

# BioSide Lines

October 2006

The Newsletter of the Office of Biological Safety, UW-Madison Safety Department  
[www.fpm.wisc.edu/biosafety](http://www.fpm.wisc.edu/biosafety)

## Transport Precautions for Small Animals

What safety precautions should be used for transporting animals that have been administered infectious or potentially-infectious material? What about animals that may carry zoonotic disease? Are there different precautions for animals that have been administered hazardous chemicals or radioactive materials? This article outlines recommended precautions for transport of small animals such as rodents.

If possible, transport hazardous material to be administered to animals to the animal facility rather than transporting animals after treatment. It is much easier to contain test tubes and bottles than it is to contain active animals. Some situations, however, require transport of animals that may carry disease or of animals post-treatment with hazardous materials.

The following precautions are recommended when transporting animals that are infectious or potentially-infectious:

- Staff who do the transport should be experienced, knowledgeable about handling that type of animal, and trained regarding the hazards of the pathogen(s) involved.
- Follow Departmental/School policies or standard operating procedures for animal transport.
- Secure (e.g., tape) the lids of the cages. Place the cages in a sturdy container (e.g., covered plastic tote) or a heavy-duty bag. The sturdy container is preferable to a bag.
- Disinfect surfaces including the outer container/bag before leaving the animal housing area. Use a disinfectant suitable for the pathogen(s) involved. If uncertain about which disinfectant is appropriate, use one that has broad-range efficacy, such as bleach (use a low concentration since NaOCl is an irritant) or a peroxygen compound (e.g., Virkon S).
- Carry hazard and contact information. Place biohazard signage on the inner container when transporting animals infected with a pathogen.
- Within a building, transport cages on a cart and avoid common usage elevators, if possible. Use dedicated vehicles for transport between buildings. Use of personal vehicles is not recommended and requires prior approval and inspection of the vehicle by the animal use and care committee.
- Do not wear personal protective equipment (PPE) such as gloves and lab coat/smock outside of the animal housing area. PPE is not necessary if the surfaces have been appropriately disinfected. Even if you use fresh gloves and lab coats that you know are not contaminated, other people do not know that this is the case and may fear that you are spreading contamination.
- Bring spill supplies including PPE, disinfectant, and absorbent material along with you in case an incident occurs during transit.

These precautions are also appropriate for animals that have been treated with hazardous chemicals or radioactive materials. Hazardous chemicals (or active metabolites) and radioactive materials may be present in animals, on the cages, and in excreta/bedding. Surfaces are cleaned to eliminate potential contamination rather than for disinfection purposes and the training and signage need to be tailored to the specific type of hazard (chemical or radioactive versus biological). Agents and active metabolites that are volatile may require additional precautions.

Animals and bedding/wastes that are infectious or potentially-infectious usually need to be handled with heightened precautions for the life of the animal. In contrast, animals that have been administered hazardous chemicals or radioactive materials (and their bedding/wastes) often only need to be handled with special precautions for a limited time period (until the chemical is fully metabolized or the radioactive material has decayed). If feasible, delay transport of such animals so that special precautions are not needed.

Feel free to contact our office for further discussion or if you have suggestions on transport precautions to share. Look for a future BioSide Lines article describing recommended precautions for transport of large animals such as monkeys.

## Biosafety in Instructional Activities

The Institutional Biosafety Committee (IBC) recently discussed oversight of biological safety in instructional activities at UW-Madison. At this time, the IBC decided not to implement a formal review process for instructional activities, such as currently is done for research activities. Nonetheless, students must be given information about the nature of the hazardous materials used in the classroom and ways to prevent an exposure.

Ensuring that appropriate precautions are used in the classroom ultimately falls to the immediate instructor, but more generally is the responsibility of the individual who plans the curriculum content and selects the materials to be handled. For certain situations, it is important that students have the opportunity to handle hazardous materials using correct procedures that protect themselves and their classmates. In other situations, handling of hazardous materials may be restricted to a demonstration by the instructor. And for some situations, a surrogate can be substituted. For example, a simulation could be developed or a substance of lesser hazard substituted, such as rabbit blood instead of human blood, or an animal pathogen instead of a human pathogen (e.g., duck hepatitis B virus instead of human HBV). Caution is always needed when students are given undefined environmental (e.g., soil or water) or clinical samples and asked to culture unknown microorganisms.

