# The Princeton University Biosafety Manual

## I. INTRODUCTION

### A. Scope

This Manual is applicable to all laboratory, research, service and support activities that may involve exposure to biohazardous agents or materials and that come under the purview of the Institutional Biosafety Committee (IBC).

Activities which are those specifically addressed are those involving:

work with recombinant DNA
various bacterial, fungal, and parasitic agents
Live viruses
experimentally infected research animals
Human blood and tissues
Receipt, handling, and disposal of biological materials

The Manual does not address issues of radiation or chemical safety. These are covered in the University Radiation Safety Manual and the Chemical Hygiene Plan and can be accessed here.

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### B. Regulatory Forces and Guidelines

Guidelines developed by the National Institutes of Health (NIH) and the Centers for Disease Control and Prevention (CDC) form the basis for the biosafety practices included in this manual. These guidelines must be followed to ensure the continuation of grant funds from federal agencies.

The NIH Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines):

Mandate the establishment of an Institutional Biosafety Committee (IBC) for the review and oversight of biological research
Outline roles and responsibilities for biosafety
Establish the practices, procedures, and conditions under which **recombinant DNA work** must be conducted.

The companion guidelines from CDC-NIH, Biosafety in Microbiological and Biomedical Laboratories (BMBL) address the appropriate measures and facilities for **work with all microbial agents,** including bacterial, viral, fungal, parasitic, and rickettsial agents.

For **work with human blood and some other body fluids and tissue,** the requirements of the Occupational Exposure to Bloodborne Pathogens standard from the Occupational Safety and Health Administration (OSHA) apply. Special training, medical surveillance, procedures, and equipment that must be in place are described in Section II of the Manual.

The obtaining, possession, use, or transfer of any **select biological agent or toxin** is strictly regulated by federal code and regulations. It requires federal permits and inspection as well as significant measures of lab security, personnel training, and

accurate record keeping regarding the status of possessed materials. Further information on select agents and toxins is found in Section IIC of the Manual.

**Handling and disposal of bio hazardous waste** is regulated and monitored by the NJ Department of Environmental Protection under the Regulated Medical Waste rules found in the NJ Administrative Code at 7:26-3A. The procedures for biological waste handling outlined in Section IV F of the Manual comply with the requirements of these rules.

The requirements for **packaging and shipment of biomedical materials** are provided in the Public Health Service regulation 42 CFR Part 72 Interstate Shipment of Etiologic Agents and parts of the Department of Transportation Hazardous Materials regulation 49 CFR, Parts 171-180. Information on shipping procedures that comply with these regulations is found in Section IV (G and H) of the Manual.

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## C. The Biological Safety Program at Princeton University

The biological safety program at Princeton University developed from the University's commitment to address and comply with the NIH Guidelines regarding safe research with rDNA and associated viral materials. Oversight of Princeton University's biological safety program is provided by the Institutional Biosafety Committee (IBC). The key components of the program are:

The Institutional Biosafety Committee (IBC)
Office of Research and Project Administration (ORPA)
The Department Chair
The Principal Investigator
The Researcher or User
Environmental Health and Safety (EHS)
Occupational Medicine
Campus Veterinarian

The roles and responsibilities of each are described below:

### The Institutional Biosafety Committee (IBC):

The IBC membership includes representative faculty and administrators, the University Biosafety Officer, a University Physician, the Campus Veterinarian, and representatives from Princeton Township and Borough. The committee's current membership is listed in the current University Register. The IBC:

Oversees the biological safety program
Reviews research proposals involving rDNA and other biological agents and materials, and approves those that comply with NIH and CDC guidelines and University policy
Adopts policies supporting the safe use of biological materials and the elimination or reduction of exposure to potentially biohazardous materials or agents addresses biosafety issues related to experimentally-infected laboratory animals

### Office of Research and Project Administration (ORPA) – Contact Joseph Broderick, Secretary of the IBC and IACUC at 258-3976:

Initiates the registration of biological research (Memorandum of Understanding and Agreement [MUA] process) by providing department chairs with the registration material
Accepts all MUAs and Annual Registrations for research proposals submitted by Principal Investigators and departments and coordinates their review by the IBC
Accepts research proposals involving the use of animals and coordinates their review by the Institutional Animal Care and Use Committee (IACUC)

**Department Chairperson**

Receives from ORPA the material for registration of biological research
Ensures that MUA forms are completed by each Principal Investigator conducting applicable research
Submits completed MUAs and annual registration forms to ORPA

**Principal Investigator**

Completes a *Memorandum of Understanding and Agreement (MUA)* for all research proposals involving the use of biological materials or agents
Accepts direct responsibility for the health and safety of those working with biological materials in his/her laboratory
Ensures proper lab orientation, training, and instruction for laboratory personnel in safe practices and protocols, including, instruction in good microbiological techniques and practices needed to work safely with the biological agents and materials involved
Ensures that laboratory personnel receive any necessary medical surveillance
Ensures compliance by laboratory personnel with the relevant regulations, guidelines, and policies
Ensures biosafety cabinets are certified as needed and personal protective equipment is provided and used
Reports immediately to OPRA any significant violations of the NIH Guidelines, problems with containment and any significant research - related accidents or illinesses

**Researcher or User:**

Participates in appropriate training and instruction
Becomes familiar with all biological agents being used in the lab and the potential risks associated with exposure
Follows all laboratory practices and protocols and complies with all applicable guidelines and policies
Completes any necessary medical surveillance
Reports all accidents, spills, or contamination incidents to supervisor

**Environmental Health and Safety (EHS) – Contact Jacqueline Wagner (Biosafety Officer) at 258-1427:**

Consults with researchers on issues of biosafety and the safe use of biological materials in the laboratory
Develops protocols and procedures to address issues of biosafety
Provides training in safe use and practices for those involved in work with potentially biohazardous materials and activities
Advises researchers on proper waste disposal methods based on federal and state regulations and established University practice
Provides oversight of the BBP program and manages on-line web-based training program for those with potential exposure
Conducts periodic inspection of labs using biological materials

**Employee Health– Contact Peggy Henke (Office Manager), Sara Ingraffia (RN), or Alice Kerwick (RN) at 258-5035:**

Advises on need for medical surveillance and/or immunization for those personnel exposed or potentially exposed to biological agents
Provides medical review and medical surveillance, as appropriate, for live virus workers, those exposed to laboratory animals, and those in the BBP Program

**Campus Veterinarian – Contact Peter Autenried at 258-7857**

Advises investigators and animal care personnel on the potential biohazards and risk of physical injury associated with laboratory animals and on the procedures for reducing or eliminating exposure
Provides training to all animal users in bio methodology and safe animal handling

**Other Committees (Human Subjects, Animal Care and Use (IACUC), Radiation Safety)**

Consults and coordinates with the IBC on any proposals under their purview which involves the use of potentially biohazardous materials or activities

# II. BIOHAZARDOUS RESEARCH PROJECT REGISTRATION AND APPROVAL

## A. Introduction

Each Principal Investigator (PI) is responsible for the preparation of a Memorandum of Understanding and Agreement (MUA) for **all** research involving biological materials or agents including the assignment of the required Biosafety Level to the proposed research. This includes research involving:

- Recombinant DNA, including experiments that are specifically exempt under the *NIH Guidelines*
- Bacterial, fungal, parasitic, or other potentially infectious agents
- Live viruses
- Human blood and tissue

The IBC will review all submitted MUAs; confirm, where applicable, that exempt status is appropriate for certain rDNA work; and consider approval for those MUAs that are complete and which provide for safe handling of potentially biohazardous materials under the appropriate Biosafety Level.

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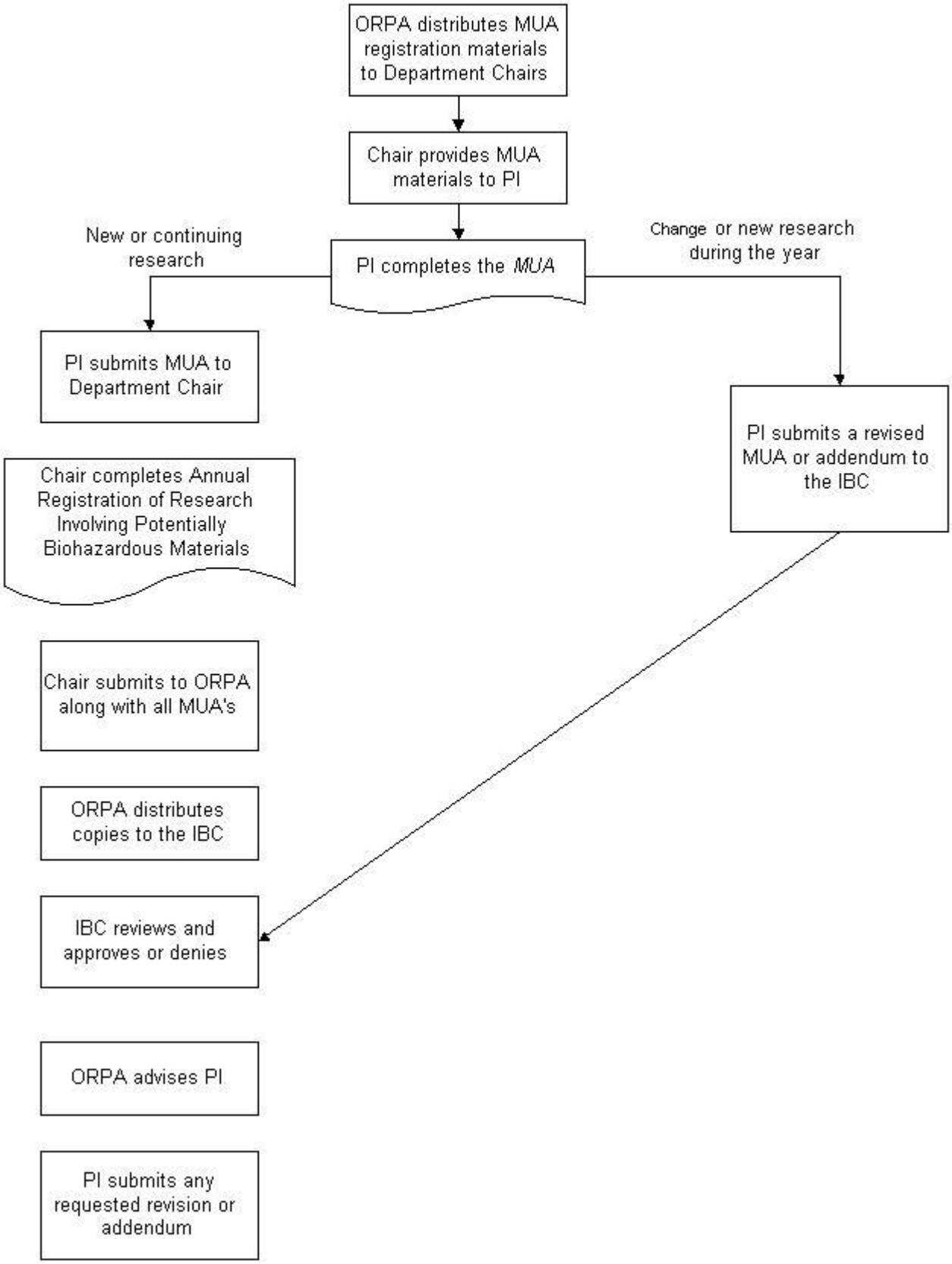
## B. Registration and Approval Process

