

**DREXEL**

**SELECT AGENTS  
POLICIES AND PROCEDURES MANUAL**

**Last Revised February 10, 2014**

## 1. Background

The U.S. Departments of Health and Human Services (HHS) under the control of the Center for Disease Control (CDC) and the Animal and Plant Health Inspection Service (APHIS)/United States Department of Agriculture (USDA) have established new safeguards for the possession, use, and transfer of select biological agents and toxins (select agents) that could pose a threat to public, animal and plant health and safety. This new rule will continue to strengthen programs aimed at protecting the American people from acts of terrorism and these safeguards will help protect the food supply without sacrificing valuable research being done on these agents. The rule updates the previous select agent rule by requiring facilities to register with HHS' Centers for Disease Control and Prevention (CDC) if they **possess** a select agent or agents that pose a potential threat to human health. **The new rule became effective February 7, 2003. The Final Rules were published in the Federal Register on March 18, 2005 and were most recently updated on October 16, 2008.**

## 2. The Law

On June 12, 2002, President Bush signed the "Public Health Security and Bioterrorism Preparedness Response Act of 2002" (Public Law 107-188). The law is designed to improve the ability of the United States to prevent, prepare for, and respond to bioterrorism and other public health emergencies. Section 202(a) of the Law requires that all persons possessing biological agents or toxins deemed a threat to public health to notify the Secretary, Department of Health and Human Services (HHS). Section 213(b) of Law requires all persons possessing biological agents or toxins deemed a threat to animal or plant health and to animal or plant products notify the Secretary, United States Department of Agriculture (USDA).

APHIS and CDC implemented the provisions of Public Law 107-188, the "Public Health Security and Bioterrorism Preparedness Response Act of 2002" (The Act) through a series of regulations. These regulations culminated with the publication of the final Select Agents Regulations (42 CFR Part 73, 7 CFR Part 331, 9 CFR Part 121) in the Federal Register on March 18, 2005. The Final Rules were published in the *Federal Register* on March 18, 2005 and became effective on April 18, 2005. Updates are published from time to time and can be found on the CDC's website.

For more information on the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (Public Law 107-188) visit: <http://www.cdc.gov/od/sap/address.htm>.

For information on Laboratory Security and Emergency Response Guidance for Laboratories Working with Select Agents visit: [http://www.cdc.gov/od/ohs/biosfty/bmbf5/bmbf\\_5th\\_edition.pdf](http://www.cdc.gov/od/ohs/biosfty/bmbf5/bmbf_5th_edition.pdf)

## 3. Intent of the Law

Traditional laboratory biosafety guidelines published Drexel University's Laboratory Safety Manual emphasizes the use of optimal work practices, to minimize risks of unintentional infection or injury for laboratory workers and to prevent contamination of the outside environment. Although clinical and research microbiology laboratories might contain dangerous biologic, chemical, and radioactive materials, to date, only a limited number of reports have been published of materials being used intentionally to injure laboratory workers or others (1--6). However, recently, concern has increased regarding possible use of biologic, chemical, and radioactive materials as terrorism agents (8,9). In the United States, recent terrorism incidents (10) have resulted in the substantial enhancement of

existing regulations and creation of new regulations governing laboratory security to prevent such incidents.

The Public Health Security and Bioterrorism Preparedness and Response Act of 2002\* (the Act) require institutions to notify the US Department of Health and Human Services (DHHS) or the US Department of Agriculture (USDA) of the possession of specific pathogens or toxins (i.e., select agents\*\*), as defined by DHHS, or certain animal and plant pathogens or toxins (i.e., high-consequence pathogens), as defined by USDA. The Act provides for expanded regulatory oversight of these agents and a process for limiting access to them to persons who have a legitimate need to handle or use such agents. The Act also requires specified federal agencies to withhold from public disclosure, among other requirements, site-specific information regarding the identification of persons, the nature and location of agents present in a facility, and the local security mechanisms in use. In addition, the Uniting and Strengthening America by Providing Appropriate Tools Required To Intercept and Obstruct Terrorism (USA PATRIOT) Act of 2001<sup>§</sup> prohibits restricted persons from shipping, possessing, or receiving select agents. Violation of either of these statutes carries criminal penalties.