Staff from the Office of Biological Safety are available to assist instructors with ensuring that students will not be exposed to biological hazards. A variety of options typically are available to mitigate the risks. We welcome the opportunity to meet with instructors to discuss precautions that are commensurate with the materials and alternative methods that could be used. Instructors may arrange a consultation by contacting OBS (263-2037).

## A Primer on Federal Permit Requirements

Research at a University often is performed in collaboration with other domestic and international colleagues. An exchange of materials frequently requires importation or transportation domestically across state lines of pathogenic organisms or of materials that potentially contain these organisms. These shipments may be subject to federal regulations, including the need to obtain a permit from one of three agencies; the Centers for Disease Control and Prevention (CDC), Animal and Plant Health Inspection Service - Veterinary Services (APHIS/VS), or APHIS - Plant Protection and Quarantine (APHIS/PPQ). Permits, if required, must be obtained by the recipient prior to acquiring the regulated materials and federal agency review of the application may trigger an inspection of facilities prior to approval. Be sure to ask for support from the Biosafety Office at any point in the process but especially if a permit application brings about a facility inspection.

The first thing to ascertain, in order to understand if a permit is necessary, is whether the material you want to receive is deemed to pose a potential risk to humans, animals, or plants. This key decision, which is not always intuitive, will also identify the applicable regulations. Permits from both the CDC and APHIS/VS may be required if the pathogen of concern affects both humans and animals. Furthermore, select agent pathogens (microbes that have the potential to be used as biological weapons) have their own regulations *in addition to* the permitting requirements.

### CDC Permits

The CDC regulates the movement of **Agents Causing Disease in Humans** – microorganisms and microtoxins, including bacteria, bacterial toxins, viruses, fungi, rickettsiae, protozoans, and parasites. In addition to the organisms, the CDC also regulates the movement of the following:

**Biological Materials:** This includes unsterilized specimens of human and animal tissues (such as blood, body discharges, fluids, excretions or similar materials) containing human pathogens.

**Host and Vectors:** Any animal (such as nonhuman primates or turtles) or arthropod known or suspected of being infected with an organism capable of causing disease in humans may require a permit, as well as any snail species capable of transmitting human diseases. A permit is not required for any material that has been rendered sterile.

### Importation vs. Transportation of Human Pathogens

In most instances the CDC requires permits only for the importation of the above mentioned materials. As is normally the case, it is the receiver (importer) who must obtain the permit. The CDC guidance document states, "The importer is legally responsible for assuring that the foreign personnel package, label, and ship the infectious materials according to Federal and international regulations". It is important that you communicate with your shipper and ensure that they are fully aware of the requirements since you, as the receiver, assume specific legal obligations and liabilities.

Note that the permit application specifically asks if the material is a select agent. For some organisms, such as some vaccine strains and *Clostridium* species, this may not be obvious. In signing the permit application, the recipient vouches that the organism is or is not a select agent. Be certain that you know what you are receiving. Receiving a select agent without federal approval can have serious consequences.

Currently, a permit is not required to transport human pathogens or materials containing human pathogens within the U.S., unless 1) the SARS virus is involved; or, 2) the person wants to send to or receive from ATCC (American Type Culture Collection) or BEI Resource (Biodefense Emerging Infections). These exceptions are subject to change and CDC should be contacted for up-to-date information. In general, if you're receiving a human pathogen from someone within the U.S., and they state that a permit is needed, it is best to take that advice seriously and look into the matter.

**Shipping CDC-Regulated Materials:** Packages containing human pathogens are subject to Department of Transportation (DOT) Hazardous Materials Regulations (49 CFR 171-180). The International Air Transport Association (IATA) Dangerous Goods Regulations apply to materials shipped by air and are more stringent than DOT regulations. Additional regulations apply to transportation of specific organisms listed in Interstate Shipment of Etiological Agents (42 CFR 72) mainly concerning CDC notification of damaged packages or packages that fail to arrive within 5 days of expected date.