The annual registration and MUA approval process begins each fall with the distribution of the MUA registration materials by ORPA to the chairperson of each department conducting research with rDNA and other potentially infectious agents. **Additional requirements referred to in the MUA for research involving live viruses or human blood or tissue, (as outlined below) will need to be fulfilled for final approval to be given.**

The chart provided below indicates the steps involved in this process:

# Annual Registration and MUA Approval



Copies of the MUA and Annual Registration forms can be downloaded from the ORPA web site at http://www.princeton.edu/~orpa1/ibc.htm or can be obtained from ORPA. To assist in the completion of the MUA, the *Synopsis of Recombinant DNA Guidelines and Biosafety Policies* is also provided at the above website or from ORPA. In addition, to assist the Principal Investigator in determining the appropriate Biosafety Level for the proposed research, the PI is directed to the *Agent Summary Statements in the BMBL* and Appendix B, classification of *Human Etiologic Agents on the Basis of Hazard* in the NIH Guidelines.

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### C. Additional Approvals and Requirements

**Select Biological Agents and Toxins**

The US Department of Health and Human Services (HHS) and the US Department of Agriculture (USDA) have developed a list of select biological agents and toxins that have the potential to pose a severe biosecurity threat to public health, animals, and agricultural crops. As directed by the US Patriot Act, HHS and USDA have adopted strict regulations for the obtaining, possession, use, or transfer of any of these selected agents. Failure to comply with the established regulations can result in significant civil and criminal penalties.

Therefore, any investigator considering the use of select agents or toxins must contact the University Biosafety Officer (Jacqueline Wagnrer at 8-1427 or jw6@princeton.edu) to discuss the specifics of the requirements. HHS regulations in 42 CFR Part 73 Possession, Use, and Transfer of Select Agents and Toxins and the companion USDA regulations in 9 CFR Part 121 require federal registration and inspection; restricted lab access; development of written and strictly followed safety and security plans; personnel background checks by the FBI (including fingerprinting); specialized training; strict recordkeeping and reporting of agent use, transfer, loss, or destruction.

In determining whether to use select agents, researchers are encouraged to give careful consideration to the personal responsibilities, financial costs, and lengthy application and permit process involved with compliance. Any plans for use of select agents could easily take several months to get the appropriate permits and approvals and establish the security and protocols necessary to comply with the regulations. Sources of research funds to cover the cost of facility security improvements will need to be identified.

There is a small quantity exemption available for some of the select toxins. If the aggregate amount of toxin in the possession of a researcher can be kept below the specified exempt quantity (see agent listing), most of the rules do not apply. It should be noted that even when taking advantage of the small quantity exemption, the investigator is required to establish an inventory system to ensure the limit is not exceeded. Regardless of the amount, the University Biosafety Officer must be contacted prior to beginning work

See Select Agents Program for more information about the select agent requirements.

## Alphabetical List Of Select Agents And Toxins

**( as per the Final Select Agent Rules published 3/18/05 )**

Except for exclusions listed in the Appendix, the viruses, bacteria, fungi, toxins, genetic elements, recombinant nucleic acids, and recombinant organisms specified in this list are HHS, USDA or HHS/USDA overlap select agents and toxins.

**Genetic Elements, Recombinant Nucleic Acids, and Recombinant Organisms**

Nucleic acids that can produce infectious forms of any of the select agent viruses.
Recombinant nucleic acids that encode for the functional form(s) of any of the select agent toxins if the nucleic acids:
- can be expressed *in vivo* or *in vitro*, or
- are in a vector or recombinant host genome and can be expressed *in vivo* or *in vitro*.

Select agents that have been genetically modified.

## APPENDIX

**Exclusions:**

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 nonfunctional toxins.
The following toxins (in the purified form or in combinations of pure and impure forms) if the aggregate amount under the control of a principal investigator does not, at any time, exceed the amount specified:

100 mg of Abrin
0.5 mg of Botulinum neurotoxins
100 mg of *Clostridium perfringens* epsilon toxin
100 mg of Conotoxins
1,000 mg of Diacetoxyscirpenol
100 mg of Ricin
100 mg of Saxitoxin
100 mg of Shigatoxin
100 mg of Shiga-like ribosome inactivating proteins
5 mg of Staphylococcal enterotoxins
100 mg of Tetrodotoxin
1,000 mg of T-2 toxin

The following attenuated strains are exempt if used in basic or applied research, as positive controls, for diagnostic assay development, or the development of vaccines and therapeutics:

*Coccidioides posadasii* Δchs5 strain

Conotoxins specifically *excluded* are: the class of sodium channel antagonist μ-conotoxins, including GIIIA; the class of calcium channel antagonist ω-conotoxins, including GVIA, GVII, MVIIA, MVIIC, and their analogs or synthetic derivatives; the class of NMDA-antagonist conantokins, including con-G, con-R, con-T and their analogs or synthetic derivatives; and the putative neurotensin agonist, contulakin-G and its synthetic derivatives.

*Yersinia pestis* strains which are Pgm - due to a deletion of a 102-kb region of the chromosome termed the *pgm* locus (i.e., Δ*pgm*). Examples are *Y. pestis* strain E.V. or various substrains such as EV 76. *Yersinia pestis* strains (e.g., Tjiwidej S and CDC A1122) devoid of the 75 kb low-calcium response (Lcr) virulence plasmid.

*Bacillus anthracis* strains devoid of both plasmids pX01 and pX02 & *Bacillus anthracis* strains devoid of the plasmid pX02 (e.g., *Bacillus anthracis* Sterne, pX01 +pX02 -).

*Brucella abortus* Strain 19 & *Brucella abortus* strain RB51 (vaccine strain). *Coxiella burnetii* Phase II, Nine Mile Strain, plaque purified clone 4.

*Francisella tularensis* subspecies *novicida* (also referred to as *Francisella novicida*) strain, Utah 112 (ATCC 15482) & *Francisella tularensis* subspecies *holartica* LVS (live vaccine strain; includes NDBR 101 lots, TSI-GSD lots, and ATCC 29684) & *Francisella tularensis* ATCC 6223 (also known as strain B38).

Rift Valley fever virus, MP-12 vaccine strain.

Venezuelan Equine Encephalitis (VEE) virus vaccine candidate strain V3526 & Venezuelan equine encephalitis virus, TC-83 strain.

Highly pathogenic avian influenza (HPAI) virus, recombinant vaccine reference strains of the H5N1 and H5N3 subtypes.

Japanese encephalitis virus, SA14-14-2 strain..

The medical use of toxins for patient treatment is exempt.

**Live Viruses**

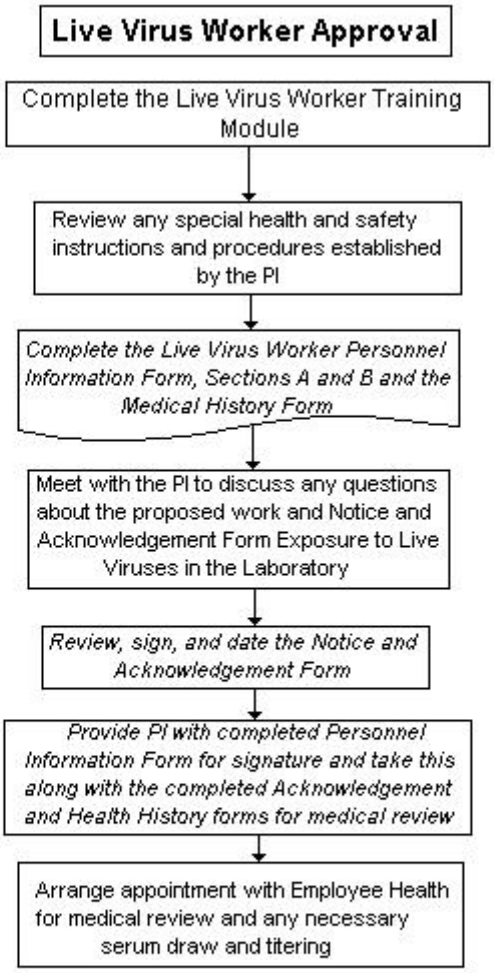
Individuals who will be working with certain live viruses in the laboratory must successfully complete the web-based training and medical review and informed consent process prior to such work. Further information and directions for completing this process are found in the *Live Virus Worker Program Instructions and Requirements.*

Successful completion of the web training will be automatically recorded in the training data base and the training will conclude by directing the individual to complete the necessary forms and medical review.