## References

1. Török TJ, Tauxe RV, Wise RP, et al. Large community outbreak of salmonellosis caused by intentional contamination of restaurant salad bars. *JAMA* 1997;278:389--95.
2. Kolavic SA, Kimura A, Simons SL, Slutsker L, Barth S, Haley CE. Outbreak of *Shigella dysenteriae* type 2 among laboratory workers due to intentional food contamination. *JAMA* 1997;278:396-8.
3. US Nuclear Regulatory Commission. Report to Congress on abnormal occurrences July--September 1995; dissemination of information. *Federal Register* 1996;61:7123--4.
4. US Nuclear Regulatory Commission. Incident investigation report: ingestion of phosphorus-32 at Massachusetts Institute of Technology, Cambridge, Massachusetts, identified on August 19, 1995 [NUREG-1535]. Washington, DC: US Nuclear Regulatory Commission, 1995.
5. US Nuclear Regulatory Commission. Preliminary notification of event or unusual occurrence PNO-1-98-052. Subject: intentional ingestion of iodine-125 tainted food (Brown University), November 16, 1998. Washington, DC: US Nuclear Regulatory Commission, 1998.
6. US Nuclear Regulatory Commission. National Institutes of Health issuance of director's decision under 10 CFR Sec. 2.206. *Federal Register* 1997;62:50018--33.
7. Public Law 107--188, June 12, 2002.

*\*\*Throughout this report, the term select agent refers to specifically regulated pathogens and toxins as defined in Title 42, Code of Federal Regulations (CFR), Part 73, including pathogens and toxins regulated by both DHHS and USDA (i.e., overlapping agents and toxins). The reader should note that 42 CFR Part 73 has not been published yet, and is still under federal review with anticipated publication in December 2002.*

*§Public Law 107--56, October 26, 2001.*

## **4. DREXEL UNIVERSITY'S SELECT AGENTS POLICIES FOR RESEARCHERS AND THEIR STAFF**

### **4.1 Standard Operating Procedures**

- 4.1.1** The Drexel University (DU) and Drexel University College of Medicine (DUCOM) Policies on the possession, use, transfer and receiving select agents are provided to assist the investigators in meeting the regulatory mandate of 42 Code of Federal Regulation (CFR) 73 and, therefore, include information regarding personnel, risk

assessments, and inventory controls. These guidelines are intended for laboratories where select agents are used under biosafety levels (BSL) 2, 3, or 4 to take into serious consideration of the following security policies and procedures:

- Risk and threat assessment;
- Facility security plans;
- Physical security;
- Data and electronic technology systems;
- Security policies for personnel;
- Policies regarding accessing the laboratory and animal areas;
- Specimen accountability;
- Receipt of agents into the laboratory;
- Transfer or shipping of select agents from the laboratory to another institution;
- Emergency response plans; and
- Reporting of incidents, unintentional injuries, and security breaches.

**4.1.2** Investigators who use university facilities to, handle, transfer, receive, or store select agents listed below (section 5.0), irrespective of the purity and quantity, must register with the Office of Research prior to acquiring or purchasing any amount of material or purity of Select Agents. To register, use the "Select Agent Inventory and Declaration Form", which is posted on the Office of Research website [www.drexel.edu/research](http://www.drexel.edu/research). To obtain the form click on Research – Compliance – Biosafety and "Select Agent Inventory and Declaration Form". complete, mail or fax the form to the Office of Research. The Office of Research will send a copy of this form to the Department of Environmental Health and Safety (DEHS) for inventory and tracking purposes. All inventory accounting, tracking and inspections will be done by the DEHS.

