HARVARD
Campus Services
ENVIRONMENTAL HEALTH & SAFETY

Harvard University

Biosafety Manual

Laboratory Safety
46 Blackstone Street, Cambridge, MA 02139 | T: 617.496.3797 | F: 617.496.5509
www.ehs.harvard.edu | email: lab_safety@harvard.edu

Table of Contents

Chapter 1 Introduction and Roles of Key Personnel

This Biosafety Manual provides a review of pertinent federal and state government regulations, information about safe work practices, safety equipment and personal protective equipment, and guidance for researchers on submitting a Biological Research Registration to the Institutional Review Board for approval.

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

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 receive 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 (HMS/HSDM) 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.

Chapter 2 NIH Recombinant DNA Guidelines

The NIH Guidelines for Research Involving Recombinant DNA Molecules (***http://www4.od.nih.gov/oba/rac/guidelines/guidelines.html***) contain procedures for the containment of rDNA research. The Guidelines apply to all institutions that receive NIH funding for rDNA. All Investigators at the institution must comply with the Guidelines even if their individual research is not funded by NIH. Consequences of noncompliance include suspension, limitation, or termination of NIH funds for rDNA research at the institution, or a requirement for prior NIH approval of rDNA projects at the institution.

The original guidelines were issued in 1976 due to public concern for safety, environmental impact, and ethical implications of rDNA research. The purpose of the guidelines is to specify safe handling practices and containment levels for rDNA molecules, organisms and viruses containing rDNA molecules, and transgenic animals.

Responsibilities under the Guidelines:

1. The Institution must:
    a. establish an Institutional Biosafety Committee (IBC). The Harvard Committee on Microbiological Safety (COMS) is the IBC for multiple institutions.
    b. ensure compliance with the NIH Guidelines by investigators
    c. report any significant problems, violations or significant research-related accidents or illnesses to NIH within 30 days

2. The Institutional Biosafety Committee must:
    a. review, approve and oversee rDNA research to ensure compliance with the Guidelines
    b. determine necessity of health surveillance of personnel
    c. ensure training for IBC members, staff, PIs, and laboratory staff
    d. set biosafety containment levels as required by the Guidelines for some experiments under III-D-4-b

3. The Principal Investigator must:
    a. be proficient in good microbiological techniques
    b. supervise staff to ensure safety practices are followed c. instruct laboratory staff on:
        i. the risk of agents used in the lab
        ii. safe work practices
        iii. emergency procedures for spills and exposures
        iv. the reasons for vaccinations and serum collection, when applicable d. ensure that:
        i. proper biosafety, biowaste, and shipping procedures are followed by staff
        ii. SOPs are developed and followed for spills, exposure, loss of containment, and reporting research-related accidents and illnesses
        iii. biological containment is maintained
        iv. unsafe work errors are corrected
    e. determine whether their research is subject to Section III-A, B, C, D or E of the Guidelines
    f. propose containment levels in accordance with NIH Guidelines and a

risk assessment
   g. submit a research registration to COMS for approval; obtain approval before initiating research if section III-A, B, C or D applies
   h. seek NIH approval for research falling under sections III-A, III-B, and III-C
   i. notify the Biosafety Officer or COMS of:
      i. changes to research before modifications are implemented
      ii. any significant research-related accidents and illnesses
      iii. any significant problems with containment procedures
      iv. violations of NIH guidelines

4. The Harvard Biosafety Office must:
   a. conduct lab inspections
   b. develop emergency and reporting procedures
   c. investigate lab accidents
   d. report rDNA incidents, violations of the Guidelines to COMS
   e. provide general biosafety training

5. The NIH Office of Biotechnology Activities (OBA) must:
   a. manage the Recombinant DNA Advisory Committee (RAC)
   b. conduct trainings of IBCs
   c. review human gene transfer protocols
   d. review the following rDNA experiments
   e. deliberate transfer of drug resistance that could compromise disease control
   f. cloning toxins with LD50 < 100 ng/Kg body weight
   g. DNA from restricted agents transferred to nonpathogenic prokaryotes or lower eukaryotes
   h. DNA from nonpathogenic prokaryotes or lower eukaryotes transferred to restricted agents
   i. use of restricted poxviruses in presence of helper virus

Levels of Review:

Levels of external federal review required for rDNA experiments are summarized below:

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

Levels of IBC review required for rDNA experiments are summarized in the table below:

Review	Experimen	Section
IBC 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
IBC 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 may require 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.

Risk Assessment and Containment Level

A risk assessment must be conducted to determine the appropriate Biosafety Level (BL1- BL4) of the agent used in your research.

1. Determine the NIH Risk Group (RG) of the agent – Appendix B of the Guidelines.
2. Evaluate the following characteristics of the agent: virulence, pathogenicity, infectious dose, environmental stability, exposure route, communicability, volume/concentration, and availability of vaccine or treatment.
3. Evaluate the gene product for toxicity, allergenicity, activity, e.g. oncogenic.
4. Determine the level of containment necessary BL1, BL2, or BL3. Harvard does not have a BL4 facility.

Viral Vectors Safety Resources

1. Lentiviral Vector Safety Guidance
   - RAC Guidance Document Biosafety Considerations for Research with Lentiviral Vectors
   - RAC discussion of Lentivirus Containment
   - Consideration of Biosafety Level Assignment for Lentiviral Vectors at Vanderbilt University
   - Lentiviral vectors and containment issues
   - Lentivirus vector discussion questions

2. Adenoviral Vector Safety
   - NIH RAC Report Assessment of Adenoviral Vector Safety and Toxicity

3. Additional Information
   - General Information about Mammalian Virus Vectors (University of Rochester)
   - Stanford University Working with Viral Vectors

Incident Reporting to NIH

The following incidents must be reported to NIH OBA within 30 days:

1. any significant problems or violations of the NIH Guidelines, e.g. failure to adhere to the containment and biosafety practices in the Guidelines
2. any significant research-related accidents and illnesses, e.g. spill or accident leading to personal injury or illness or a breach in containment, e.g. escape or improper disposition of a transgenic animal.