Completing this live virus worker process:

- Provides the individual with information on the risks and the necessary safety measures associated with the work
- Acknowledges the individual's acceptance of risks and responsibilities for the work
- Initiates the necessary medical review provided through Employee Health at McCosh Health Center

The procedure to be followed by the live virus worker to complete this process is outlined in the chart that follows:




The live virus worker informs the PI and Employee Health when the worker:

Becomes pregnant
Is exposed to live virus by accident or injury
Has a change in immune status

**Human Blood and Tissue**

In any laboratory where work involves the use of and/or exposure to human blood, certain other body fluids, or unfixed human tissue, there is the danger of exposure to bloodborne pathogens, the disease-causing microorganisms that may be found in such material. Work with any of these materials in a laboratory setting usually requires that workers be enrolled in the Bloodborne Pathogens Program. The BBP Program ensures compliance with the federal Occupational Health and Safety Administration (OSHA) Bloodborne Pathogens Standard (29 CFR 1910.1030).

The Bloodborne Pathogens Program requires each department or laboratory to develop an Exposure Control Plan that documents how the risk of exposure will be reduced or eliminated. Specifically, the Plan:

Defines who has potential exposure and what tasks or duties cause exposure
Indicates the engineering and work practice controls in place
Describes the personal protective equipment provided and used
Describes the good housekeeping practices initiated
Provides for the offer of hepatitis B (HBV) vaccination to those exposed
Provides for medical follow-up after exposure
Provides for proper hazard signage and labeling
Provides for initial and annual training and necessary record-keeping

EHS has developed a model plan that can be tailored to the needs of the department or lab. A copy of the model plan can be found at http.//web.princeton.edu/sites/ehs/biosafety/ModelEXCNP_FY2010 (3).DOC.

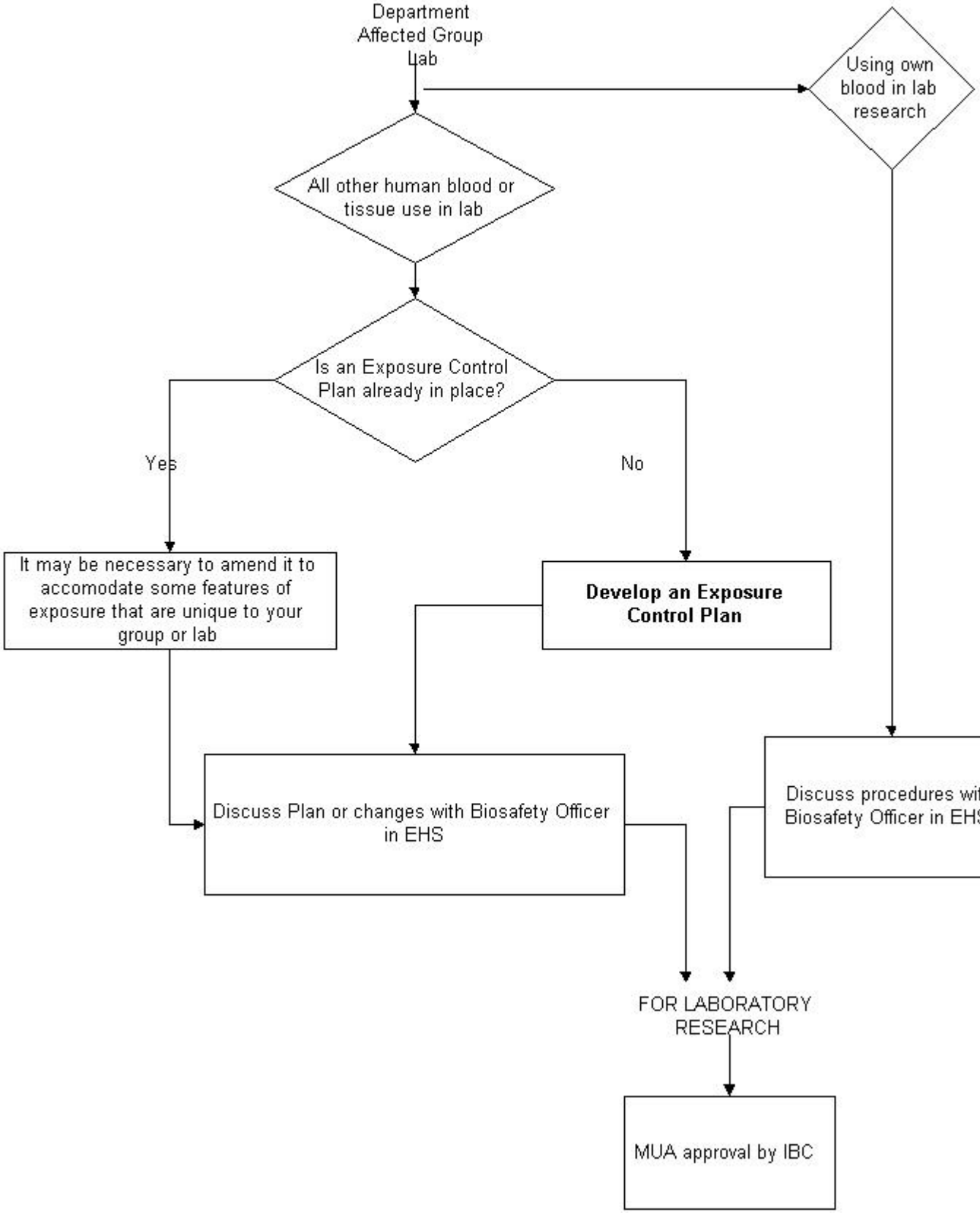
As part of this plan, the potentially exposed individuals must:

Complete the on-line interactive web-based training, Protection Against Bloodborne Pathogen, which includes offer of Hepatitis B vaccination and registration in the Bloodborne Pathogens Program
Use appropriate personal protective equipment and follow established safe work practices

Report all exposures to the Employee Health at McCosh Health Center for post-exposure treatment

The following chart indicates the steps a PI must take to obtain approval of work using human blood and tissue:

# Human Blood and Tissue Approval



In addition, **when blood or tissue donors are involved,** the Principal Investigator must:

Submit the research proposal through ORPA to the Review Panel for Human Subjects.
Get the informed consent of prospective donors and inform them of the requirement for pre-testing every six months for HIV and hepatitis B and C.
Donors will not be able to donate without agreeing to pre-testing.
Contact Employee Health at McCosh Health Center to arrange for pre-testing. (Drawing of blood and pre-testing is performed only by McCosh personnel.) After test results are confirmed negative, then up to 200 ml of blood can be drawn for research. If the results are positive, then blood would
not be drawn for research use. New Jersey law requires that the treating physician notify the proper state agency regarding persons who have tested positive for HIV, and this will be done by McCosh personnel.
**NOTE:** McCosh will monitor the donors' charts. The investigator's grant will be charged for costs of pre-testing and blood draws.
Get assurance that, when human blood or blood products are received from sources outside the University, donors (or blood products) have been tested for HIV and hepatitis B and C and found to be negative. When such testing is impractical or impossible, requests for exemptions to this requirement are to be made to the Biosafety Committee.

**Biohazards Associated with Animal Handling**

When research involves exposure to and handling of animals, there are considerations that must be given to the potential allergens, zoonoses, and physical hazards, e.g. bites and scratches, that may be encountered by researchers and staff.

All staff, faculty, and students who have direct contact with animals are enrolled in the Occupational Health and Safety Program. Enrollment is initiated by the individual completing the web-based training, *Health and Safety for Animal Workers.*

Successful completion of the web training will be automatically recorded in the training data base and the training will conclude by directing the individual to complete the necessary forms and medical review. The web training and medical review must be completed before the individual will be provided access to the animal facility.