**4.1.3** Purchase and use of select agents require registration of the facilities with the CDC/USDA. This registration is done **ONLY** by the Office of Research Compliance. The registration requires completion of CDC/USDA "Select Agent Form", completion of Table 4A, approval of engineering controls, Department of Justice approval of individuals who will be working with select agents and their finger print records. All of these forms require Office of Research approval and signature of the Responsible Official. Therefore, it is imperative that investigators discuss with Office of Research should they need to use select agents in their research projects.

The Office of Research and the Department of Environmental Health and Safety (DEHS) shall provide any assistance required for completing these requirements and forms. Please call 215-255-7857 for assistance.

**4.1.3** In order to comply with Federal regulations, the university has appointed a Responsible Official (RO) and an alternate for this RO. They are Vice Provost for Research, Drexel University, Sreekant Murthy, Ph.D., Vice Provost for Research Compliance and Jonathan M. Chase, respectively.

**4.1.4** No select agent, irrespective of purity and quantity should be transferred to or from Drexel University or Drexel University College of Medicine without prior registration with the Office of Research Compliance, RO's approval and the CDC/USDA. Guidance documents and the form for receiving and shipping are posted on the website: <http://www.selectagents.gov/TransferForm.html>. Authorization from the Office of Research Compliance is required before transferring the agent to another facility or receiving the select agent from another facility. This authorization is required

because the Office of Research must register the laboratory (facility) with the CDC/USDA when any of the select agents above the exempt level is added to the list. Only the Office of Research Compliance through RO will coordinate all requests for CDC or USDA approval regarding the procurement, transfer or destruction of Select Agents.

- 4.1.5** Institutional Biosafety Committee must approve the use of a select agent before work can begin. Biosafety committee meets once a month. The process for submission of Biosafety protocols for committee review is posted on the Office of Research website <http://www.drexel.edu/research/>. To obtain guidance and forms click on Research – Compliance – Biosafety and Biosafety Guidelines.
- 4.1.6** Purchase of select agents in any quantity and purity requires approval from the Office of Research. The Office of Research will send a copy of the purchase order to the DEHS for tracking and maintaining an inventory of all select agents to ensure compliance with respect to the aggregate amount of a select agent used in our university. It is the aggregate amount of select agent toxins that determines whether the university has to register with CDC/USDA.
- 4.1.7** Use of Small Value Purchase Orders or use of a Purchasing Card is permitted within the policies of the purchasing department, but require prior permission from the Office of Research before a select agent is ordered. Signature of Vice Provost for Research Compliance on the small value purchase order or a memo detailing the purchase of select agent through purchasing card is sufficient to purchase. The Office of Research will send a copy of the approved request to DEHS for maintaining the inventory and tracking of select agents. Policies on small value purchase orders and purchasing cards are posted on the website: <http://www.drexel.edu/procurement/>.

#### **4.2 Security of Select Agents – Investigator’s Responsibilities**

- 4.2.1** All select agents must be kept in a secure place under lock and key. Establish appropriate security plans, which include periodic testing to determine the effectiveness through test procedures, which can vary from a simple check of keys, locks, and when necessary, alarms to a full scale laboratory exercise.
- 4.2.2** Ensure that there are sufficient controls to prevent access by non-authorized personnel:
- Control access to the area as suggested by the Drexel University Department of Public Safety (DPS)
  - Restrict access to select agents to workers who are authorized and required to perform work in the area.
  - Limit the access of non-laboratory personnel.
  - Keep the room locked at all times.
  - Record all entries, including entries by visitors, maintenance workers, repairmen and others needing one-time or occasional entry.
  - Freezers, refrigerators, cabinets, and other containers where stocks of select agents should be locked at all times.
  - Screen all packages being removed or brought into the laboratory or facility.
  - Have an emergency plan in place in case of an emergency.
  - Report incidents to appropriate department, administrators, or agencies