The following incidents require immediate reporting to NIH OBA:

1. Spills or accidents involving rDNA requiring BL2 containment resulting in an overt exposure, e.g. needlestick; splash in eyes, nose, mouth; or accidental aerosolization/inhalation

2. Spills or accidents involving rDNA requiring BL3 or BL4 containment resulting in an overt exposure or potential exposure, e.g. spills of high risk recombinant materials occurring outside of a biosafety cabinet

Minor spills of low-risk agents, contained and properly disinfected, generally don't need to be reported- consult NIH OBA if uncertain. The incident report to NIH OBA can be submitted by either the Institution, IBC, BSO, or PI. The report should include the response made to mitigate the problem and preclude its reoccurrence

NIH Guidelines Appendices

Appendix A Exemptions: Natural Exchangers

Appendix B Classification of Etiologic Agents

Appendix C Exemptions under IIIF

Appendix D Major Actions

Appendix E Certified Host-Vector Systems

Appendix F Biosynthesis of Toxic Molecules

Appendix G Physical Containment

Appendix H Shipment

Appendix I Biological Containment

Appendix J Biotechnology Research Subcommittee

Appendix K Large Scale Physical Containment

Appendix L Gene Therapy Policy Conferences

Appendix M Points to Consider in Human Gene Transfer Research

Appendix P Physical and Biological Containment: Plants

Appendix Q Physical and Biological Containment: Animals

Chapter 3 Infectious Agents and Biosafety Levels

Infectious materials are classified into risk groups based on their relative hazard. The CDC Biosafety in Microbiological and Biomedical Laboratories (BMBL, 5th Ed.) outlines safe lab practices, lab facilities, and safety equipment for four biosafety levels that provide appropriate containment for the various risk group agents (RG1-RG4). The BMBL also describes animal biosafety levels for the use of research animals. The summary tables below were adapted from BMBL, 5th Edition.

SUMMARY OF RISK GROUPS

RG1	Agent not associated with disease in healthy adult humans; *B. subtilis, E. coli K-12,* AAV, ecotropic avian sarcoma virus
RG2	Associated with human disease which is rarely serious and preventive or therapeutic interventions are often available; Human adenoviruses, human herpesviruses (except herpes B), *Staphylococcus aureus,* amphotropic murine leukemia virus, influenza viruses type A, B, and C
RG3	Serious or lethal human disease; preventive or therapeutic interventions may be available; *Mycobacterium tuberculosis*, VEE, *Francisella tularensis*
RG4	Serious or lethal human disease; preventive or therapeutic interventions are usually not available; Ebola, Marburg, Lassa, and Herpes B virus

SUMMARY OF RECOMMENDED BIOSAFETY LEVELS FOR INFECTIOUS AGENTS

BSL	AGENT	PRACTICES	PRIMARY BARRIERS AND SAFETY EQUIPMENT	FACILITIES (SECONDARY BARRIERS)
1		Standard Microbiological Practices	None required	Laboratory bench and sink required
2	percutaneous injury, ingestion, mucous membrane exposure	BSL-1 practice plus: • Limited access • Biohazard signs • "Sharps" precautions • Biosafety manual defining any needed waste decontamination or medical surveillance policy	Primary barriers: • Class I or II BSCs or other physical containment devices used for all manipulations of agents that cause splashes or aerosols of infectious materials PPEs*: • Laboratory coats; gloves; face protection as needed	BSL-1 plus: • Autoclave available
3	potential for aerosol transmission	BSL-2 practice plus: • Controlled access • Decontamination of all waste • Decontamination of laboratory clothing before laundering • Baseline serum	Primary barriers: • Class I or II BSCs or other physical containment devices used for all open manipulation of agents PPEs: • Protective laboratory clothing; gloves; respiratory protection as needed	BSL-2 plus: • Physical separation from access corridors • Self-closing, double-door access • Exhaust air not recirculated • Negative airflow into lab
4	Aerosol-transmitted laboratory infections have occurred	BSL-3 practices plus: • Clothing change before entering • Shower on exit • All material decontaminated on exit from facility	Primary barriers: • All procedures conducted in Class III BSCs or Class I or II BSCs in combination with full-body, air-supplied, positive pressure personnel suit	BSL-3 plus: • Separate building or isolated zone • Dedicated supply and exhaust, vacuum, and decontamination systems • Other requirements

* PPE – Personal Protective Equipment

SUMMARY OF RECOMMENDED BIOSAFETY LEVELS FOR ACTIVITIES IN WHICH EXPERIMENTALLY OR NATURALLY INFECTED VERTBRATE ANIMALS ARE USED

ABSL	Routes of Transmission	PRACTICES	PRIMARY BARRIERS AND SAFETY EQUIPMENT	FACILITIES (SECONDARY BARRIERS)
1		Standard animal care and management practices, including appropriate medical surveillance programs	As required for normal care of each species	Standard animal facility: • No recirculation of exhaust air • Directional air flow recommended • Hand washing sink is available
2	percutaneous injury, ingestion, mucous membrane exposure	ABSL-1 practice plus: • Limited access • Biohazard warning signs • "Sharps" precautions • Biosafety manual • Decontamination of all infectious wastes and of animal cages prior to washing	ABSL-1 equipment plus primary barriers: • Containment equipment appropriate for animal species PPEs*: • Laboratory coats, gloves, face and respiratory protection as needed	ABSL-1 plus: • Autoclave available • Hand washing sink available • Mechanical cage washer recommended
3	potential for aerosol transmission	ABSL-2 practice plus: • Controlled access • Decontamination of clothing before laundering • Cages decontaminated before bedding removed • Disinfectant foot bath as needed	ABSL-2 equipment plus: • Containment equipment for housing animals and cage dumping activities • Class I, II or III BSCs available for manipulative procedures (inoculation, necropsy) that may create infectious aerosols. PPEs: • Appropriate respiratory protection	ABSL-2 facility plus: • Physical separation from access corridors • Self-closing, double-door access • Sealed penetrations • Sealed windows • Autoclave available in facility
4	Aerosol transmission	ABSL-3 practices plus: • Entrance through change room where personal clothing is removed and laboratory clothing is put on; shower on exiting • All wastes are decontaminated before removal from the facility	ABSL-3 equipment plus: • Maximum containment equipment (i.e., Class III BSC or partial containment equipment in combination with full body, air- supplied positive-pressure personnel suit) used for all procedures and activities	ABSL-3 facility plus: • Separate building or isolated zone • Dedicated supply and exhaust, vacuum and decontamination systems • Other requirements outlined in the text

