially infectious materials to humans, animals, and plants, genetically modified materials, animal carcasses, and human and animal tissues (pathological waste).

Always use personal protective equipment (lab coat, safety glasses, latex or nitrile gloves) when collecting and handling biological waste.

Solid Biological Waste Collection and Handling:

- Collect BL1 and BL2 waste in red-lined Stericycle biowaste cardboard boxes or reusable plastic bins for pick-up and off-site treatment.
- When containers are 3/4 full, tie off the red bag liner with a single knot and tuck bag completely inside the container. If using cardboard boxes, tape the cover or box closed with packaging tape. For the plastic reusable containers, snap the cover flaps shut.
- BL2+ and BL3 solid waste should follow established lab specific SOP's for disposal.

Contact the biosafety@harvard.edu if you plan on performing on-site treatment of solid biological waste.

Incinerate Only Biological Waste

- Incinerate Only Waste includes all animal carcasses, body parts, tissues, organs, and surgical specimens. These types of waste must be segregated for incineration.
- Incinerate Only Waste must be collected in Stericycle cardboard boxes using **two** red bag liners.
- A Stericycle "Incinerate Only" sticker must be placed on the box to identify the required treatment method.

To avoid nuisance odors, package and transfer waste from freezers/refrigerators to the cardboard boxes according to the Stericycle pick-up schedule. Contact the EH&S Office for Stericycle scheduling information: Longwood (617) 432-1720, Cambridge (617) 495-2345.

Mixed Biohazardous Waste

- Animal or human tissue treated with chemical fixative is processed as solid chemical waste. Label the hazardous waste, with the appropriate chemical hazard and identify the waste as non-infectious animal/human tissue.

Do not autoclave materials treated with a chemical fixative.

- Mixed biological, chemical and/or radioactive waste requires special procedures for decontamination and disposal. Contact the EH&S Office or refer to the [Laboratory Waste Guide](#) for guidance.

Do not autoclave materials treated with a chemicals or radionuclides.



Liquid Biological Waste

- Liquid biological waste must be treated with an appropriate disinfectant before sink disposal. COMS has approved the use of Bleach (sodium hypochlorite solution) for disinfecting genetically modified cultures, BL1 and BL2 liquid biological waste for sink disposal. Use a final concentration of 10% bleach to liquid waste. Use fresh bleach from the manufacturer's container since a prepared 10% bleach solution has a shelf life of only 24 hours.
- Allow a minimum contact time of 20 minutes before drain disposal.
- Carefully pour the disinfected liquid waste down the sink drain and flush with generous amounts of water.
- Autoclaving genetically modified cultures, BL1, and BL2 liquid waste is also a COMS approved method for disinfecting liquid waste prior to sink disposal. Follow lab-specific procedures for autoclaving liquid waste.

**Do not autoclave liquid waste that has been
treated with a chemical disinfectant.**

BL3 Biological Waste

Biological waste from BL3 laboratories must be decontaminated and the process validated following established lab specific procedures prior to removal containment.



Biological Spill Procedures

Spills involving genetically modified or infectious cultures, should be reported immediately to Harvard EH&S.

Biosafety Level 1 and 2 Biological Spills

Inside the Biosafety Cabinet

- Remove contaminated clothing and wash exposed skin, if applicable.
- Wear gloves and lab coat.
- Pick up any sharp items, e.g., broken glass or needles, with forceps place in a sharps container.
- Cover spill with paper towels and pour an appropriate disinfectant such as 10% bleach, around and over the spill.
- Allow suitable contact time, 20 minutes at a minimum.
- Wipe up the spill from the outside edge working towards the center of the spill.
- Discard disposable materials used to clean up the spill in a red biowaste bag.
- Wipe the surrounding area and the spill area again with disinfectant.
- Disinfect or autoclave any non-disposable materials used.
- Report the spill to your supervisor.

Outside of the Biosafety Cabinet

- Alert others in the area, and request they vacate the area.
- Remove contaminated clothing and wash exposed skin with soap and water.
- Exit the lab and place “Do Not Enter” signage on the door.
- Report the spill to your supervisor.
- Allow aerosols to settle for at least 30 minutes before re-entering the lab.
- Wear gloves, lab coat, and face protection.
- Pick up any sharp items, e.g., broken glass or needles with forceps or dustpan and brush and place in a sharps container.
- Cover spill with paper towels and pour disinfectant, e.g., 10% bleach, around and over the spill.
- Allow suitable contact time, at a minimum 20 minutes.
- Wipe up the spill from the outside edge working towards the center of the spill.
- Discard disposable materials used to clean up the spill in a biowaste bag.
- Wipe the surrounding area and the spill area again with disinfectant.
- Disinfect or autoclave any non-disposable materials used.
- Report the spill to your supervisor.