- 4.2.3** Ensure that all laboratory workers and visitors understand security requirements and that all employees and students are trained and equipped to follow established procedures. Security plan should be an integral part of daily operations. New employees and students should receive training when they first begin work, and all employees should receive training at least annually thereafter. Training should be updated as policies and procedures change. All training should be documented by maintaining records of training schedules and employee/student attendance.
- 4.2.4** Make sure to screen all employees and other personnel who require access to select agents or who enter the laboratory. Employees and students must wear a visible identification badge with a photo.
- 4.2.5** Immediately report to the Office of Research if select agents are stolen or found missing. Please be advised that Office of Research must report such incidences to the CDC/USDA when they occur. The CDC/USDA guidance to report theft, loss or release of select biological agents and toxins is posted on the website: <http://www.selectagents.gov/TheftLossRelease.html>
- 4.2.6** When select agents are completely used, report to the DEHS. It helps the DEHSto make appropriate changes to the inventory.
- 4.2.7** Investigators are not permitted to dispose select agents on their own. Contact the DEHSto dispose the unused select agent(s). Disposal of select agents must be reported to the CDC/USDA. Office of Research is responsible for reporting disposal of agents.
- 4.2.8** Maintain and update records of transfers, acquisitions, purchases, inventories, stocks, use, and destruction of select agents.
- 4.2.9** Ensure that individuals working in your laboratory are aware of restrictions on transferring, receiving, storage, safe work practices, and use of select agents. Train all personnel with access to the Select Agent in:
- Inventory management (security, written inventory, etc.)
  - Safe work practices
  - Personal protective equipment (if required)
  - Emergency Procedures in the event of a spill or exposure
  - Signs and symptoms of exposure
  - Vaccination requirements (if any)
  - Written disposal and deactivation procedures
- 4.2.10** Complete and maintain an annual inventory of select agents. Submit a copy of the annual inventory to the DEHS.
- 4.2.11** Ensure that the laboratory has a copy of the Chemical Hygiene Plan that addresses personal protection, training, and safe work practices are in place when working with biological toxins. Copies of Chemical Hygiene plan is posted on the website: <http://www.drexelsafetyandhealth.com/index.asp?page=labsafety.asp> Click on the appropriate link to download the desired plan.
- 4.2.12** If you are not using a select agent, you must complete the demographic information on the Select Agent Inventory form and sign "Select Agent Inventory and Declaration Form" and send the form to the DEHS. To down load this form, go to the Office of Research website: <http://www.drexel.edu/research/>. To obtain the form, click on

Research – Compliance – Biosafety and “Select Agent Inventory and Declaration Form” Complete and mail the form to DEHS. The address is: Department of Environmental Health and Safety, 400 N. 31<sup>st</sup> Street, Philadelphia, PA 19104.

## **5. Possession, Use, and Transfer of Select Agents and Toxins**

This document establishes requirements regarding possession and use within the Drexel University and Drexel University College of Medicine (hitherto referred to as “institution”), receipt from outside, and transfer within the university and transfer within the United States of select agents and toxins. This includes requirements concerning registration of individual laboratories with the CDC, security risk assessments, safety plans, security plan, emergency response plans, training, transfers, record keeping, inspections and notifications. This document provides guidelines to implement provisions of the Public Health Security and Bioterrorism preparedness and Response Act of 2002 designed to provide protection against misuse of select agents and toxins whether inadvertent or the result of terroristic act or criminal act against the United States. This rule (42 CFR Part 73) became effective February 7, 2003 with the most recent published update published on October 16, 2008. The provisions of this act is consistent with the intent of the Act, that the institution and the authorized individuals within the institution are allowed to conduct activities regulated by this rule only if they are conducted for scientific and lawful purposes in accordance with the part 73 regulations.

## **6. List of Select Agents and Toxins**

The CDC and USDA have categorized the list based on where the application needs to be sent. Some agents are regulated by CDC alone, some by USDA alone and some are overlapping agents which are regulated by either CDC or USDA. The Office of Research shall determine where the agent and the investigator have to be registered or registration to be amended.