The medical review includes:

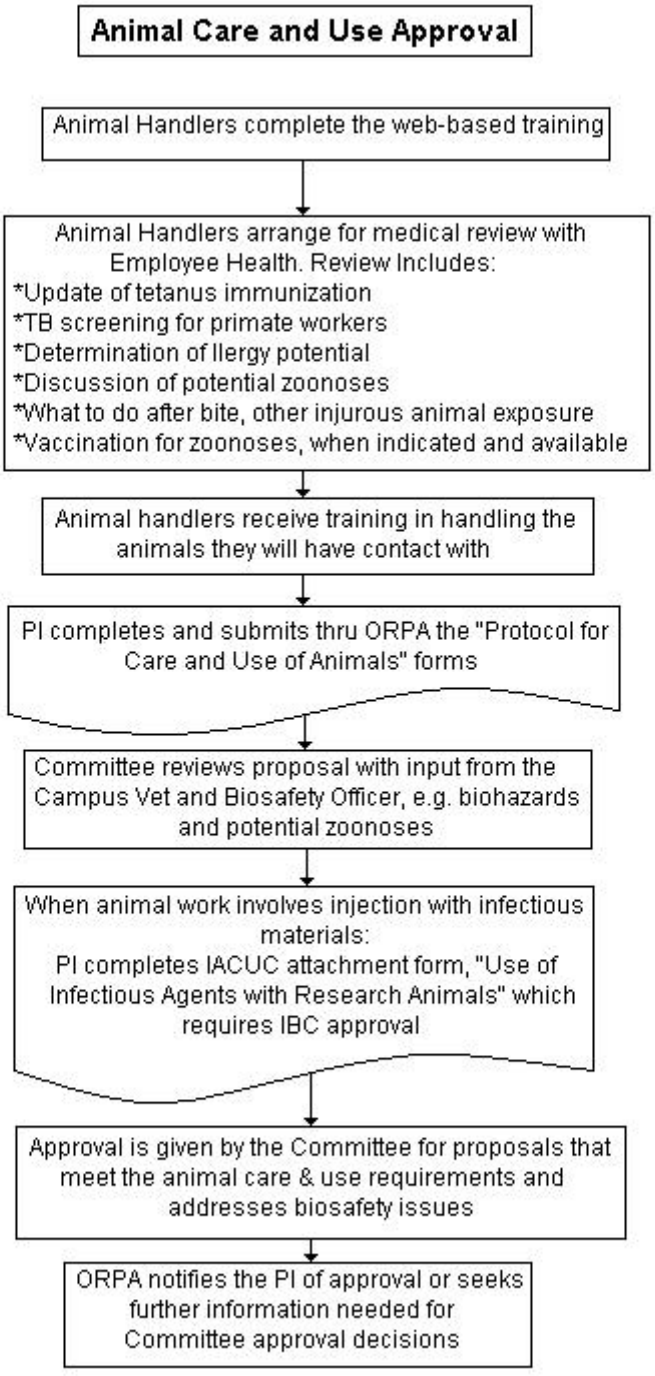
Update of tetanus immunizations
TB screening for primate workers
Discussion of allergen exposure and potential zoonoses
What to do if bitten, or after other injury with animals or contaminated caging/equipment
Vaccination for zoonoses, when indicated and available
Completion of the *Animal Worker Personnel Information Form* and the *Health History Form.*

Personnel also receive training by the Campus Veterinarian in biomethodology and safe handling techniques for those animals with which they will have contact.

All research involving the care and handling of animals is reviewed and approved by the Institutional Animal Care and Use Committee (IACUC). Hazards associated with animal exposure are addressed through this committee.

IACUC Protocol Forms and attachments need to be completed and submitted to ORPA. The necessary forms can be found and completed online.

The following chart indicates the steps of the review and approval process:




## III. WORKING SAFELY WITH BIOLOGICAL MATERIALS

## A. Exposure Control

The term "containment" is used in describing safe methods for managing infectious agents in the laboratory environment where they are being handled or maintained. The purpose of containment is to reduce or eliminate exposure of laboratory workers, other people, and the outside environment to potentially hazardous agents.
The three elements of containment include laboratory practice and technique, safety equipment, and facility design.

### Laboratory Practice and Technique

The most important element of containment is strict adherence to standard microbiological practices and techniques. Persons working with infectious agents or infected materials must be aware of potential hazards, and must be trained and proficient in the practices and techniques required for handling such material safely. The PI or laboratory supervisor is responsible for providing or arranging for appropriate training of personnel.

Each PI should identify specific hazards that will or may be encountered, and consider practices and procedures needed to minimize or eliminate risks. Personnel should be advised of special hazards and are expected to follow the required practices and procedures.

### Safety Equipment (Primary Barriers)

Safety equipment includes biological safety cabinets, enclosed containers, and other engineering controls designed to eliminate or minimize exposures to hazardous biological materials. The biological safety cabinet (BSC) is the principal device used to provide containment of infectious splashes or aerosols generated by many microbiological procedures. More information on BSCs may be found in Section IV.B.

Safety equipment may also include items for personal protection such as personal protective clothing, respirators, face shields, safety glasses or goggles. In some situations, personal protective clothing may form the primary barrier between personnel and the infectious materials.

### Facility Design (Secondary Barriers)

The design of a facility is important in providing a barrier to protect those working inside and outside the laboratory and to protect people or animals in the community from infectious agents which may be accidentally released from the laboratory. Facilities must be commensurate with the laboratory's function and the recommended biosafety level for the agent being manipulated.

The secondary barrier(s) needed will depend on the risk of transmission of specific agents. For example, all Princeton University research falls within Biosafety Levels 1 and 2 (see Biosafety Levels below) and exposure risks involve direct contact with the agents, or inadvertent contact through contaminated work environments. Secondary barriers in these laboratories includes separation of the laboratory work area from public access, availability of a decontamination facility (e.g., autoclave) and handwashing facilities.

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## B. Laboratory Biosafety Levels

CDC-NIH has established **four levels of biosafety**, based on the degree of hazard associated with an organism, to describe the combination of laboratory practices and techniques, safety equipment, and facilities needed to protect against exposure. These four biosafety levels (BSL) require successively more restrictive practices and facilities as work moves from the least restrictive BSL1 to work with the highest hazard level of BSL4. Exposure to biohazardous agents is intended to be prevented or limited by establishing and following the appropriate biosafety level practices and conditions. Research in Princeton University facilities is currently limited to BSL1 and BSL2. (See Section IV.A. for an outline of good practices at BSL1 and BSL2).

**BSL1** applies to the basic level of containment and essentially represents good microbiological practice with no special primary or secondary barriers required. This applies to work with defined and characterized strains of viable microorganisms not known to consistently cause disease in healthy adult humans. This includes such organisms as the bacteria Bacillus subtilis, Vibrio harveyi, or host/vector strains of E coli and yeast Saccharomyces cerevisiae.

**BSL2** applies to work with a broad spectrum of moderate-risk agents that are generally present in the environment at large and are associated with human disease of varying severity.

All of the viral agents used in campus research, such as adenovirus, cytomegalovirus, and other herpes viruses fall within the BSL2 level of work. Other microorganisms assigned to this containment level include salmonella spp., toxoplasma spp., hepatitis B, and HIV. With the use of good microbiological techniques, much of this work can be done on open bench tops as long as there is limited potential for splashes and aerosol creation. **In addition to BSL1 conditions,** this level of work also requires that:

- Laboratory personnel have specific training in handling any pathogenic agents used
- Access to the laboratory is limited when BSL2 work is being done
- Gloves and other suitable personal protective equipment are worn
- Extreme precautions are taken with contaminated sharps
- Biosafety cabinets are used when there is potential for splash or aerosol creation

**BSL3** and **BSL4** apply to work with exotic agents of increasingly greater potential for causing serious human illness or death. No work at the BSL3 or 4 is currently being done and facilities that would meet the requirements of these biosafety levels are not available at Princeton.

A good summary of requirements at each laboratory biosafety level can be found at http://bmbl.od.nih.gov/sect3tab1.htm.

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### C. Animal Biosafety Levels

A similar set of four biosafety levels are provided for work with vertebrate animals infected with agents which may infect humans. These **Animal Biosafety Levels, ABSL 1 thru 4**, provide for practices, equipment, and facilities that are comparable to the laboratory biosafety levels described above. However, there are unique hazards associated with infected animals that must be understood by those personnel with animal contact and addressed in the animal facility. Animal activity can create aerosols and bites and scratches can occur.

See http://www.cdc.gov/od/ohs/biosfty/bmbl4/bmbl4s3t.htm for a good summary of the Animal Biosafety Levels.

# IV. Laboratory Procedures and Equipment

## A. Guidelines for Good Laboratory Practices at BSL1 and BSL2*

**(Excerpted from the** *CDC/NIH Biosafety in Microbiological and Biomedical Laboratories* **and the** *NIH Guidelines for Research Involving Recombinant DNA Molecules***)**

***Indented and bulleted items indicate additional requirements for work at BSL2.**

1. Immediately notify the laboratory supervisor or Principal Investigator (PI) in case of an accident, injury, illness, or overt exposure associated with laboratory activities. As appropriate, proceed to McCosh Health Center for any necessary medical surveillance and/or treatment. **Note:** The University is required to report to regulatory officials any significant research-related accidents/injuries and violations of NIH Guidelines so it is important that the lab notify the Office of Research and Project Amniistration (OPRA), Institutional Biosafety Committee (IBC) immediately under such circumstances.

2. For those intending to work with live viruses or research animals: complete the Live Virus Worker and/or the Animal Worker web-based training (See http://web.princeton.edu/sites/ehs/biosafety/livevirusworker/intro.htm or http://web.princeton.edu/sites/ehs/biosafety/animalworker/intro.htm) and the required medical review with Employee Health at McCosh Health Center. For live virus work, serum draw and titering may be required or desired depending on the virus involved. (See more information at http://www.princeton.edu/sites/ehs/biosafety/livevirusworker/lvprograminfo.htm or http://web.princeton.edu/sites/ehs/biosafety/biosafetypage/animal.htm).

3. For those intending to work with blood or human tissue: complete the Protection Against Bloodborne Pathogens web-based training and entry into the Bloodborne Pathogens Program. (See http://web.princeton.edu/sites/ehs/biosafety/bloodpathogens/Training/BBPIntro.htm )

4. Be aware that access to the laboratory is limited or restricted at the discretion of the laboratory director when experiments or work with cultures or specimens is in progress. Laboratory should have doors to control access.

5. Understand that the PI and/or lab supervisor must ensure that all laboratory personnel receive appropriate initial training, necessary on-going training, and supervision regarding on hazards associated with the agents involved; the necessary precautions to prevent exposures; and exposure evaluation procedures.

6. Understand that personal health status may impact an individual's susceptibility to infection or necessary medical surveillance and any conditions in this regard should be discussed with lab supervisor and healthcare personnel in Health Services as appropriate.