* PPE – Personal Protective Equipment

Resources for assigning risk group/biosafety level

1. The NIH Guidelines Appendix B assigns risk groups to some biological agents.
2. The BMBL provides Agent Summaries that indicate the appropriate biosafety level for some infectious agents.
3. The American Biological Safety Association (ABSA) website provides a searchable database of biological agents and their assigned biosafety levels by country.
4. Based on a risk assessment and review of the above sources, the PI will propose a biosafety level that COMS will evaluate.

Human blood, blood products, body fluids, tissues, and cells

Biosafety level 2 practices and containment must be followed when handling human materials that may contain bloodborne pathogens, e.g. HBV, HCV and HIV. The OSHA Bloodborne Pathogens Standard (29 CFR 1910.1030) applies to all occupational exposure to blood or other potentially infectious materials. Under the OSHA BBP Standard employers are required to develop a written Exposure Control Plan, offer employees the hepatitis B vaccination, and provide annual training. For more information on the OSHA BBP standard see the Harvard University Exposure Control Plan.

OSHA considers both primary and established human cell lines to potentially contain bloodborne pathogens unless tests have shown them to be free of BBP.

Cultured cells and tissue

Cultured cells which are known to contain or be contaminated with a biohazardous agent (e.g. bacteria or viral) are classified in the same biosafety level as the agent. Cell lines that are not human or non-human primate cells and which do not contain known human or animal pathogens are designated biosafety level 1.

The following cells and tissue must be handled using BL2 practices and containment.

- Human and non-human primate primary cells, established cell lines, and unfixed tissue
- Cell lines exposed to or transformed by a human or primate oncogenic virus
- Cells, cell lines or tissue infected with pathogens requiring BL2 containment.

Select agents

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 EHS if you discover select agents in your laboratory that have not been registered.

HHS SELECT AGENTS AND TOXINS (Target humans)

Abrin
Botulinum neurotoxins
Botulinum neurotoxin producing species of *Clostridium* Cercopithecine herpesvirus 1 (Herpes B virus)
Clostridium perfringens epsilon toxin
Coccidioides immitis Coccidioides posadasii Conotoxins
Coxiella burnetii
Crimean-Congo haemorrhagic fever virus
Diacetoxyscirpenol
Eastern Equine Encephalitis virus
Ebola viruses *Francisella tularensis* Lassa fever virus Marburg virus Monkeypox virus
Reconstructed replication competent forms of the 1918 pandemic influenza virus containing any portion of the coding regions of all eight gene segments (Reconstructed 1918 influenza virus) Ricin
Rickettsia prowazekii
Rickettsia rickettsii
Saxitoxin
Shiga-like ribosome inactivating proteins
Shigatoxin
South American haemorrhagic fever viruses: Flexal, Guanarito, Junin, Machupo, Sabia
Staphylococcal enterotoxins
T-2 toxin
Tetrodotoxin
Tick-borne encephalitis complex (flavi) viruses: Central European Tick-borne encephalitis, Far Eastern Tick-borne encephalitis, Kyasanur Forest disease, Omsk Hemorrhagic Fever, And Russian Spring and Summer encephalitis
Variola major virus (Smallpox virus) and Variola minor virus (Alastrim)
Yersinia pestis

OVERLAP SELECT AGENTS AND TOXINS (Target humans & animals)

Bacillus anthracis
Brucella abortus Brucella melitensis Brucella suis
Burkholderia mallei (formerly *Pseudomonas mallei*)
Burkholderia pseudomallei (formerly *Pseudomonas pseudomallei*) Hendra virus
Nipah virus
Rift Valley fever virus
Venezuelan Equine Encephalitis virus

USDA SELECT AGENTS AND TOXINS (Target Animals)

African horse sickness virus African swine fever virus Akabane virus
Avian influenza virus (highly pathogenic) Bluetongue virus (Exotic)
Bovine spongiform encephalopathy agent
Camel pox virus
Classical swine fever virus
Ehrlichia ruminantium (Heartwater)
Foot and mouth disease virus
Goat pox virus
Lumpy skin disease virus
Japanese encephalitis virus
Malignant catarrhal fever virus (Alcelaphine herpesvirus type 1) Menangle virus
Mycoplasma capricolum subspecies capripneumoniae (contagious caprine pleuropneumonia)
Mycoplasma mycoides subspecies *mycoides* small colony (*Mmm*SC) (contagious bovine pleuropneumonia)
Peste des petits ruminants virus
Rinderpest virus
Sheep pox virus
Swine vesicular disease virus
Vesicular stomatitis virus (exotic): Indiana subtypes VSV-IN2, VSV-IN3
Virulent newcastle disease virus[1]

[1] A virulent Newcastle disease virus (avian paramyxovirus serotype 1) has an intracerebral pathogenicity index in

day-old chicks (Gallus gallus) of 0.7 or greater or has an amino acid sequence at the fusion (F) protein cleavage site that is consistent with virulent strains of Newcastle disease virus. A failure to detect a cleavage site that is consistent with virulent strains does not confirm the absence of a virulent virus.