Biosafety Level 3 (BL3) Biological Spill

Follow your laboratory-specific SOP for BL3 biological spills.



Biological Risk Assessment

Infectious Agents and Biosafety Levels

The CDC Biosafety in Microbiological and Biomedical Laboratories, 5th Ed. (BMBL) outlines laboratory practices, facility requirements, and safety equipment for working with infectious agents. The BMBL classifies infectious agents into four risk groups based on the agents' ability to infect and cause disease in a susceptible human or animal host, virulence as measured by the severity of the disease, and the availability of preventive measures and effective treatments for the disease.

Risk groups address the risk to both the laboratory worker and the community. Biosafety levels (BSL) provide a description of containment and work practices required to safely manipulate these agents. The risk group of an agent does not necessarily equate to the BSL. A risk assessment incorporating the agent, procedures, and available engineering controls will determine the appropriate BSL for a particular agent. The NIH rDNA Guidelines and BMBL also provide general containment requirements and safe work practices for the research use of [plant pathogens](#) and [arthropods](#).

Harvard University laboratories support research utilizing BSL1, BSL2 and BSL3 containment and work practices. There are no BSL4 labs at Harvard.

Summary of Risk Groups

RG1	Agents not associated with disease in healthy adult humans
RG2	Agents associated with human disease that is rarely serious and for which preventive or therapeutic interventions are often available
RG3	Agents associated with serious or lethal human disease for which preventive or therapeutic interventions may be available
RG4	Agents likely to cause serious or lethal human disease for which preventive or therapeutic interventions are usually not available

Provided on the next page is Table 2. Summary of Recommended Biosafety Levels for Infectious Agents from CDC BMBL, 5th Edition p. 59



Tissue and Cell Culture

Human and Non-Human Primate Materials

The manipulation of human and non-human primate materials including, blood, unfixed tissues, established and immortalized cell lines places laboratory workers at risk due to potentially infectious agents that can reside in these materials. Due to this potential for exposure, materials of primate origins must be treated as if they were known to be infectious.

Unless a thorough risk assessment and pathogen screening has been conducted both human and non-human primate materials should be handled with Biosafety level 2 (BL2) practices and containment.

Human materials specifically fall under the OSHA Bloodborne Pathogens (BBP) Standard.

OSHA BBP Standard

- All human cell lines are considered potentially infectious and fall under the OSHA BBP standard unless pathogen testing and clearance has been conducted and documented for a specific cell line.
- Employers are required:
 - To personalize a laboratory specific [Exposure Control Plan](#)
 - Offer personnel with occupational exposure appropriate vaccination and retain a record thereof with the [Hepatitis B offer form](#)
 - Provide annual training, BBP pathogen training is incorporated in Laboratory Biosafety and the refresher training. Training is completed and documented via the [EHS TMS](#).
 - Update the Exposure Control Plan as needed, and at least annually
 -

Other cultured cells and harvested tissues

- Other mammalian cell lines or tissues that are not of human or non-human primate origin, and do not contain known human or animal pathogens are designated Biosafety level 1.
- Cultured cells and any harvested tissues that have been administered or manipulated with an infectious agent (e.g. bacteria or viral based vector) are classified in the same biosafety level as the administered agent.



Select Agents and Exempted Quantities of Select Agent Toxins

Select Agents are federally regulated agents that have potential use in biological warfare. Health and Human Services (HHS) regulates select agents targeting humans, the United States Department of Agriculture (USDA) regulates select agents targeting animals, and the USDA Plant Protection and Quarantine (PPQ) regulates select agents targeting plants. Before possessing, using, sending, or receiving select agents, the institution and Principal Investigator must register with CDC, APHIS, and/or USDA to receive official authorization for each individual requesting access to select agents. Requirements include background checks on those authorized to access select agents, security plans and inventories. Immediately notify the Biosafety Office if you discover select agents in your laboratory that have not been registered.