- Only personnel advised of the special hazards and meeting any specific entry requirements, i.e., appropriate immunizations, serum sampling, are permitted in the laboratory. Understand and follow all biosafety procedures provided by the PI and/or supervisor.
- Be aware that any possession or use of select biological agents or toxins requires special federal government registration and inspection; restricted lab access; written and strictly followed safety and security plans;

personnel background checks and training; accurate records and/or reporting of agent use, transfer, loss, or destruction. Any plans for obtaining such materials must be discussed with the Biosafety Officer and approved by the IBC.

- Ensure that **when infectious agents are in use** in the laboratory, a biohazard sign is posted on the lab access door. This sign identifies the agent(s) in use, the biosafety level, any required immunizations, the PI's name and telephone number, and any PPE that must be worn in the laboratory.

7. Wash hands frequently and always after handling viable material or animals, after removing gloves, and before leaving the laboratory. A sink for handwashing is present in each laboratory.

- Consider foot, knee, or automatically operated handwashing sinks.
- Know the location of a readily accessible eyewash station.

8. Do not eat, drink, smoke, chew gum, handle contact lenses, or apply cosmetics in the laboratory. Persons wearing contact lenses in the laboratory should also wear goggles or a face shield.

9. Do not bring any food, medications, or cosmetics, into the laboratory for storage or later use. Food is stored outside the work area in cabinets or refrigerators designated specifically for that purpose.

- Do not bring animals unrelated to experimental work into the laboratory.

10. Do not pipette by mouth; only mechanical pipetting devices are permitted.

11. Perform all procedures carefully to minimize the creation of splashes or aerosols.

12. Establish and follow policies for safe handling of sharps. Use a high degree of caution when handling any contaminated sharp item, such as needles and syringes, slides, pipettes, capillary tubes, and scalpels. Substitute plasticware for glass whenever possible. Handle broken glassware with brush and dustpan, tongs, or forceps - not directly with hands.

13. Do not bend, shear, break, recap, or remove used needles from disposable syringes or otherwise manipulate such units by hand before disposal. Dispose of needles and syringes in the puncture resistant container provided in the laboratory for this purpose. Place full containers in an autoclave bag and sterilize before disposal in medical waste boxes.

**Restrict needles and syringes or other sharp instruments in the laboratory for use only when there is no alternative, such as for parenteral injection, phlebotomy, or aspiration of fluids from laboratory animals and diaphragm bottles.**

Use only needle-locking syringes or disposable syringe-needle units (i.e., needle is integral to the syringe) for injection or aspiration of infectious material.

14. Use of lab coats, gowns, or other designated laboratory uniform is recommended to prevent contamination or soiling of street clothing.

Wear lab coats, gowns, smocks, or other provided protective garments while working with hazardous materials. When leaving the lab, remove and

leave coats and other protective clothing in the lab for either disposal or laundering.

15. Wear gloves if the skin on the hands is broken or if a rash is present. Protective eyewear should be worn for procedures that involve anticipated splashes of microorganisms or other hazardous materials to the face.

Wear gloves when manipulating infectious materials or agents or when hands must otherwise contact contaminated surfaces. Remove and change gloves when overtly contaminated or when torn or punctured. Do not wear contaminated gloves outside the lab. Do not wash or reuse disposable gloves. Consider alternatives to latex gloves to prevent allergic response. Wear appropriate face protection (goggles, mask, face shield or other splatter guard) for anticipated splashes or sprays of infectious materials to the face when agents **must** be handled outside the BSC. Persons wearing contact lenses should also wear eye protection.

16. Decontaminate equipment and work surfaces at completion of work, at the end of the day, and following spills of viable materials. If a spill occurs, cover the spill with paper towels and soak the towels with a 1 to 10 dilution of chlorine bleach or other suitable disinfectant. Allow the material to soak for approximately 20 minutes before discarding materials in biohazard bag. Bench tops are impervious to water and resistant to solvents, acids, alkalis, and chemicals used for surface decontamination. Laboratory surfaces and spaces between fixtures are designed to be easily cleaned; no carpets or rugs.

17. Work on open bench tops is permitted; use of special containment equipment such as a biological safety cabinet (BSC)is not generally required for agents assigned to BL1.

**Work in the open laboratory is permitted, except that** a properly maintained **biological safety cabinet is required whenever:**

Procedures with a potential for creating infectious aerosols or splashes are conducted. These may include **centrifuging, grinding, blending, vigorous shaking or mixing, sonic disruption, opening containers of infectious materials** whose internal pressures may be different from ambient pressures, **inoculating animals intranasally,** and **harvesting infected tissues from animals or embryonate eggs.**

**High concentrations or large volumes of infectious agents are used** . Such materials may be centrifuged in open laboratory if sealed rotor heads or centrifuge safety cups are used, and if these rotors or safety cups are opened only in a biological safety cabinet.

**Be aware that air sampling studies have shown that most of the common manipulations of bacterial and viral cultures in research laboratories release aerosols of viable organisms. This must be considered when evaluating need for use of the biological safety cabinet or other physical containment device**.

18. Dispose of all regulated medical wastes (potentially biohazardous) and associated wastes as outlined in the provided Laboratory Waste Streams charts developed for all laboratories using biological materials (see http://web.princeton.edu/sites/ehs/biosafety/biosafetypage/disposalchart.htm)and for Chemistry and other departments where some labs use biological materials (see http://web.princeton.edu/sites/ehs/biosafety/biosafetypage/disposalchart2.htm).

Cover containers of all cultures, tissues, specimens of body fluids, or other potentially infectious waste to prevent leakage during collection, handling, processing, storage, transport, or shipping.

19. Have an insect and rodent control program in place. Ensure screens are fitted on exterior windows that open into the lab.

Revised 9/07

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## B. Biological Safety Cabinets (BSCs)

### Types of BSCs

BSCs are classified as Class I, Class II or Class III cabinets. When properly maintained and operated, they effectively contain and capture microbial contaminants and infectious agents using HEPA (High Efficiency Particulate Air) filters. (See Figure 1.) Biosafety cabinets should not be confused with clean benches which only protect the material being worked with and are not suitable for work with infectious or toxic material. (Although clean benches, like BSCs, have HEPA-filtered air, with clean benches the air flows over the experimental material toward the user rather than being drawn away.) BSCs should also not be confused with conventional fume hoods that do not filter microorganisms.

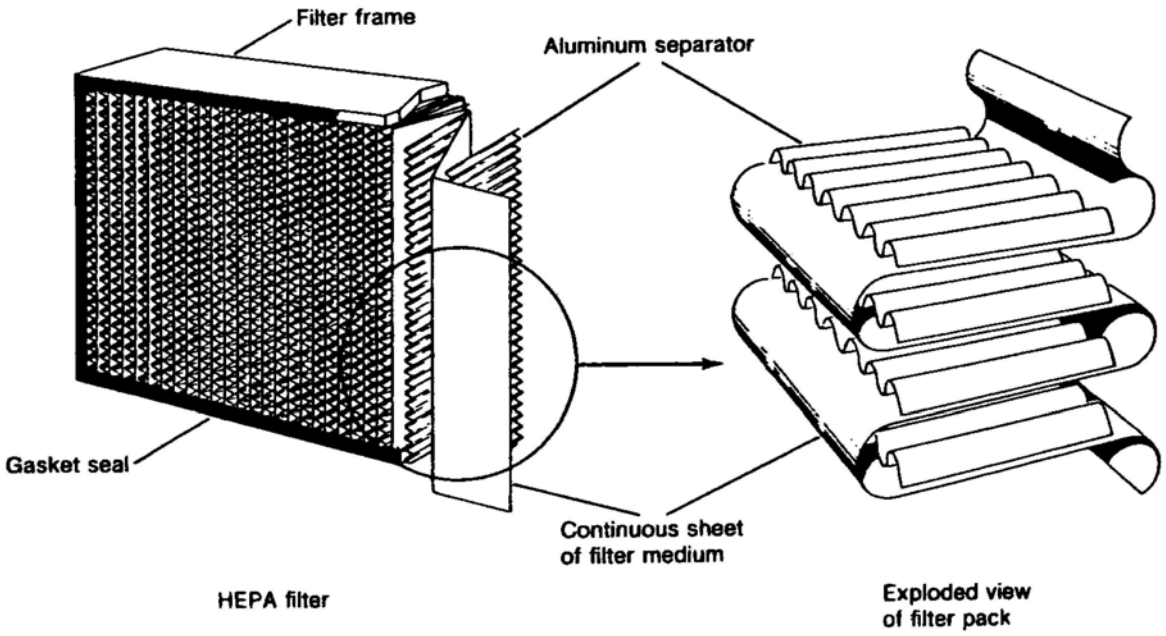
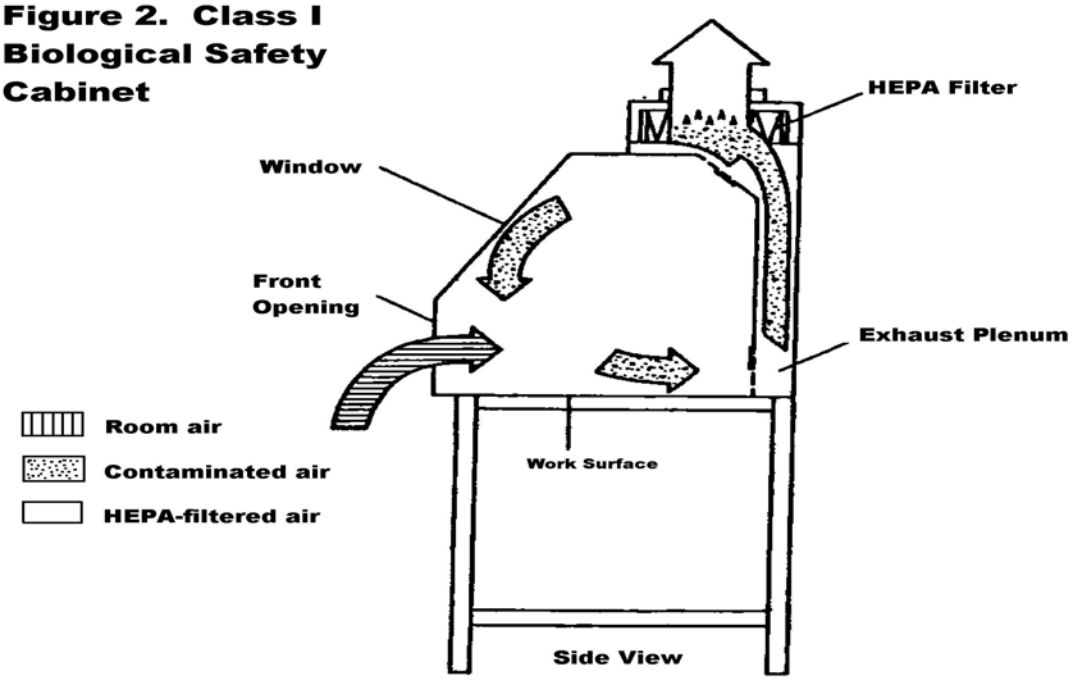