### **CDC / HHS Select Agents and Toxins**

Abrin

Botulinum neurotoxins

Botulinum neurotoxin producing species of Clostridium

Cercopithecine herpesvirus 1 (Herpes B virus)

Clostridium perfringens epsilon toxin

Coccidioides posadasii/Coccidioides immitis

Conotoxins

Coxiella burnetii

Crimean-Congo haemorrhagic fever virus

Diacetoxyscirpenol

Eastern Equine Encephalitis virus

Ebola virus

Francisella tularensis

Lassa fever virus

Marburg virus

Monkeypox virus

Reconstructed replication competent forms of the 1918

pandemic influenza virus containing any portion of the

coding regions of all eight gene segments (Reconstructed 1918 Influenza virus)

Ricin

Rickettsia prowazekii

Rickettsia rickettsii  
Saxitoxin  
Shiga-like ribosome inactivating proteins  
Shigatoxin  
South American Haemorrhagic Fever viruses  
Flexal  
Guanarito  
Junin  
Machupo  
Sabia  
Staphylococcal enterotoxins  
T-2 toxin  
Tetrodotoxin  
Tick-borne encephalitis complex (flavi) viruses  
Central European Tick-borne encephalitis  
Far Eastern Tick-borne encephalitis  
Kyasanur Forest disease  
Omsk Hemorrhagic Fever  
Russian Spring and Summer encephalitis  
Variola major virus (Smallpox virus)  
Variola minor virus (Alastrim)  
Yersinia pestis

**OVERLAP (CDC and USDA) Select Agents and Toxins**

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

**USDA Select Agents and Toxins**

African horse sickness virus  
African swine fever virus  
Akabane virus  
Avian influenza virus (highly pathogenic)  
Bluetongue virus (exotic)  
Bovine spongiform encephalopathy agent  
Camel pox virus  
Classical swine fever virus  
Ehrlichia ruminantium (Heartwater)  
Foot-and-mouth disease virus

Goat pox virus  
Japanese encephalitis virus  
Lumpy skin disease virus  
Malignant catarrhal fever virus  
(Alcelaphine herpesvirus type 1)  
Menangle virus  
Mycoplasma capricolum subspecies capripneumoniae  
(contagious caprine pleuropneumonia)  
Mycoplasma mycoides subspecies mycoides small colony (Mmm SC) (contagious bovine  
pleuropneumonia)  
Peste des petits ruminants virus  
Rinderpest virus  
Sheep pox virus  
Swine vesicular disease virus  
Vesicular stomatitis virus (exotic): Indiana subtypes  
VSV-IN2, VSV-IN3  
Virulent Newcastle disease virus 1

**USDA Plant Protection and Quarantine (PPQ)**

**Select Agents and Toxins**

Peronosclerospora philippinensis (Peronosclerospora  
sacchari)  
Phoma glycinicola (formerly Pyrenochaeta glycines)  
Ralstonia solanacearum race 3, biovar 2  
Rathayibacter toxicus  
Sclerophthora rayssiae var zea  
Synchytrium endobioticum  
Xanthomonas oryzae  
Xylella fastidiosa (citrus variegated chlorosis strain)

## 7. HOW TOXINS ARE FEDERALLY-REGULATED

Toxins are regulated based on potency and quantity (as opposed to potency only or LD50 values). If investigators at Drexel University **do not** at any time **have more** than the following aggregate\* amounts (in the purified form or in combinations of pure and impure forms) the university is excluded from requirements of the regulation for possession and registration.

Abrin	100 mg
Botulinum neurotoxins	0.5 mg
<i>Clostridium perfringens</i> epsilon toxin	100 mg
Conotoxins	100 mg
Diacetoxyscirpenol	1000 mg
Ricin	100 mg
Saxitoxin	100 mg
Shiga-like ribosome inactivating proteins	100 mg
Shigatoxin	100 mg
Staphylococcal enterotoxin	5 mg
Tetrodotoxin	100 mg
T-2	1,000 mg

\* The toxins are not regulated if the amount under the control of a principal investigator, treating physician or veterinarian, or commercial manufacturer or distributor does not exceed, at any time, the amounts indicated in the table below.