A few common examples are listed below.

- Botulinum neurotoxins
- Botulinum neurotoxin producing species of *Clostridium*
- Conotoxins (Short, paralytic alpha conotoxins containing the following amino acid sequence X1CCX2PACGX3X4X5X6CX7)
- *Francisella tularensis*
- Lassa fever virus
- Reconstructed 1918 pandemic influenza virus containing any portion of the
- *Bacillus anthracis*
- *Bacillus anthracis* Pasteur strain
- *Brucella melitensis*
- Avian influenza virus
- Classical swine fever virus
- Foot-and-mouth disease virus*
- coding regions of all eight gene segments (
- Ricin
- SARS-associated coronavirus (SARS-CoV)
- Staphylococcal enterotoxins A,B,C,D,E subtypes
- Tetrodotoxin
- Variola major virus (Smallpox virus)
- Variola minor virus (Alastrim)
- *Yersinia pestis*
- *Brucella abortus*
- *Brucella suis*
- Newcastle disease virus



The select agent regulations also apply to Genetic Elements, Recombinant Nucleic Acids, and Recombinant Organisms as described below:

- Nucleic acids (synthetic or naturally derived, contiguous or fragmented, in host chromosomes or in expression vectors) that can encode infectious and/or replication competent forms of any of the select agent viruses.
- Nucleic acids (synthetic or naturally derived) that encode for the functional form(s) of any of the toxins listed if the nucleic acids are in a vector or host chromosome and/or can be expressed *in vivo* or *in vitro*.
- Listed viruses, bacteria, fungi, and toxins that have been genetically modified.

Exclusions

The select agent regulations do not apply to:

- Any select agent or toxin that is in its naturally occurring environment provided it has not been intentionally introduced, cultivated, collected, or otherwise extracted from its natural source.
- Non-viable select agent organisms or non- functional toxins.

The HHS secretary may exclude attenuated strains or toxins if it is determined that they do not pose a public health threat.

Exempt Quantities of Select Agent Toxins

Select Agent Toxins are identified by the US federal government as toxins with the potential to be used in biological warfare. Only toxins listed here are controlled as Select Agent Toxins. CDC allows for the storage and use of these toxins in limited amounts without the full regulatory burden of registration with the CDC/USDA and the associated security requirements.



Select Agent Toxin Exempt Quantities

Toxin	Amount
Abrin	100 mg
Botulinum neurotoxin	0.5 mg
Short, paralytic alpha conotoxins	100 mg
Diacetoxyscirpenol (DAS)	1000 mg
Ricin	100 mg
Saxitoxin	100 mg
Staphylococcal Enterotoxins (Subtypes A, B, C, D, and E)	5 mg
T-2 toxin	1000 mg
Tetrodotoxin	100 mg

NOTE: The following forms of these toxins are also exempt.

- Any toxin that is in its naturally occurring environment provided it has not been intentionally introduced, cultivated, collected, or otherwise extracted from its natural source.
- Nonfunctional toxins.

Requirements

- The Principal Investigator must register select agent toxin work with COMS.
- The maximum allowable amount listed above may never be exceeded.
- An inventory must be kept for all toxins used and the quantities on hand.
- Toxins must be stored in secondary containment with restricted access (locked freezer, lock box, etc.)
- A toxin specific SOP for handling each toxin being used in the laboratory must include the following:
 - Personal Protective Equipment for research personnel
 - Safe handling, Storage, and Use in the laboratory
 - Decontamination/Inactivation and Disposal procedures
- Laboratory-specific safety training:
 - Inventory record keeping
 - Toxin characteristics and hazards
 - Proper equipment and PPE usage associated with procedures being performed.
- Only trained staff approved by the PI may have access to the materials.
- Any destruction of exempt quantities of select agent toxins must be documented on the select agent toxin destruction form.
- Any transfer of select agent toxins must be documented on the select agent toxin transfer form.



Shipping Biological Materials

Shipments of research materials that may be classified as hazardous materials or dangerous goods by the US Department of Transportation (DOT) and the International Air Transport Association (IATA) must be managed in accordance with a very strict set of requirements. Individuals who, package, label, transport, or prepare paperwork for a shipment must complete function specific training every 2 years and follow all DOT/IATA regulations.

The shipper of any biological material is ultimately responsible for the package throughout its shipment. The responsibilities of the shipper include:

CLASSIFYING the material correctly.