**Figure 1.** Diagram of HEPA filter. These filters are typically constructed of continuous sheets of paper-thin filter medium, pleated to increase surface area, divided by aluminum separators, and affixed to a frame.

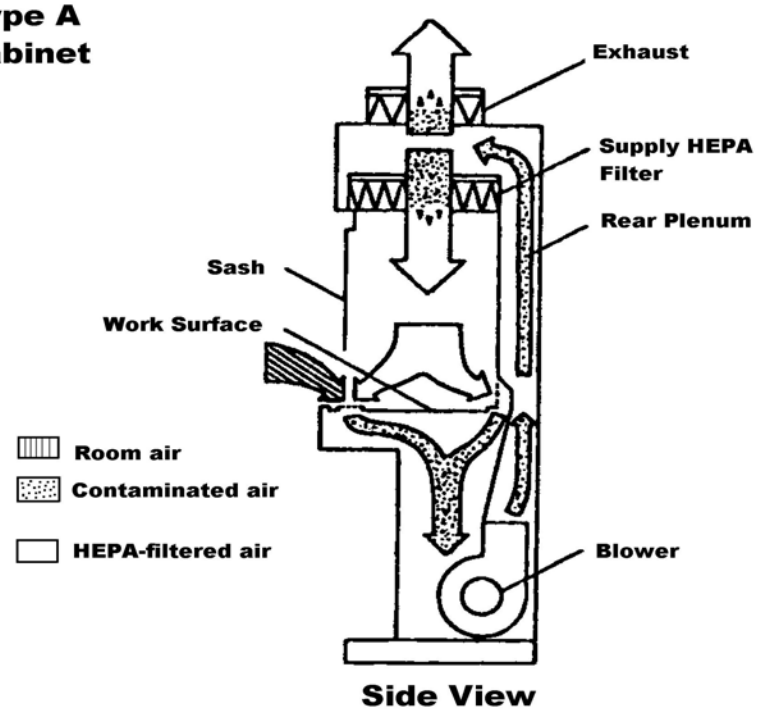
**Class I BSCs** provide personnel and environmental protection, but not product protection. (See Figure 2).

**Figure 2. Class I Biological Safety Cabinet**




**Class II BSCs** are the most commonly used BSC on campus. These cabinets provide personnel, environmental and product protection. (See Figure 3). Only those which are hard ducted to the outside and provide a face velocity of 80 to 125 feet per minute should be used when working with volatile chemicals. Additionally, cabinets are not designed to prevent ignition of volatile flammable chemicals.

**Figure 3. Class II, Type A Biological Safety Cabinet**




**Working in a BSC**

1. Turn the cabinet on for at least 10 - 15 minutes prior to use, if the cabinet is not left running.
2. Disinfect work surface with 70% alcohol or other suitable disinfectant.
3. Consider the materials necessary for the planned work in the cabinet.
4. Place items into the cabinet so that they can be worked with efficiently without unnecessary disruption of the air flow, working with materials from the clean to the dirty side.
5. Wear appropriate personal protective equipment. At a minimum, this will include a buttoned laboratory coat and gloves.
6. Adjust the working height of the stool so that the worker's face is above the front opening.
7. Delay manipulation of materials for approximately one minute after placing the hands/arms inside the cabinet.
8. Minimize the frequency of moving hands in and out of the cabinet.
9. Do not disturb the airflow by covering any of the grillwork with materials.
10. Work at a moderate pace to prevent the air flow disruption that occurs with rapid movements.
11. Wipe the bottom and side of the hood surfaces with disinfectant when work is completed.

**NOTE:** Be very careful when using small pieces of materials such as kimwipes in the hood. These can be blown into the hood and disrupt the motor operations.

**Certification of the BSC**

Certification is a series of performance tests on the BSC to confirm that it will provide the user and experimental material the protection for which it is designed. The air flows, filters, and cabinet integrity are checked to ensure that the cabinet meets minimum performance standards. Certification is arranged through the department and provided by an outside vendor.

BSCs intended for user protection must be certified:

After they are received and installed (before use with infectious materials)
After filter changes
Annually

Biological safety cabinets intended only for protection of the experimental material are certified at the discretion of the Principal Investigator.

BSC decontamination (using the paraformaldhyde gas production process) is also provided by an outside vendor and needs to be done:

Before any maintenance work requiring disassembly of the air plenum, including filter replacement
Prior to cabinet recertification
Before moving the cabinet to a new laboratory

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## C. Decontamination

### Definitions

**Decontamination** is a process or treatment that renders an instrument or environmental surface safe to handle. A decontamination procedure can be as simple as clean-up with detergent and water or as thorough as sterilization. Sterilization, disinfection, and antisepsis are all forms of decontamination.

**Sterilization** is the use of physical or chemical processes to destroy all microbial life, including highly resistant forms, such as bacterial spores.

**Disinfection** is the elimination of essentially all pathogenic non-spore forming microorganisms but not necessarily all microbial forms from work surfaces and equipment. Effectiveness is influenced by a number of factors, including: types and numbers organisms; amount of organic matter; the object being disinfected; the disinfectant being used; exposure time, temperature and concentration.

**Antisepsis** is the application of a liquid antimicrobial to skin or other living tissue to inhibit or destroy microorganisms. Examples include hand washing with germicidal solutions or swabbing skin before an injection.

### When to Decontaminate

All material and equipment contaminated with or containing potentially infectious agents should be decontaminated:

Upon completion of procedures involving the use of biologically-active materials
In the event of spills of such materials
At least daily

Before being washed, stored, or discarded

In most Princeton University laboratories, decontamination is accomplished by **steam heat sterilization in an autoclave**, or by surface application of or placement in a **chemical disinfectant solution**, such as 1:10 bleach solution or its equivalent.

### Autoclave Use

Autoclaving (saturated steam under pressure of approximately 15 psi to achieve a chamber temperature of at least 250oF for a designated time) is the preferred and most convenient method to rapidly destroy all forms of microbial life. However, to do this, the autoclave process must reach proper temperature and time and also prevent the entrapment of air in the bag or container of treated material.

Material to be sterilized must come into contact with live steam.
Bags or containers should be left open during autoclaving or water (~200ml) should be added to sealed bags to generate steam.
Heat indicator tape should be used with each autoclave load to indicate that sterilization has been completed.
Autoclave sterility monitoring should be conducted on a regular basis using biological indicators (such as B. stearothermophilus spore strips) placed among treated materials and at locations throughout the autoclave. The spores, which are more resistant to heat than most microbials, provide validation of general microbial destruction when they are effectively inactivated (250 deg. F for 13 minutes) by autoclave operation.

### Chemical Disinfectant Use

The most practical use of chemical disinfectants is for surface decontamination and, when used in sufficient concentration, as a decontaminant for liquid wastes prior to final disposal down the drain.

## GENERAL RECOMMENDATIONS:

### Liquid Decontamination

Add liquid chlorine bleach to provide a final 1:10 dilution
Let stand at least 20 minutes
Discard down the drain

### Surface Decontamination

Wipe with 1:10 dilution of chlorine bleach, or
Wipe with iodophor disinfectant (per label concentration), or
Wipe with 70% alcohol

See Table 1, Table 2, Table 3 for further information on disinfectants.

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## D. Exposure to Infectious Agents

In the event of an exposure to an infectious agent or material, the following guidelines should be used:

### Intact skin

Remove contaminated clothing
Vigorously wash contaminated skin for 1 minute with soap and water

**Broken, cut or damaged skin or puncture wound**

Remove contaminated clothing
Vigorously wash contaminated skin for 5 minutes with soap and water
Seek medical attention at McCosh Health Center

**Eye**

Immediately flush eyes for at least 15 minutes with water, preferably using an eyewash; if no eyewash is available, pour water on the eye(s) for 15 minutes, rinsing from the nose outward to avoid contamination of the unaffected eye.
Hold eyelids away from your eyeball and rotate your eyes so that all surfaces may be washed thoroughly.
Seek medical attention at McCosh Health Center

**Ingestion or Inhalation**

Seek medical attention at McCosh Health Center
Do not induce vomiting unless advised to do so by a health care provider

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## E. Biological Material Spills

### Spills and Preparing for Them

In the event of a spill of biological material, the individual(s) who caused the spill is responsible for the clean-up. Princeton University does not have a spill response team.