USDA PPQ SELECT AGENTS AND TOXINS (Target plants)
Peronosclerospora philippinensis (Peronosclerospora sacchari)
Phoma glycinicola (formerly *Pyrenochaeta glycines*)
Ralstonia solanacearum race 3, biovar 2
Rathayibacter toxicus Schlerophthora rayssiae var *zeae Synchytrium endobioticum Xanthomonas oryzae*
Xylella fastidiosa (citrus variegated chlorosis strain)

GENETIC ELEMENTS, RECOMBINANT NUCLEIC ACIDS, and RECOMBINANT ORGANISMS

1. 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.
2. 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*
3. Listed viruses, bacteria, fungi, and toxins that have been genetically modified.

Exclusions

1. The select agent rule does not include 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.
2. The select agent rule does not include non-viable select agent organisms or non- functional toxins.
3. 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 Toxins

The listed toxins are exempt from CDC and USDA registration requirements if the maximum allowable exempt quantity per Principal Investigator is not exceeded. PI's must keep toxin locked and maintain inventories to ensure maximum exempted amount is not exceeded.

Toxin	Maximum Exempted Amount per PI
Abrin	100 mg
Botulinum neurotoxins	0.5 mg
Clostridium perfringens epsilon toxin	100 mg
Conotoxins	100 mg
Diacetoxyscirpenol (DAS)	1000 mg
Ricin	100 mg
Saxitoxin	100 mg
Shiga-like ribosome inactivating proteins	100 mg
Shigatoxin	100 mg
Staphylococcal enterotoxins	5.0 mg
Tetrodotoxin (TTX)	100 mg
T-2 toxin	1000 mg

Chapter 4 Committee on Microbiological Safety (COMS)

Investigators must register all research studies involving recombinant DNA, microbiological agents, potentially infectious materials, and human studies with the Harvard University Committee on Microbiological Safety (COMS). The registration forms must be submitted to your biosafety officer who in turns submits the form with their containment level recommendations to COMS.

COMS requires annual laboratory inspections of BL2 and BL3 labs and biennial inspections of BL1 labs.

Links to COMS resources:

COMS Registration Forms
Biosafety Officer Contact Information
COMS Home Page

Chapter 5 Training

Initial training for all new personnel working with biological materials is provided in a classroom setting by EHS on the Cambridge, Longwood and Southborough campuses. EHS provides initial generic environmental and occupational health and safety training covering regulations and guidelines, safe work practices, and exposure controls.

On the Longwood campus, permanent IDs with key card access will not be granted to laboratory employees until all of the required training is completed. Incoming graduate students are required to attend classroom training as a group as arranged by EHS.

Annual BBP training is available to all personnel through on-line training or classroom training provided by EHS.

Laboratory-specific or job-specific training:

As required by OSHA, a Supervisor or his/her designee must provide training on specific job hazards to supplement EHS generic training. The PI or his/her designee must provide laboratory-specific training to personnel on the type of experiments being conducted, the nature of the material and equipment used and their associated hazards, safe work practices, waste management, and dealing with accidents including reporting requirements. This training should be documented.

Chapter 6 Medical Surveillance

A medical surveillance program is provided through University Health Services (UHS) for personnel who are occupationally at risk of exposure to bloodborne pathogens (BBP). The program includes free hepatitis B vaccine offer and post-exposure evaluation with follow up. See the Harvard University Exposure Control Plan for more information.

A medical surveillance program for personnel that have direct contact with research animals is provided at the Cambridge, Southborough and Longwood campuses. The program includes disease-specific occupational health advice, Animal Biosafety Level 2 training, vaccination offers, pre-screening questionnaires, and post-exposure medical treatment. The Longwood Campus animal facility occupational health program is provided by Tom Winters, MD, of OEHN.

Vaccination for various infectious agents used in the laboratory, e.g., vaccinia, attenuated rabies, and measles, is offered to all at-risk employees as recommended by COMS. UHS provides medical treatment and post-exposure evaluation after an exposure to infectious agents or rDNA for students and employees working in BL1 or BL2 laboratories.

A detailed Occupational Health Response Program has been developed for each BL3 laboratory. In addition to being offered recommended vaccinations, BL3 laboratory personnel may have baseline serum samples collected, as appropriate, and tests for agents handled in the lab, e.g. TB skin test. The medical surveillance program and post- exposure evaluations for BL3 laboratory personnel is administered by Tom Winters, MD, of OEHN.

Chapter 7 Biosafety Cabinets and Other Safety Equipment

Biosafety cabinets (BSC) control airborne contaminants during work with infectious material through the use of laminar airflow and high efficiency particulate air (HEPA) filtration. The Class II BSC is the most commonly used BSC at Harvard. It is designed to protect personnel and the environment from infectious materials inside the cabinet and to protect the material inside the cabinet from contamination from the lab environment.

BSC Location in the Laboratory and Certification

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, high traffic areas, and laboratory equipment, e.g. centrifuges, that create turbulence. A BSC in a BL1 and BL2 laboratory must be professionally certified after installation, annually, and after being moved. A BSC in a BL3 laboratory must be certified after installation, every six months, and after being moved. A BSC must be professionally decontaminated before moving.