PACKAGE and secure the material for shipment by using the correct Packing Instructions as provided in the EHS provided function specific shipping training.

LABEL the outer package appropriately.

DOCUMENT by completing the air waybill and other shipping paperwork as required.

Import & Export Requirements for Research Materials

In addition to the DOT/IATA training and packaging requirements for shipments of biologics and other dangerous goods, Import and Export requirements may apply when shipping research materials internationally. Import and Export requirements vary based on the port of entry (import location). Check with your contact in the receiving country to make sure they have the required permits in place to receive the research materials being sent. Below we provide some export and import guidance for the United States.

Export License

All shipments being sent from the US to a foreign country, including Canada, should be evaluated by a Harvard University Export Control Officer. The Department of Commerce requires export licenses for a wide variety of disease causing agents, the genetic material from these agents and other products derived therefrom. This includes agents that affect humans, plants, and animals.

Harvard University Export Control Officers by School:

FAS/SEAS: **Gearoid (Griff) Griffin**, Research Integrity Officer
phone: (617) 495-9204 email: gearoid_griffin@harvard.edu

HSPH: information can be found [online](#)

Contact Eileen Nielsen, Director of Sponsored Projects Compliance

Email: enielsen@hsph.harvard.edu

HMS/HSDM: information can be found [online](#)

Contact email: export_control@hms.harvard.edu



Import Permits

Contact biosafety@harvard.edu for assistance if an import permit is required. All agencies listed below may require an inspection of the importer's facility and safety validation from the EHS department.

Centers for Disease Control (CDC)

Items Requiring CDC Import Permits:

- Any infectious (etiologic) agent known or suspected to cause disease in humans.
- Unsterilized specimens of human and animal tissues (such as blood, body discharges, fluids, excretions or similar material) containing an infectious or etiologic agent.
- Hosts and Vectors:
 - Animals: Any animal known or suspected of being infected with an organism capable of causing disease in humans may require an import permit. Importation of live turtles of less than 4 inches in shell length and live nonhuman primates is regulated by the CDC, Division of Global Migration and Quarantine (phone number: 404-498-1600 and website: <http://www.cdc.gov/ncidod/dq/>).
 - 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 on their [website](#).
 - Arthropods: Any living insect or other arthropod that is known or suspected of containing an etiologic agent (human pathogen).
 - Snails: Snail species capable of transmitting a human pathogen.

Importation permits are issued only to the importer, who must be located in the United States. A CDC Import Permit can be obtained on their website:

<http://www.cdc.gov/od/eaipp/importApplication/agents.htm>

CDC Contact Information

Phone: (404) 718-2077; Fax: (404) 471-8333

Email: ImportPermit@cdc.gov

United States Department of Agriculture, Animal and Plant Health Inspection Service, Veterinary Services (USDA/APHIS/VS)

USDA/APHIS/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.

Animal Products Requiring a USDA Import Permit

Generally, a USDA veterinary permit may be needed for materials derived from animals or exposed to animal-source materials. Materials which require a permit include, animal tissues, blood, cells or cell lines of livestock or poultry origin, antibodies for *in vivo* use in non-human species, and bulk shipments of test kit reagents. Veterinary biological products (vaccines, bacterins, antisera, diagnostic kits, and other products of biological origin) produced in other countries may be imported into the United States for research and evaluation if a permit is obtained.



To Obtain a USDA Import Permit for Animal Products:

[Apply on-line for a VS import permit](#), or obtain a permit application by writing the Import/Export Animal Products Program:

USDA, APHIS, VS, NCIE Products Program
4700 River Road, Unit 40
Riverdale, MD 20737-1231

For further information, contact Animal Products Program at (301) 734-3277.

Animal Products NOT Requiring a USDA Import Permit

Animal products that do not need a USDA import permit, but will be reviewed at the port of entry by USDA inspectors, include the numbered guidelines listed below.