NOTE: Botulinum neurotoxin is only considered a select toxin under the Select Agent regulations when the amount under the control of a physician exceeds 0.5 mg. Additionally, all dermatology clinics using FDA-approved botulinum toxin preparations in accordance with labeling instructions are excluded from the requirements to register under the Select Agent regulations and DO NOT need to submit a letter to CDC or USDA to declare exemption from registration with the Select Agent Program.

## 8. RECOMBINANT ORGANISMS/MOLECULES

- a. Genetically modified microorganisms or genetic elements from agents in these lists that have the potential to encode for a factor associated with disease.
- b. Genetically modified microorganisms or genetic elements that contain nucleic acid sequences coding for any of the toxins on these lists, or their toxic subunits.

## 9. EXCLUSIONS FROM THE REGULATION

- a. Select agents or toxins that are in their naturally occurring environment, provided that it has not been intentionally introduced, cultivated, collected, or otherwise extracted from its natural source.
- b. Non-viable select agent organisms or nonfunctional toxins.
- c. The vaccine strain of Junin virus (Candid #1).
- d. It is possible under the new rule to apply for exclusion for any attenuated agent or toxin using an appropriate form obtainable from CDC.
- e. Exclusions for specific strains may be granted if the attenuated Strain I is determined not to pose a significant public health or safety threat. Exclusions will be published in the

notice section of the Federal Register and will be listed on the CDC website at <http://www.cdc.gov/od/sap>.

## **10. TOXIN EXEMPTIONS**

- a) Under the regulations toxins listed above are exempt from the Select Agents registration with the Federal government as long as the amount in possession does not exceed the aggregate amount listed above whether the toxin is pure or impure form. For example, possession of a select agent such as a milligram of tetrodotoxin does not require registration with the Federal government, but requires registration with the university Office of Research. This is done to ensure inventory control and tracking so the cumulative/aggregate amount in the university does not exceed the exempt level.

Investigators can keep exempt quantities of select agents (as long as the aggregate amount does not exceed the exempt limits) in their laboratory for any length of time; however, they must follow the security, inventory control and tracking policies enumerated in this document.

- b) Principal investigators in possession of any of the toxins listed above, irrespective of the quantity or purity of the toxin must complete the "Select Agents Inventory and Declaration Form". Signed completed forms must be submitted to the Office of Health and Safety. To download the form, please go to <http://www.research.drexel.edu/compliance/biosafety/guidelines.aspx>.
- c) The DEHS must be notified prior to each toxin acquisition purchase or transfer, regardless of the quantity procured or transferred. The notification must include the name of the toxin, source and quantity. Purchase or acquisition should occur only after receiving the approval from Office of Research.
- d) Principal investigators must maintain an inventory log for each toxin listed above. The log should have the date, the quantity of each purchase, source, date of purchase, amount of toxin used in the experiment and how the sample was destroyed or disposed.
- e) The EHS department shall periodically conduct audits to verify the maintenance of the toxin inventory logs and to verify the storage, usage and disposal of toxins.
- f) Principal investigators are responsible to ensure security of the toxins by limiting access to the toxin storage and use locations.
- g) Principal investigators must inform DEHS when they are no longer in possession of select agent toxins
- h) If the amount of toxin exceeds the exemption quantity, prior approval from the Office of Research and Federal Select Agent Program coordinated through the Office of Research Compliance and RO must be obtained before acquiring the material.

## **11. REGISTRATION**

All laboratories within the institution which intends to possess or use, receive from within or outside the institution or transfer within or outside the institution any select agent or toxin above the exempt levels as specified in Section 9 above, must be registered with the CDC or

USDA. Investigators are not permitted to register their labs directly with the CDC or USDA. Only the Office of Research Compliance is authorized to register, make amendments to registration, approve receipt and transfer of select agents and toxins. For instructions to register, possess, use and transfer of select agents contact the Office of Research Compliance at 215-255-7857.