Safe and Effective Use of the BSC

1. Before beginning work:
   a. Monitor alarms, pressure gauges, or flow indicators for any changes.
   b. Shut off the UV light.
   c. Turn the cabinet on and let it run for 3-5 minutes.
   d. Wipe work surface with an appropriate disinfectant, e.g. 70% ethanol.
   e. Place a pan with disinfectant and/or a sharps container inside the BSC. Avoid using the vertical pipette discard containers on the floor outside the BSC.
   f. Plan your work and place everything needed for the procedure inside the BSC. Wipe items with disinfectant before placing in BSC.
2. Avoid airflow disruption that could affect the level of protection provided by the BSC:
   a. Keep the BSC free of clutter, e.g. extra equipment and supplies
   b. Don't place objects over the front air intake grille.
   c. Don't block the rear air intake grille.
   d. Limit traffic in the area when the BSC is in use
   e. Make sure lab door is closed, and avoid opening and closing door if located near the BSC.
   f. Move arms slowly when removing or introducing items.
   g. Keep all materials at least 4 inches inside the sash.
   h. Place a centrifuge or blender that creates air turbulence in the back 1/3 of the cabinet and stop other work while the equipment is running.
   i. Don't operate a Bunsen burner in the cabinet.
3. While working:
   a. Work as far to the back of the BSC workspace as possible.
   b. Segregate contaminated and clean items. Work from "clean to dirty."
   c. Clean up all spills in the cabinet immediately. Allow cabinet to run for 3-5 minutes before resuming work.
4. After completing work:
   a. Wipe down all items with an appropriate disinfectant before removing. Remove all materials and wipe all interior surfaces with an appropriate disinfectant, e.g. 70% ethanol.
   b. Periodically decontaminated under work grilles.

Aerosol-proof rotors and safety cups for centrifuges

Aerosols may be created during centrifugation from poorly sealed or capped tubes and from tubes breaking. Please follow the procedures below when centrifuging biohazardous materials:

1. Use aerosol-proof rotors or safety buckets with caps that seal with O-rings.
2. Before use inspect O-rings and safety caps for cracks, chips, and erosion.
3. Use tubes with threaded caps. Avoid overfilling the tube and getting caps/closures wet. Wipe tubes down with disinfectant after filling.
4. Load and unload rotors and buckets inside the BSC
5. Balance buckets, tubes and rotors before centrifuging.
6. Disinfect the centrifuge after use.
7. Place small, low-speed centrifuges in a BSC during use to contain aerosols.
8. Filter the exhaust air from high-speed centrifuges.

Other safety equipment for aerosol-producing devices

The use of certain devices, e.g. blenders, homogenizers, sonicators (ultrasonic disrupters) can produce aerosols. To reduce exposure to aerosols, these devices should be used in a biosafety cabinet whenever possible.

Safety blenders and the BeadBeater homogenizer (BioSpec Products) are designed to prevent leakage of aerosols. The devices should be used in the BSC to prevent accidental release of aerosols.

Sterilization of inoculating loops or needles in an open flame generates small-particle aerosols that may contain viable microorganisms. The use of a shielded electric incinerator minimizes aerosol production during loop sterilization. Alternatively, disposable loops and needles can be used.

Chapter 8 Safe Work Practices and PPE

PPE is used to protect personnel from contact with infectious agents and hazardous materials. Supervisors are responsible for conducing workplace assessments and to select and train employees in the use of PPE e.g. lab coats, gloves, safety glasses, face shields, etc. PPE must not be taken home or worn outside the laboratory in non- laboratory areas. For assistance in selecting PPE, contact the EHS Office.

Recommended PPE:

1. Laboratory garments, e.g. lab coats, scrubs, and gowns, are long-sleeved and used to prevent contamination of the skin and street clothes. If splashes may occur, the garment must be fluid-resistant. If required, lab coats should be provided for visitors, maintenance and service workers.
2. Gloves must be worn when working with biohazards. Temperature resistant gloves must be worn when handling hot material or dry ice. If personnel develop or have latex allergies, then nitrile gloves should be used in the lab with biohazards instead of latex gloves. Gloves should overlap the sleeve of the lab garment. Double-gloving adds further protection and is recommended in some circumstances, e.g. for BL3 laboratories, or if a spill or splash may occur.
3. Face protection, e.g. goggles or safety glasses with side shields in combination with masks, or face shields, or other splatter guards are required for anticipated splashes or sprays of infectious material.
4. Respirators may be necessary in some cases, e.g. for BL3 laboratories. Personnel who require respiratory protection must be evaluated by a physician and trained in respirator selection and usage. Personnel required to wear tight-fitting respirators must be fit-tested by the EHS Office.

Sharps Precautions:

1. Avoid the use of needles and other sharps whenever possible. Many glass items have plastic alternatives that should be used.
2. If the use of sharps is unavoidable, take extra precautions and dispose in a red biosharps container immediately after use.
3. Needles must never be recapped, removed from the syringe, sheared, bent or broken. If a needle must be recapped, use a one-handed method or a mechanical device, e.g. forceps.
4. Use syringes with a luer lock system to prevent the needle from detaching from the syringe during use.
5. Use a mechanical device to remove scalpel blades, never use your fingers.
6. Contact the EHS Office for help in evaluating or selecting safer medical devices, e.g. safe needles.

Safe Work Practices:

Proper work practices protect you and others from exposure to infectious materials, reduce the possibility of cross-contamination, and improve the quality of the work performed.

1. Label all equipment used to store infectious materials with a biohazard warning label
2. Keep an uncluttered work space
3. Plan work procedures with safety in mind
4. Remove PPE and wash hands when leaving the lab

5. Don't eat, drink, smoke, apply cosmetics, and handle contact lenses in the lab
6. Don't mouth pipette
7. Decontaminate work surfaces at the end of an experiment and after a spill occurs
8. Decontaminate reusable PPE as soon as possible after it has been contaminated. Lab coats can be spot treated with 10% bleach or autoclaved before laundering
9. Protect house vacuum lines and vacuum pumps by using a hydrophobic HEPA filter installed between the collection flask and vacuum source
10. Change gloves often and as soon as possible when visibly contaminated
11. Minimize aerosol production by working carefully
12. Perform procedures that may result in aerosols in a BSC
13. Use aerosol-proof rotors or safety cups when centrifuging and load and unload them in a BSC

Longwood Lab Hazard Inventory and Door Placard Database (LabPoint)

As required by the Boston Fire Department (BFD), each laboratory must **annually** update their hazardous substance and biological material inventory and post updated door placards each year by April 1. The door placard contains the biosafety level, entry requirements, and office and after-hours contact numbers for the PI and the second in charge of the laboratory in the PIs absence.