Click on the links below and follow the instructions provided for writing a letter to be attached to the outside of the package for review by USDA inspectors at the port of entry:

- [1100](#) Human Pharmaceuticals and Human Vaccines Containing Animal Components
- [1101](#) Human and Non-Human Primate Material (excluding cell cultures)
- [1102](#) Feline and Canine Material
- [1103](#) Live Laboratory Mammals and Their Material (for research purposes)
- [1104](#) Amphibians, Fish, Reptiles, Shellfish and Aquatic Species (includes venom)
- [1105](#) Chemically Synthesized Materials
- [1110](#) Microbially Produced Materials
- [1114](#) Recombinant Microbes and Their Products
- [1116](#) Non-pathogenic Microorganisms
- [1119](#) Pet chews/Treats made of Antlers or Rawhide
- [1120](#) Cell Cultures/Lines, Recombinant Cell Cultures/Lines, and Their Products (for *in vitro* use)
- [1121](#) Test Kits
- [1122](#) Animal Feeds, Feed Supplements, and Pre-Mixes

To Obtain a USDA Import Permit for Veterinary Biologics:

Apply on-line for a [VS import permit](#), or submit applications for a Permit for Research and Evaluation, as well as a [Permit for Transit Shipment](#), to:

Center for Veterinary Biologics
4700 River Rd., Unit 148
Riverdale, MD 20737-1231



Fish & Wildlife Service and National Marine Fisheries Service

Fish and Wildlife Service permits are required for marine mammals, certain fish, and certain live animals, including bats. Call 1-800-344-WILD for further information

Contact information:

Website: <http://www.fws.gov/permits/ImportExport/ImportExport.html>

Permit Division, Office of Protected Resources, National Marine Fisheries

Service (301) 713-2355 or 713-2289 and/or Fish and Wildlife Service, Office of Management Authority (703) 358-2104.

Select Agents

Individuals wishing to import select agents and toxins must be registered with CDC's

Select Agent Program (<http://www.cdc.gov/od/sap>) in accordance with 42 CFR Part

73 (Possession, Use, and Transfer of Select Agents and Toxins; Interim Final Rule). Also, In accordance with 42 CFR Part 73.16(a), an APHIS/CDC Form 2 must be completed and submitted to the CDC Select Agent Program and granted approval prior to the shipment of the select agents or toxins under the import permit. Please contact the EHS Office (617-432- 1720) for more information on select agent registration and transport requirements.

FDA Import Permits

All food (except most meat and poultry), drugs, biologics, cosmetics, and medical devices require a permit or registration before importation into the US. See

<http://www.fda.gov/ora/import/> for more information.



List of Regulations and Guidelines

The following is a summary of federal, state, and local agency regulations and guidelines that either regulate or provide guidance 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), 5th Edition, 2009. 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 DNA Molecules (NIH Guidelines). This document provides guidelines for constructing and handling recombinant DNA molecules (rDNA) and organisms containing rDNA. Although these guidelines are not subject to regulatory enforcement, institutions that receive any NIH funding for rDNA research are required to comply with these guidelines as a condition of funding. This document requires that each institution establish an Institutional Biosafety Committee with the authority to approve proposed rDNA research using the NIH guidelines as the minimum standard.
- Occupational Safety and Health Administration: Bloodborne Pathogens Standard. 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.
- Boston Public Health Commission: Recombinant DNA Technology: Use Regulations (passed March 22, 1994) and Biological Laboratory Regulation (passed September 19, 2006). These regulations require that all institutions in the City of Boston that work with recombinant DNA molecules or that operate BSL-3 or BSL-4 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 March 30, 2004) 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.
- Cambridge Public Health Department Cambridge Biosafety Regulation and Recombinant DNA Technology Ordinance establishes strict oversight of university and commercial laboratories that engage in recombinant DNA research. The requirements set forth in the city ordinance are based on the widely employed National Institutes of Health (NIH) Guidelines for Research Involving DNA Molecules



- 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 record keeping.
- Select Agent Rule, Department of Health and Human Services: 42 CFR Parts 42 and 43 Possession, Use, and Transfer of Select Agents and Toxin; Final Rule; and the Department of Agriculture's Animal and Plant Health Inspection Service: 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. 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.

Other Regulatory Requirements

- U.S. Department of Transportation and the International Air Transportation Authority: These organizations have strict requirements governing the 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.
- U.S. Department of Commerce: The DOC has specific regulatory requirements for exportation of biological materials. These regulations are both agent and country specific and must be followed strictly.
- Massachusetts Department of Public Health (DPH): The MADPH regulates the management of biological wastes in the state (105 CMR 480) and also inspects BSL3 laboratory spaces on a regular basis.
- Institutional Biosafety Committee, COMS: 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.