## **12. SECURITY RISK ASSESSMENT**

No person within the institution is authorized to possess, use, transfer or have access to a select agent or toxin unless approved by the Department of Justice, CDC or USDA. Certain individuals may be restricted from possession, use and transfer of select agents and toxins. When an application is made for security risk assessment, the Office of Research Compliance or certain Federal agencies may restrict or deny access if the applicant is classified as a restricted person as defined in 18 U.S.C. 175b.

## **13. RESPONSIBLE OFFICIAL**

Institutions conducting regulated research activities are required to identify and authorize an individual who has the authority and responsibility to ensure that the requirements of the regulations are met, on behalf of the institution. The Institution has appointed a Responsible Official (RO) and an alternate for this RO. They are Vice Provost for Research Compliance, Drexel University, Sreekant Murthy, Ph.D., and Director of Safety and Health, Drexel University, Jonathan M. Chase, respectively.

## **14. SAFETY**

The institution adheres to the safety standards pertaining to the possession and use of microbiological agents, possession, use and handling of toxins, occupational exposure to hazardous chemicals, recombinant DNA in microbiological and biomedical laboratories and the provisions there in regards to security, physical containment, biological containment. These provisions are designed to implement the mandate in the Act to establish safety provisions commensurate with the risk of the biological agent or toxin poses to the public health and safety.

In order to comply with these regulations, the RO and the AROs conduct regular inspections to ensure compliance with all of the procedures and protocols of the safety plan. If the inspection results in some violations, the investigator will be required respond immediately to those concerns to ensure that safety provisions are met.

It is imperative to understand that the safety procedures and other provisions to contain risk is not limited to the select agents listed above (see section 5 above). Laboratory manipulation of microbes can alter their characteristics, either intentionally or inadvertently, so as to increase their virulence, pathogenicity, or host range or alter their mode of transmission or route of exposure in ways that increase risks to human, animal and plant health. In particular, the resulting organism could present risks equal to or even greater than the current select agents and toxins.

In this institution, at present we are not authorized to conduct the following experiments. We need to obtain approval from the HHS Secretary through CDC, which will consult outside experts prior to giving approval for the following experiments:

- i. Experiments utilizing recombinant DNA that involve the deliberate transfer of a drug resistance trait to select agents that are not known to acquire the trait naturally, if such acquisition could compromise the use of the drug to control disease agents in humans, veterinary medicine, or agriculture.

- ii. Experiments involving the deliberate formation of recombinant DNA containing genes for the biosynthesis of select toxins lethal for vertebrates at an LD50 < 100 ng/kg body weight.

This is to ensure that these categories of experiments with select agents and toxins involving recombinant DNA (as defined in the NIH Guidelines) are conducted only if safe to do so.

Also, be mindful that the regulations have provisions within to include possible future specifications of additional types of experiments that might warrant stringent security in the interest of safety.

#### **14.1 Biosafety Standards**

This manual describes the Institution's requirements and standards to secure and work with pathogens, select agents and toxins at BSL2 and BSL3 facilities.

#### **14.2 Biosafety Level Definitions**

**Biosafety Levels (BSL).** A combination of work practices and physical containment requirements designed to reduce the risk of laboratory infection when working with infectious material. The degree of protection recommended is proportional to the risk associated with an agent. There are four biosafety levels, BSL1-BSL4, where BSL-1 is the lowest level of protection.

##### **14.2.1. Biosafety Level 1**

Biosafety Level 1 is suitable for work involving well-characterized agents not known to consistently cause disease in immunocompetent adult humans, and present minimal potential hazard to laboratory personnel and the environment. BSL-1 laboratories are not necessarily separated from the general traffic patterns in the building. Work is typically conducted on open bench tops using standard microbiological practices. Special containment equipment or facility design is not required, but may be used as determined by appropriate risk assessment. Laboratory personnel must have specific training in the procedures conducted in the laboratory and must be supervised by a scientist with training in microbiology or a related science.