### **APHIS/VS Permits**

The APHIS/VS has responsibility for regulating movement of materials that contain (or potentially contain) livestock and poultry pathogens, with the term livestock referring to any bovine, ovine, caprine, porcine, and equine animal. This purview includes the organisms themselves, materials derived from them, and their vectors. The regulations define a vector as animals such as mice, pigeons, guinea pigs, insects, etc., "which have been treated or inoculated with organisms, or which are diseased or infected with any contagious, infectious, or communicable disease of animals or poultry". A special note should be made about recombinant microbes as well as RNA and DNA derived from a pathogen. As a general rule, if the DNA, RNA or plasmids were derived from an animal pathogen, then the permit requirement applies. Recombinant microbes that contain genes related to pathogenicity or virulence or express antigens of livestock or poultry disease agents also require a permit.

There is more. In addition to requiring permits for receiving animal pathogens and their hosts and vectors, APHIS/VS requires permits for materials derived from animals or exposed to animal-source materials. These 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, and antisera.

While this list is broad, there are significant exceptions described in guidance documents issued by the USDA. Exceptions that may be of importance in a University setting are outlined below. As is often the case, the exceptions help define the rules.

**Human Pharmaceuticals and Vaccines:** Pharmaceuticals and vaccines intended for humans and packaged in their final dosage form, even if they contain animal components, are not regulated by the USDA. However, pharmaceutical ingredients that contain animal components still require a permit due to potential presence of an animal pathogen and possible diversion for animal use.

**Human and Non-Human Primate Material:** Human or non-human primate material are not regulated unless it has a potential or actual pathogen or is produced in tissue culture. Materials produced in tissue culture are regulated if techniques employ animal-derived materials such as fetal bovine serum.

**Live Laboratory Mammals and Their Products:** Exempted are rodents and rabbits, and their blood, tissue, DNA, extracts, antibodies, feces, sera, and antisera. USDA does not have jurisdiction over these unless they were inoculated with or exposed to any livestock pathogens.

**Microbially Produced Material:** Biochemicals, or other materials produced by microbes (usually *E. coli* or yeasts) do not require a permit as long as the microbe that was used does not express genetic material of a livestock or poultry disease.

**Recombinant Microbes and their Products:** Recombinant non-pathogenic bacteria/yeasts (such as *E. coli* and *Saccharomyces cerevisiae*) and their products that are not related to livestock or avian species or disease causing agents and that do not contain animal products such as albumin or serums may be brought into the country without a permit.

**Cell Cultures/Lines and their Products (including recombinant forms):** Cell lines and other products of cell lines, including monoclonal antibodies, which are not derived from livestock or avian species, have not been exposed to livestock or avian pathogens exotic to the U.S., and do not produce antigens or contain genes of livestock or avian pathogens or do not produce monoclonal antibodies directed against livestock or avian pathogens do not require a permit.

**Importation vs. Transportation:** The need to obtain a permit is independent of whether the materials are to be imported or are from a domestic source. However, items entering the U.S. are subject to USDA inspection upon arrival at a port of entry. To facilitate clearing customs when it is determined that the imported material does not require a permit, the shipping documents must include a detailed description of the material as well as a declaration that the material is exempt from the permit requirements.

Shipping Requirements for Animal Pathogens: Animal pathogens, like human pathogens, are subject to DOT and IATA shipping regulations whether an APHIS/VS permit is required or not. Remember that permits are only required for pathogenic materials that affect agriculturally important species. DOT and IATA regulations do not make this distinction.

### **APHIS/PPQ Permits**

APHIS/PPQ requires permits for the importation, transport across state lines and environmental release of any organisms that impact plants. This oversight is not limited simply to plant pathogens, but also includes other plant pests such as insects, mites, snails, slugs, earthworms, microbes pathogenic to invertebrates, biological control organisms, parasitic plants, and noxious weeds. Plant pests that have been determined by PPQ to be widely present within the destination state are likely to be issued permits more promptly and with minimal containment requirements, but require a permit none-the-less.

APHIS/PPQ also requires permits for importation (but not interstate transportation) of plants and plant products, and for soil. These phytosanitary permits are different from the plant pest permits. If you intend to isolate and/or culture live organisms from soil, then you must obtain both a permit to receive soil as well as a plant pest permit.