Chapter 9 Waste Management

Biohazardous waste includes all waste that may contain or had contained biohazardous materials or rDNA.

Liquid Waste for Drain Disposal

Liquid biohazardous waste from a BL3 laboratory is autoclaved following lab-specific SOPs prior to disposal. Autoclaves in BL3 labs are validated and annually calibrated. An On-Site Treatment log is kept per MDPH regulations.

Listed below are two COMS-approved options for treating rDNA, BL1 and BL2 liquid waste for drain disposal:

I. SOP for bleach disinfection of rDNA, BL1 and BL2 liquid waste for drain disposal

1. Effectiveness:
   Bleach, a sodium hypochlorite solution (NaOCl), is a broad-spectrum disinfectant that is an effective disinfectant for enveloped viruses (e.g. HIV, HBV, HSV), vegetative bacteria (e.g. *Pseudomonas, Staphylococcus, and Salmonella*), fungi (e.g. *Candida*), mycobacterium (e.g. *M. tuberculosis* and *M. bovis*), and non-enveloped viruses (e.g. Adenovirus and Parvovirus).
   Austin A1 mercury-free bleach and Clorox bleach EPA registration numbers are 1672-20004 and 5813-50, respectively.
2. Recommended Personal Protective Equipment:
   a. Lab coat
   b. Latex or nitrile gloves c.
   Safety glasses
3. Concentration:
   The appropriate concentration of sodium hypochlorite for disinfecting liquid BL1 and BL2 waste, e.g. supernatants from cell culture, is 5000 ppm, approximately 0.5%. Household bleach is 5.2 - 6.1 % sodium hypochlorite, therefore a 1:10 (v/v) dilution of bleach to liquid biological waste is appropriate.
4. Contact time:
   An appropriate contact time of sodium hypochlorite with liquid waste is 20 minutes before drain disposal. After 20 minutes of contact, disinfected liquid waste is poured down the sink and the drain is flushed with water.
5. Stability and Storage:
   Bleach should be stored between 50 and 70°F. According to Clorox, undiluted household bleach has a shelf life of six months to one year from the date of manufacture, after which bleach degrades at a rate of 20% each year until totally degraded to salt and water, and a 1:10 bleach solution has a shelf life of 24 hours. Some manufacturer-prepared 1:10 bleach solutions, e.g. Bleach-Rite, contain a stabilizer that increases the shelf life to approximately 18 months.
6. Massachusetts Medical and Biological Waste Regulations 105 CMR 480.200 (F) Biotechnology By-product Effluents:
   a. Following this SOP will meet the requirements in 105 CMR 480.200 (F) for drain disposal of BL1 and BL2 liquid waste.
   b. According to Steven Hughes of the MDPH, an On-site Treatment Log and validation is not required for chemical disinfection of BL1 and BL2 liquid waste for drain disposal given that the IBC approves this SOP and an EPA

registered disinfectant is used.

7. Additional Information: See the bleach MSDSs.

II. SOP for autoclaving rDNA, BL1, and BL2 liquid waste for drain disposal

1. Effectiveness:
   Autoclaving is an effective means of sterilizing BL1 and BL2 liquid waste. Sterilization refers to the complete killing of all living organisms, including spores. The autoclave is periodically validated for effectiveness by using a biological indicator, e.g. *Geobacillus sterothermophilus* spores.
2. Recommended Personal Protective Equipment:
   a. Lab coat
   b. Latex or nitrile gloves c.
   Heat resistant gloves d. Safety glasses
3. Procedure:
   a. Collect BL1 and BL2 liquid waste in autoclavable, leak proof containers that are never more than ¾ full.
   b. Place containers in an autoclavable tray in the autoclave. LOOSEN each container top and place indicator tape on each top.
   c. Adequate cycle time varies depending on load, type of autoclave, and secondary containment. Based on spore testing, determine the appropriate cycle time to sterilize liquid waste for your autoclave. Typical cycle times for sterilizing liquid waste range from 45 to 90 minutes at 250°F.
   d. Autoclave temperature should be 250°F (121°C) and autoclave pressure should be 15 psi.
   e. Pour sterilized liquid waste down the sink and flush the drain with water.
4. Massachusetts Medical and Biological Waste Regulations 105 CMR 480.200 (F) Biotechnology By-product Effluents:
   a. Following this SOP will meet the requirements in 105 CMR 480.200 (F) for drain disposal of BL1 and BL2 liquid waste.
   b. According to Steven Hughes of the MDPH, an On-site Treatment Log is not required for autoclaving BL1 and BL2 liquid waste for drain disposal given that the IBC approves this SOP.

Sharps waste collection and handling procedures:

Biohazardous sharps waste describes material used with rDNA, BL1, BL2, or BL3 material that have sharp edges capable of causing punctures or cuts, including, but not limited to the following: needles, syringes, scalpels, razor blades, slides, coverslips, Pasteur pipettes, capillary tubes, and broken glass and plastic. Plastic serological pipettes are considered “sharps waste” if they are broken and have a sharp edge.

1. Collect biohazardous sharps in a rigid, red biosharps container. To avoid injury, please do NOT clip, bend, shear, or separate needles from syringes and do NOT recap needles.
2. Please do not overfill the biosharps container.
3. When the container is ¾ full, close it, and place the container in a Stericycle biowaste box or reusable bin.

4. Biosharps containers located in a BL2+ or BL3 laboratory must follow lab-specific SOPs.

To request red biosharps containers on the Longwood campus, use the hazardous waste online form or call the EHS Office. On the Cambridge campus, labs can purchase sharps containers from VWR: (800) 932-5000 or www.vwr.com.