Minimize the consequences of any spill of biological material by performing all work on plastic-backed liner to absorb spills
Have a simple spill kit on hand including:
- Chlorine bleach or some other concentrated disinfectant
- A package or roll of paper towels
- Autoclavable bags
- Rubber gloves
- Forceps for pick-up of broken glass

### Spills Inside a Biological Safety Cabinet

1. **LEAVE THE CABINET TURNED ON**
   While wearing gloves, spray or wipe cabinet walls, work surfaces, and equipment with disinfectant equivalent to 1:10 bleach solution. If necessary, flood the work surface, as well as drain pans and catch basins below the work surface, with disinfectant for a contact time of at least 20 minutes
2. Soak up disinfectant and spill with paper towels. Drain catch basin into a container. Lift front exhaust grill and tray and wipe all surfaces. Ensure that no paper towels or solid debris are blown into the area beneath the grill.

3. Autoclave all clean-up materials before disposal in the biohazard waste container. Wash hands and any exposed surfaces thoroughly after the clean-up procedure.

**Small Spill of Material Outside of a Biological Safety Cabinet (Spill that can be covered by a few paper towels)**

1. Wearing gloves and a lab coat, cover the spill with paper towels and gently apply disinfectant, proceeding from the outer edge of the spill to its center. Leave in place for 20 minutes.
2. Pick up the towels and discard into a biohazard container. Pick up any pieces of broken glass with forceps and place in sharps container.
3. Re-wipe the spill area with disinfectant and thoroughly wash hands after glove removal.

**Large Spill of BL2 Material (>500ml) Outside of a Biological Safety Cabinet**

1. Hold your breath and leave the room immediately.
2. Warn others to stay out of the spill area to prevent spread of contamination; post a sign stating: **"DO NOT ENTER, BIOHAZARD SPILL"**, contact (name and phone #) for information".
3. Remove any contaminated clothing and put into a biohazard bag for later autoclaving.
4. Wash hands and exposed skin and inform your PI or supervisor about the spill
5. Put on protective clothing (lab coat, gloves and, if indicated, surgical mask, eye protection, shoe covers) and assemble clean-up materials.
6. Wait 30 minutes before re-entering the contaminated area to allow dissipation of aerosols.
7. Cover the spill with paper towels and gently apply disinfectant, proceeding from the outer edge of the spill to its center. Leave in place for 20 minutes
8. Collect all treated material and discard in a biohazard container. Pick up any broken glass with forceps and place them into a sharps container.
9. Re-wipe the spill area with disinfectant and wash hands thoroughly at completion of clean-up.

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## F. Biological Waste Handling

**Biohazardous Waste (Regulated Medical Waste)**

Some wastes associated with biological materials must be disposed of in special ways because they may have been contaminated with infectious organisms or agents. These potentially infectious or biohazardous materials are defined by NJ regulations as **Regulated Medical Waste**. These wastes include the following:

All sharps, e.g. glass implements, needles, syringes, blades, etc. coming from facilities using infectious materials
Biologically-cultured stocks and plates, human blood or tissues

For disposal of these wastes, the lab personnel:

1. Sterilize or disinfect waste materials associated with viral, bacterial or other agents infectious to humans (by autoclave or chemical treatment equivalent to 1:10 bleach solution).

2. Place all biohazardous wastes, except for sharps, directly into the red bag-lined medical waste boxes provided by Building Services.
3. Place sharps into labeled sharps containers which when filled are placed into the medical waste box.
4. When the Medical Waste box is filled, seal the bag liner and box and notify janitor for pick-up.

**IMPORTANT LABELLING REQUIREMENT: Lab personnel must apply an adhesive-backed label completed with generator information to each bag or container (such as autoclaved bags or filled sharps containers) placed into the medical waste box. Building Services provides such a label that has space to record Date, Building, Lab #, and Contact Person. Apply this label to all containers placed inside the medical waste box AND to the exterior of the sealed medical waste box before it is made available for pick-up by Building Services. Alternatively, the inner bags and containers can be marked clearly with a permanent marker to indicate "Princeton University, Princeton, New Jersey."**

5. Where pick-ups are infrequent or limited, contact Building Services to arrange for pick-up.

**Other wastes** generated in these facilities that are not contaminated with biological agents or materials **are not** treated as biohazardous and may be discarded in the regular trash container, with recyclables, or into other specially designated waste containers. These include such items as recyclable and non-recyclable waste glass, gloves, unused plates or tubes, fly media or embryo plates, etc.

In order to clarify how these various wastes are to be handled in laboratories using biological materials, the waste stream charts indicated below have been developed and put into use.

The chart developed for the Departments of Molecular Biology and EEB is intended to be used by biological laboratory facilities. The second chart was developed for the Chemistry Department and other science and engineering departments where biological cultures may be used in some laboratories. Choose the model that most clearly fits the waste being generated or call the Biosafety Officer at 8-5294 for clarification.

**Animal Bedding Waste**

This waste is picked up in a special vehicle by Princeton University Building Services personnel and is not to be mixed with other waste. All animal bedding is bagged by animal care personnel and placed in specially provided gray carts for movement to the pick-up location. Bags should be filled only to a depth and weight that will allow for effective tying of the bag by animal facility staff and for ease of handling by one person. For example, several partially-filled bags should be tied and placed in the gray carts rather than one or two full bags (bag weight should not exceed 40 pounds). This will help to prevent repetitive motion injury to staff and help to prevent bags from being ripped open while being handled.

The carts are maintained clean and in sanitary condition by the animal facility staff. Any spills of bedding when loading the truck are cleaned up by the Building Services trash crew.

**Animal Carcasses**

Freezers are provided in each animal facility for storage of carcasses that have been bagged and sealed. The frozen carcasses are picked up on a regular schedule for

appropriate disposition - either disposal by a contracted firm or use by groups such as Raptor Trust. Freezers are cleaned and defrosted as necessary by animal laboratory personnel to keep them in a sanitary condition.

### Animal Waste from BSL2 Animal Room LTL 41

Rodents housed in this animal space are considered to be potentially infectious because as part of the research protocol they are infected with Biosafety Level 2 (BSL2) animal and/or human viruses. Animal bedding, carcasses, and tissue are placed in biohazard bags by the research staff. All animal bedding is autoclaved before being placed in medical waste boxes by animal care staff and disposed of in the medical waste stream. Bagged animal carcasses and tissue are placed in the provided storage freezer in room 41 and removed by animal care staff to medical waste boxes for pick-up by Building Services as part of the medical waste stream.

### Patient Care Waste Disposal

All disposable wastes generated at McCosh Health Center from patient rooms and as part of direct patient care are considered potentially infectious and are disposed of in the medical waste stream. Syringes, needles, and other sharps are placed in the provided sharps container which, when filled and sealed are placed in the provided medical waste box. When boxes are filled and sealed, they are removed by the custodial staff outside to the locked storage shed for later pick-up by Building Services.

Patient care waste generated at other sites on campus by medical response personnel (i.e. Public Safety) are placed in biohazard bags and brought to McCosh Health Center for medical waste disposal or handled by responding EMS personnel.

A program is in place to ensure that needles and syringes generated as part of personal diabetes care will not be an exposure hazard to others. Collection containers are available from McCosh Health Center which, when filled, are returned to the Health Center for proper disposal in the medical waste stream.

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## G. Packaging and Shipping Biological Materials

### Definitions

Packaging and shipping of biological materials must be done in a way that ensures the contents will not leak and that the package will arrive in good condition.

The definitions below apply to the packaging and shipping instructions that follow:

***Etiologic agent*** means a viable microorganism or its toxin which causes, or may cause, human disease.

***Diagnostic specimen*** means any human or animal material including, but not limited to, excreta, secretion, blood and its components, tissue, and tissue fluids, etc., which is reasonably believed to contain an etiologic agent, and is being shipped for purposes of diagnosis.

***Biological product*** means a biological prepared and manufactured in accordance with regulations that govern the manufacture of vaccines, reagents, etc.

***Interstate shipping*** means shipping to or from the continental US including to other NJ locations.

**Packaging**

All biological materials including diagnostic specimens and biological products that may contain an etiologic agent must be packaged to withstand leakage of contents, shocks, pressure changes, and other conditions incident to ordinary handling and transportation (passage through cancellation machines, sorters, conveyors, etc). Contents should not leak to the outside of the shipping container, even if leakage of the primary container occurs.