Importation vs. Transportation: Permit requirements are the same for organisms whether these are received interstate or internationally with a few exceptions (honey bees, entomophagous insects, entomopathogens). Another difference is that importation permits are generally valid for 1-2 years while permits to transport pathogens are usually valid for 3 years.

Shipping requirements for Plant Pathogens: Shipping of plant pathogens and pests is not regulated by DOT and IATA, but APHIS has rules (7 CFR 330.210-212) regarding proper packaging and labeling. A limited number of package labels may be issued with the permit.

### **APHIS Permits for Genetically Modified Organisms**

This article has generally focused on permit requirements for various pathogens. A very distinct permit requirement lies in the area of Genetically Modified Organisms (GMOs). The Biotechnology Regulatory Services (BRS) of APHIS regulates the field testing (release into the environment), interstate movement, and importation of genetically engineered organisms.

Depending on the nature of the genetically engineered crop, an applicant files either a notification or a permit application. In general, most of the plants are field tested under the notification procedure, a more streamlined approval process that is used only for familiar crops and traits considered to be low risk. Permitting is used for field tests of plants that have an elevated risk, such as plants producing pharmaceutical or industrial compounds.

### **General APHIS Permit Considerations**

**Permit Conditions:** Upon receiving your permit, you should immediately read the conditions imposed on possession of the material received under the permit. These are very specific and as the permit holder you are bound by these conditions. Conditions will vary depending on the material covered by the permit and may change upon renewal. A common condition is that the regulated material may not be distributed further without APHIS approval.

**Permit Renewals:** The necessity of renewing permits is significantly different between PPQ and VS. There is no need to renew a VS permit for an animal pathogen if you are not going to receive or transport any more materials under the permit. This is true even if the materials are to be retained beyond the permit expiration date. However, the permit restrictions remain in force as long as the material is retained even if the permit has expired.

This differs significantly with the PPQ renewal requirements. PPQ requires that you renew your permit if you retain the materials. Otherwise, you are expected to destroy the regulated material when your PPQ permit expires.

**Final Word:** The permitting requirements can be complicated and are often subject to interpretation. This article can, at best, act as an introduction to the topic. The websites listed below can provide further information. In addition, contact the Biosafety Office if a question arises.

Additional information on the permit requirements can be obtained from websites:

CDC Permit Program	<a href="http://www.cdc.gov/od/eaipp/">http://www.cdc.gov/od/eaipp/</a>
APHIS/VS Permits	<a href="http://www.aphis.usda.gov/vs/import_export.htm">http://www.aphis.usda.gov/vs/import_export.htm</a>
APHIS/PPQ Permits	<a href="http://www.aphis.usda.gov/ppq/permits/">http://www.aphis.usda.gov/ppq/permits/</a>

## Safety Products/Gadgets Corner

### Laundry Service for Lab Coats

Lab coats, smocks, and scrubs serve to protect the wearer and their personal clothing from contaminants encountered during procedures. They need to be laundered periodically, particularly when they are visibly dirty. Taking a lab coat home to be washed is ill-advised. The university has the following contracts with vendors for laundry service.

- Uniform rental and laundering - contract # 04-5194, Aramark Uniform Services. A variety of protective clothing styles are available for rental. Laundry service can be arranged on a regular schedule or as needed.
- Laundry services - contract # 04-5325, Band Box Cleaners & Laundry. This contract only covers laundry service. The protective clothing is owned by the university, typically purchased by the investigator.

The Purchasing Services website, [www.bussvc.wisc.edu/purch/contract/](http://www.bussvc.wisc.edu/purch/contract/), has current information about these contracts.

### Snuff Out the Flame

In the April 2006 BioSide Lines, we discussed the hazards of using a Bunsen burner in a biosafety cabinet (BSC). Flames and alcohol pose an inherent danger. Heat may damage a HEPA filter, alcohol can easily catch on fire, and the heat may disrupt the laminar air flow on which containment depends. Alternative devices are available that cause less or no disruption of the air curtain and will not harm a biosafety cabinet.