Solid biohazardous waste collection and handling procedures:

1. Collect BL1 and BL2 waste in a red bag-lined Stericycle biowaste box or reusable bin for pick-up and off-site treatment. The inner red bag must be tied closed. If using cardboard boxes, close the box with tape and write your building and room number on the side of the box. If liquid is placed in the Stericycle boxes or reusable bins, then place enough absorbent material in the box to absorb the liquid to prevent leaking. Biowaste Plastic Bin Collection Procedures can be found on the EHS website on the Lab Waste Management page.
2. BL2+ and BL3 solid waste collection and treatment must follow lab-specific SOPs.
3. Stericycle biowaste boxes or reusable bins are picked-up for off-site Electro Thermal Deactivation (ETD) unless an **"Incinerate Only"** or **"Pathological Waste"** sticker is affixed to the box.

Incineration Only Waste

The following waste must be identified and segregated for incineration:

1. Trace chemotherapy-contaminated waste: RCRA empty drug vials, contaminated gloves and gowns, IV tubing and bags, and needles and syringes.
2. Pathological waste: human or animal body parts, organs, tissues, and surgical specimens.
3. Non-RCRA hazardous pharmaceuticals: must be characterized and certified as non-RCRA hazardous material by the generator. Excludes all DEA drugs including controlled substances.

Incinerate only waste must be collected in Stericycle cardboard boxes and an "Incinerate Only" or a "Pathological Waste" sticker must be placed on the box.

Mixed waste:

Mixed waste often requires special procedures. Please contact the EHS Office for proper disposal procedures.

1. Mixed biological/chemical waste can be disinfected by using carefully selected chemical treatments only if compatible with the other chemicals in the experiment. Handle resulting waste as hazardous chemical liquid waste. Contact the EHS office for advice on avoiding adverse chemical reactions.
2. Treat animal or human tissue in 10% formalin waste as liquid chemical waste and label the hazardous waste tag "10% formalin + non-infectious animal tissue" or "10% formalin + non-infectious human tissue."

3. Disinfect biologically contaminated radiological solid waste by soaking in a suitable disinfectant. Discard disinfectant waste in designated and posted sink if radiological contamination is within sink disposal limits.
4. Disinfect iodinated liquid waste with a phenolic disinfectant; e.g., Lysol™. Disinfect all other liquid waste with bleach (10% final concentration.) If the waste is within radiological sink disposal limits, dispose of in designated and posted sink. If levels are above sink disposal limits, then package in EHS-provided containers.

Chapter 10 Emergencies and Reporting

Each Harvard University Campus has an Emergency Response Guide flipchart that is posted in each laboratory. The guide contains procedures for spills, exposure incidents, reporting instructions, contact numbers, and the location of emergency equipment. The PI or lab safety coordinator must review the guide with new personnel.

Reporting Instructions

Report all injuries, accidents, animal bites, and exposures to your supervisor and complete the Harvard Accident Report Form or your institution's Accident Report Form if you are a tenant at Harvard Longwood Campus

Report exposure incidents involving rDNA, infectious substances, or radiation to Harvard Longwood EH&S which will notify the appropriate regulatory agency, as necessary.

Report all animal bites to your supervisor and medical treatment provider who will notify the appropriate regulatory agency, as necessary.

Injury, Medical Emergency, Animal Bite

OBTAINING MEDICAL ATTENTION

- For serious medical emergencies, go to Brigham and Women's emergency room or call 911.
- HUPD (43)2-1212 are trained in first aid and CPR/AED and can transport uncontaminated, ambulatory patients to medical treatment sites
- Medical treatment during work hours:
    - Harvard employees/students, go to Harvard University Health Services (UHS) at 275 Longwood Avenue, Vanderbilt Hall: (43)2-1370. (M/Th 9–6:30; T/W/F 9–5) or to Holyoke Center if you work in Cambridge.
    - Tenants in Harvard buildings, go to your institution's health care center. For more information, refer to Emergency Phone Numbers tab.
- Medical treatment after work hours:
    - Harvard employees/students, go to UHS at Holyoke Center, 75Mount Auburn St., Cambridge (clinicians available 24 hours).
    - Tenants in Harvard buildings should contact their institution's health care center for instructions related to after work hour emergencies.
- Harvard employees/students at the Longwood campus with animal-related injuries, medical treatment is provided by the animal facility occupational health program at 617-632-3352 (pager # 42038).

HAZARDOUS MATERIAL ON SKIN OR SPLASHED IN EYE

- 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.
- Immediately after rinsing, obtain medical attention.
- Review MSDS(s) for hazards and report the incident (see above).

NEEDLESTICK OR CUT WITH CONTAMINATED SHARP ITEM

- Immediately wash the area with soap and water for at least 15 minutes.
- Immediately after rinsing, obtain medical attention.
- Report the incident (see above).

MONKEY-RELATED INJURIES/BITES

- Immediately stop what you are doing and secure the animal in its cage.
- EYE SPLASH: immediately rinse eye for 15 minutes.
- BITE/SCRATCH/CUT: go to nearest B Virus Bite Kit
- Wash the wound with the Betadine scrub brush for 15 minutes.
- Rinse the wound with sterile saline solution and bandage with sterile gauze.
- Immediately obtain medical attention for ANY exposure or possible exposure. Report the incident (see above).

INJURY INVOLVING RESEARCH ANIMAL (If monkey-related, see above.)

- BITE/SCRATCH/CUT: wash the area with soap and water for at least 15 minutes.
- Obtain medical attention and report incident to the animal facility.

ASSISTING IN MEDICAL EMERGENCY OR PERSONAL INJURY

- See above OBTAINING MEDICAL ATTENTION.
- Do not move injured person unless there is a danger of further harm from remaining in the location. If the area is unsafe, then evacuate, close doors to area, and prevent access. Provide information to emergency responders.
- Remain with the injured person until medical assistance arrives. Initiate life-saving measures if necessary and you are trained.