Specific packaging requirements apply to materials which are known to contain, or reasonably believed to contain certain etiologic agents. See here for etiologic agents. For such materials, the following procedures apply (See Figure 1):

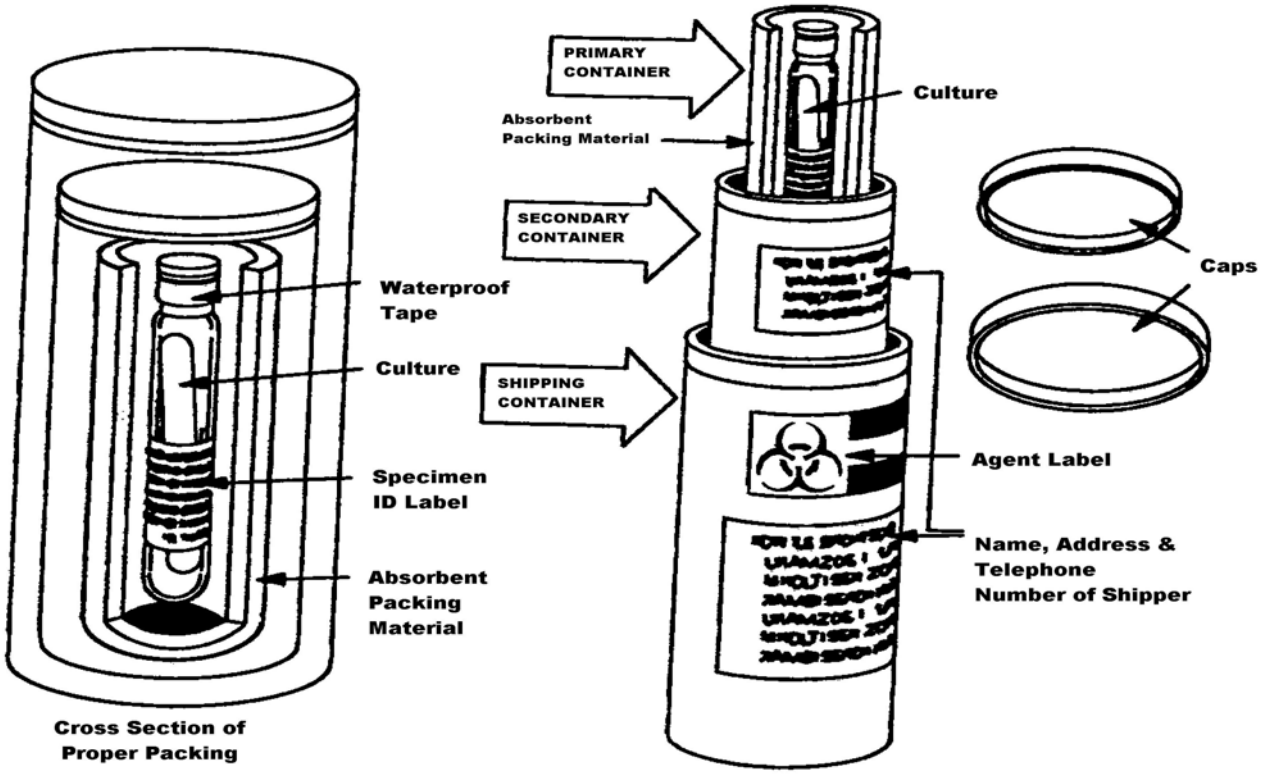


**Figure 1**

**Volume not exceeding 50 ml:**

Place material in a securely enclosed, watertight primary container (test tube, vial, etc.). Enclose this primary container in a secondary, durable watertight container. Several primary containers may be enclosed in a single secondary container as long as the total volume of material in all the primary containers enclosed does not exceed 50 ml.

Place absorbent nonparticulate material (e.g. paper toweling, not sawdust or vermiculite, etc.) in the spaces at the top, bottom and sides between the primary and secondary containers. Use enough absorbent material to absorb the entire contents of the primary container(s) in case of breakage or leakage.

Enclose each set of primary and secondary containers in an outer shipping container constructed of corrugated fiberboard, cardboard, wood or other material of equal strength. Do not use bags, envelops and similar materials.

If you package the material with dry ice, see Packaging with Dry Ice.

**Volume greater than 50 ml:**

1. Follow requirements for lesser volumes outlined above.
2. Place shock absorbent material at the top, bottom, and sides between the secondary container and the outer shipping container. (This material should at least equal the amount of absorbent material placed between the primary and secondary containers).
3. Ensure single primary containers contain no more than 1000 ml of material; however, two or more primary containers (combined volumes not exceeding 1000 ml) may be placed in a single secondary container. The maximum amount of etiologic agent which may be enclosed within a single outer shipping container must not exceed 4000 ml.

**Packaging with Dry Ice**

1. If used, place dry ice between the secondary and outside containers.
2. Place shock absorbent material so as to prevent the secondary container from becoming loose inside the outer container as the dry ice sublimates.

**Labeling**

The outer shipping container of all materials containing etiologic agents which are being shipped or transported must bear a special label, as illustrated in Figure 2. These labels are available from your laboratory supply vendor.


**Figure 2**

## H. Shipping and Transportation Methods and Requirements

### Registered mail or the equivalent

For a list of etiologic agents that use registered mail or an equivalent system which provides the sender with immediate notification of receipt see here.

### Federal Express or UPS

1. For such shipments, internationally or domestically, follow the International Air Transport Association (IATA) Dangerous Goods Regulations. (Receipt of shipment notice is not required since the shipment is traceable through the specific carrier).
2. Apply appropriate labels to the outer shipping container for packages containing dry ice and/or infectious substances as shown in Figures 3 and 4, respectively.
3. Contact the specific carrier's dangerous goods agent prior to shipment for any additional packaging and labeling requirements.

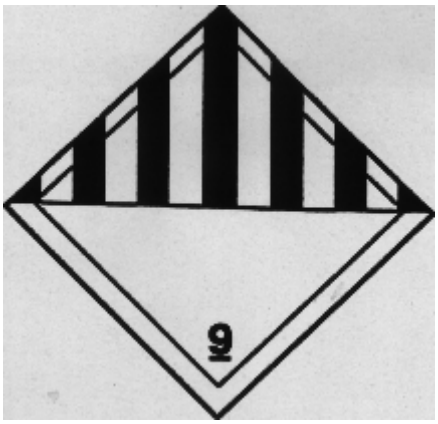


**Figure 3**


**Figure 4**

### Damaged Packages

When evidence of leakage or any other damage to packages bearing an Etiological Agents/Biomedical Material label is discovered, the carrier must promptly isolate the package and notify the Director, Centers for Disease Control and Prevention (CDC), 1600 Clifton Road N.E., Atlanta, Georgia 30333 or by telephone (404) 633-5313 (404) 633-5313 .

### Notice of Delivery

In the event that a package sent by Princeton University is not received by the recipient within 5 days following the anticipated delivery of the package, the sender must notify the Director, Centers for Disease Control and Prevention, 1600 Clifton Road N.E., Atlanta, Georgia 30333 or by telephone (404) 633-5313 (404) 633-5313 .

### Importation/Exportation of Etiologic Agents

***Importation of infectious agents, etiologic agents and vectors that may contain them*** is governed by federal regulation. In general, an importation permit is required for any infectious agent known to cause disease to man. This includes but is not limited to

bacteria, viruses, rickettsia, parasites, yeasts and molds. In some instances, an agent which is suspected of causing human disease also requires a permit.

Importation permits are issued by the U.S. Public Health Service (USPHS) only to the importer, who must be located in the United States. The importation permit, with the proper packaging and labeling, will expedite clearance of the package of infectious materials through the USPHS Division of Quarantine and Release by U.S. Customs.

Instead of an importation permit, a **Letter of Authorization** may be issued by the Centers for Disease Control and Prevention (CDC) after review of an "Application to Import an Etiological Agent". The letter is issued for materials that are judged to be noninfectious, but which might be construed to be infectious by U.S. Customs inspection personnel. Letters of Authorization may be issued for items such as formalin fixed tissues, sterile cell cultures, clinical materials such as human blood, serum, plasma, urine, cerebrospinal fluid, and other tissues or materials of human origin when there is no evidence or indication that such materials contain an infectious agent. Letters of Authorization are in effect for two years, and do not require a shipping label to be issued by CDC.

Importation permits and Letters of Authorization are issued by the CDC, Import Permit Program, 1600 Clifton Road NE, Mailstop E-79, Atlanta, Ga. 30333 after review of a completed application form. Application forms may be obtained by calling CDC at (404)498-2260 (404)498-2260 . CDC can also be contacted on the Internet at http://www.cdc.gov/od/ohs/biosfty/imprtper.htm. Completed forms may be returned to CDC by mail or FAX at 404-498-2275. Application to CDC for the importation permit should be made 10 working days in advance of the shipment date to allow time for processing, issuance and delivery of the permit and shipping labels to the permittee.

Facilities **transferring or receiving select biological agents** must be registered with the CDC or USDA and comply with elaborate regulatory requirements. See Section IIC of the Manual.

**Other Permits**

The United States Department of Agriculture (USDA), Animal and Plant Health Inspection Service (APHIS), Veterinary Service (VS) regulates the importation of animals and animal-derived materials to ensure that exotic animal and poultry diseases are not introduced into the United States.

Generally, a USDA veterinary permit is needed for materials derived from animals or exposed to animal-source materials. Materials which require a permit include, animal tissues, blood, cells or cell lines of livestock or poultry origin, RNA/DNA extracts, hormones, enzymes, monoclonal antibodies for IN VIVO use in non-human species, certain polyclonal antibodies, antisera, bulk shipments of test kit reagents, and microorganisms including bacteria, viruses, protozoa, and fungi. Exceptions to this requirement are human and non-human primate tirrues, serum, and blood. They also have information on animal products that do not require an import permit.

Various other animal materials which require a permit include dairy products (except butter and cheese), and meat products (e.g., meat pies, prepared foods) from countries with livestock diseases exotic to the U.S.

Import permit applications may be obtained from the NCIE home page or by writing the Import/Export Animal Products Program at:

USDA, APHIS, VS, NCIE

Products Program

4700 River Road, Unit 40

Riverdale, MD 20737-1231

For further information or questions concerning import applications, please contact the Animal Products Program at Area Code (301)734-3277 or by facsimile at (301)734-8226

**The importation or domestic transfer of plant and plant pests** are also regulated by the USDA. Information may be obtained by calling 1(877)770-5990 1(877)770-5990 or on the website at http://www.aphis.usda.gov/ppq/permits/index.html.

**Export of infectious materials** may require license from the Department of Commerce (DoC). Exporters of a wide variety of etiological agents of human, plant, and animal diseases, including genetic material, and products which might be used for culture of large amounts of agents will require an export license.