- The portable ceramic furnace (e.g., the Bactincinerator®) is a great alternative for microbiological uses such as flaming a loop or a culture bottle neck. An attachment allows heat fixing of microscope slides.
- Bead sterilizers have been around for about 30 years and are just now gaining in popularity. You place a dry clean instrument in the glass beads that are heated to 250°C and in 20 seconds it is sterilized.
- On-demand burners (e.g., the Touch-O-Matic®) are available for the work that requires a flame. A pilot light is constantly on, and with a touch of a switch, a small but adequate flame is generated. If the switch is turned left or right, a continuous flame is available. This small flame does not disrupt laminar air flow to the degree of the Bunsen burner. This larger flame self-extinguishes when used in on-demand mode, reducing the risk of a fire.
- Using pre-sterilized tools, such as inoculating loops and spreaders, removes the problem of having to sterilize devices in the BSC.

These alternatives to a Bunsen burner flame will assist you in keeping your lab safe and your work uncontaminated. They are available from laboratory supply vendors such as Fisher Scientific. This information is provided as a service to UW staff and students and is not an endorsement of particular products or vendors.

## ***Shipping Infectious Substance and Other Biological Materials***

The Office of Biological Safety will provide training and certification for shipping Infectious Substance and other biological materials, with a focus on safety and regulatory compliance for research laboratories. The Department of Transportation requires that persons involved in shipping hazardous materials in commerce be trained and certified in proper handling of these materials.

**Wednesday, October 11, 2006**

Union South 1:00 – 3:30 p.m.

Refreshments will be served.

All staff are welcome to attend this class for initial training or re-certification. Computer-based training is available only for those who attended the class for their initial certification.

## **HazMat Packaging Workshop**

An optional hands-on HazMat packaging workshop will be offered after the regular HazMat Shipping class. Trainees will decide how example materials should be shipped (e.g., Infectious substance; Biological substance, category B; Exempt patient specimens) and then will package the surrogate materials in appropriate containers. Feedback and tips on packaging will be provided. People with current HazMat certification may register for the workshop only.

**Wednesday, October 11, 2006**

Union South 3:30-4:30 pm

## ***Basic Biosafety Class Offered***

This class will give an overview of basic biological safety. Topics include biosafety levels and biohazard containment, good microbiological techniques, waste disposal, risk assessment, and emergency preparedness. It is intended primarily for students and staff who are new to this institution and/or new to working with biological materials. Everyone is welcome to attend.

**Tuesday, October 24 , 2006**

Union South 1:00 – 3:30 p.m.

## **Advanced Biosafety Training**

This class builds on the Basic Biosafety class and focuses on biosafety level 2 (BSL-2) precautions and containment in lab and animal research. Topics include risk assessment, proper use of containment equipment and personal protective equipment, and disinfection procedures for various types of Risk Group 2 pathogens (viruses, bacteria, fungi, parasites, prions). A major goal of the class is to provide safety information on commonly-used viral vectors since they are becoming a widespread research tool. The Basic Biosafety class should be taken prior to the Advanced Biosafety class either by attending a Basic Biosafety class or by reviewing the training available at the OBS website.

**Wednesday, November 15, 2006**

Union South 1:00-3:30 p.m.

**Registration is required for these courses.**

Contact OBS at 263-2037 or [biosafety@fpm.wisc.edu](mailto:biosafety@fpm.wisc.edu).

<b>Contacts</b>			
Jan Klein	General Contact	263-2037	biosafety@fpm.wisc.edu
Margy Lambert	Biological Safety Officer	263-9026	jklein@fpm.wisc.edu
Darren Berger	Associate Biosafety Officer	263-9013	mlambert@fpm.wisc.edu
Terry Lawrin	Facilities Engineer	263-2187	dberger@fpm.wisc.edu
Nancy Schensky	Biosafety Specialist	262-6670	tlawrin@fpm.wisc.edu
Jeff Zebrowski	Administrative Support	263-2037	nschensky@fpm.wisc.edu
Tom Kenney	Res. Compliance Specialist	890-0993	jzebrowski@fpm.wisc.edu
	Occupational Health Officer	263-2177	tkenney@fpm.wisc.edu