Biological Spill Procedures

BIOSAFETY LEVEL 1 (BL1) BIOLOGICAL SPILL

- Alert others in the area.
- Remove contaminated clothing and wash exposed skin (see INJURY PROCEDURES above).
- Wear gloves, lab coat, and face protection.
- Cover spill with paper towels and pour disinfectant, e.g., 10% bleach, around and over the spill.
- Allow suitable contact time, such as 20 minutes.
- Pick up sharp items, e.g., broken glass or needles, with forceps or dust pan and brush and place in a sharps container.
- Discard disposable materials used to clean up the spill in a red biowaste bag. Disinfect any non-disposable materials used.

BIOSAFETY LEVEL 2 (BL2) BIOLOGICAL SPILL

- Alert others in the area. Avoid inhaling airborne material while leaving the room.
- Close lab door and post Do Not Enter or place caution tape across door.
- Remove contaminated clothing and wash exposed skin with soap and water (see

INJURY tab above).

- Allow aerosols to settle for at least 30 minutes before re-entering the lab.
- Wear gloves, lab coat, and face protection (depending on nature of spill HEPA N95 respirator may be advised—refer to your lab-specific spill SOP)
- Cover spill with paper towels and pour disinfectant, e.g., 10% bleach, around and over the spill. Allow suitable contact time, such as 20 minutes.
- Pick up sharp items, e.g., broken glass or needles, with forceps or dust pan and brush and place in a sharps container.
- 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.

BIOSAFETY LEVEL 3 (BL3) SPILL

- Follow your laboratory-specific SOP for BL3 biological spills.

BLOOD SPILL

- Alert others in the area.
- Remove contaminated clothing and wash exposed skin with soap and water (see INJURY tab above).
- Wear gloves, lab coat, and face protection.
- Cover spill with paper towels and pour disinfectant, e.g., 10% bleach, around and over the spill. Allow suitable contact time, such as 20 minutes.
- Pick up sharp items, e.g., broken glass or needles, with forceps or dust pan and brush and place in a sharps container.
- 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.

Chapter 11 Shipping Biological Materials

Shipping regulated biological materials must comply with the US Department of Transportation (US DOT) and International Air Transport Association (IATA) regulations. Personnel packaging and shipping regulated biological materials must be trained every two years. Contact the EHS Office for shipping training.

Import and Export Information

Centers for Disease Control (CDC) import permit

The importation of etiologic agents regulation is contained in USPHS 42 CFR - Part 71 Foreign Quarantine; Part 71.54 Etiologic agents, hosts, and vectors.

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 (http://www.cdc.gov/od/eaipp/).
  - **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.

To Obtain a CDC Import Permit (www.cdc.gov/od/eaipp**):**

- Importation permits are issued only to the importer, who must be located in the United States. Link for fillable form: http://www.cdc.gov/od/eaipp/forms/Permit_to_Import_Transport_fillable.pdf
- Phone: (404) 718-2077**;** Fax: (404) 718-2093
- Email: importpermit@cdc.gov
- Website: www.cdc.gov/od/eaipp

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

Animal Products Requiring a USDA Import Permit

- animal tissues, blood, cells or cell lines of livestock or poultry origin,
- RNA/DNA extracts,
- hormones,
- enzymes,
- monoclonal antibodies for IN VIVO use in non-human species,
- certain polyclonal antibodies,
- antisera,
- bulk shipments of test kit reagents,
- and microorganisms including bacteria, viruses, protozoa, and fungi.

APHIS regulates veterinary biologics (vaccines, bacterins, antisera, diagnostic kits, and other products of biological origin) to ensure that the veterinary biologics available for the diagnosis, prevention, and treatment of animal diseases are pure, safe, potent, and effective.

Animal Products NOT Requiring a USDA Import Permit

- Non-human primate tissues, serum, and blood.
- Below are links to guidelines for animal products that do **NOT** need a USDA import permit, but will be reviewed at the port of entry by USDA inspectors:

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

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 Animal Products:

- To **apply on-line for a VS import permit**, go to the link http://www.aphis.usda.gov/import_export/animals/animal_import/downloads/epermitsl ttr.pdf or
- Obtain a permit application by writing:
  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

Veterinary Biologics Requiring a USDA Import Permit

- Veterinary biologics available for the diagnosis, prevention, and treatment of animal diseases including vaccines, bacterins, antisera, diagnostic kits, and other veterinary products of biological origin.
- Veterinary biological products produced in other countries may be imported into the United States for research and evaluation, transit shipment, or general sale and distribution

To Obtain a USDA Import Permit for Veterinary Biologics:

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 or submit electronically via the APHIS e-permit system.

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.shtml
- 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 agent importing

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.

Exporting: Department of Commerce (DOC)

The export of a wide variety of etiologic agents of human, plant, and animal diseases may require a license from the Department of Commerce. Information may be obtained at the Department of Commerce Bureau of Export Administration at 202-482-4811 or http://www.bis.doc.gov/Licensing/. Ellen Berkman (ellen_berkman@harvard.edu), Harvard University Attorney, helps researchers export items on the DOC Commerce Control List.

Chapter 12 Biosafety References

Guidelines for Research Involving Recombinant DNA Molecules, National Institutes of Health, April 2002

Biosafety in Microbiological and Biomedical Laboratories (BMBL), 5th Edition, Centers for Disease Control and Prevention, National Institutes of Health, February 2007

Primary Containment for Biohazards: Selection, Installation and Use of Biological Safety Cabinets, BMBL Appendix A, Centers for Disease Control and Prevention, National Institutes of Health

Massachusetts Department of Public Health 105 CMR 480.000 MINIMUM REQUIREMENTS FOR MEDICAL OR BIOLOGICAL WASTE (STATE SANITARY CODE CHAPTER VIII)

Recombinant DNA Technology: Use Regulations City of Boston, Board of Health and Hospitals, March, 1994

Revised Ordinance City Council of the City of Cambridge, February 1993

CDC and APHIS Select Agent Final Rule

Select Agent and Toxin List

A Laboratory Security and Emergency Response Guidance for Laboratories Working with Select Agents, MMWR Dec 6, 2002/51 (RR-19) 1-8