The following standard practices, safety equipment, and facility requirements apply to BSL-1:

#### **A. Standard Microbiological Practices**

1. The laboratory supervisor must enforce the institutional policies that control access to the laboratory.
2. Persons must wash their hands after working with potentially hazardous materials and before leaving the laboratory.
3. Eating, drinking, smoking, handling contact lenses, applying cosmetics, and storing food for human consumption must not be permitted in laboratory areas. Food must be stored outside the laboratory area in cabinets or refrigerators designated and used for this purpose.
4. Mouth pipetting is prohibited; mechanical pipetting devices must be used.
5. Policies for the safe handling of sharps, such as needles, scalpels, pipettes, and broken glassware must be developed and implemented. Whenever practical, laboratory supervisors should adopt improved engineering and work practice controls that reduce risk of sharps injuries. Precautions, including those listed below, must always be taken with sharp items. These include:

- a. Careful management of needles and other sharps are of primary importance. Needles must not be bent, sheared, broken, recapped, removed from disposable syringes, or otherwise manipulated by hand before disposal.
  - b. Used disposable needles and syringes must be carefully placed in conveniently located puncture-resistant containers used for sharps disposal.
  - c. Non disposable sharps must be placed in a hard walled container for transport to a processing area for decontamination, preferably by autoclaving.
  - d. Broken glassware must not be handled directly. Instead, it must be removed using a brush and dustpan, tongs, or forceps. Plasticware should be substituted for glassware whenever possible.
6. Perform all procedures to minimize the creation of splashes and/or aerosols.
  7. Decontaminate work surfaces after completion of work and after any spill or splash of potentially infectious material with appropriate disinfectant.
  8. Decontaminate all cultures, stocks, and other potentially infectious materials before disposal using an effective method. Depending on where the decontamination will be performed, the following methods should be used prior to transport:
    - a. Materials to be decontaminated outside of the immediate laboratory must be placed in a durable, leak proof container and secured for transport.
    - b. Materials to be removed from the facility for decontamination must be packed in accordance with applicable local, state, and federal regulations.
  9. A sign incorporating the universal biohazard symbol must be posted at the entrance to the laboratory when infectious agents are present. The sign may include the name of the agent(s) in use, and the name and phone number of the laboratory supervisor or other responsible personnel. Agent information should be posted in accordance with the institutional policy.
  10. An effective integrated pest management program is required.
  11. The laboratory supervisor must ensure that laboratory personnel receive appropriate training regarding their duties, the necessary precautions to prevent exposures, and exposure evaluation procedures. Personnel must receive annual updates or additional training when procedural or policy changes occur. Personal health status may impact an individual's susceptibility to infection, ability to receive immunizations or prophylactic interventions. Therefore, all laboratory personnel and particularly women of child-bearing age should be provided with information regarding immune competence and conditions that may predispose them to infection. Individuals having these conditions should be encouraged to self-identify to the institution's healthcare provider for appropriate counseling and guidance.

## **B. Special Practices**

None required.

## **C. Safety Equipment (Primary Barriers and Personal Protective Equipment)**

1. Special containment devices or equipment, such as BSCs, are not generally required.
2. Protective laboratory coats, gowns, or uniforms are recommended to prevent contamination of personal clothing.
3. Wear protective eyewear when conducting procedures that have the potential to create splashes of microorganisms or other hazardous materials. Persons who wear contact lenses in laboratories should also wear eye protection.
4. Gloves must be worn to protect hands from exposure to hazardous materials. Glove selection should be based on an appropriate risk assessment. Alternatives to latex gloves should be available. Wash hands prior to leaving the laboratory. In addition, BSL-1 workers should:

- a. Change gloves when contaminated, integrity has been compromised, or when otherwise necessary.
- b. Remove gloves and wash hands when work with hazardous materials has been completed and before leaving the laboratory.
- c. Do not wash or reuse disposable gloves. Dispose of used gloves with other contaminated laboratory waste. Hand washing protocols must be rigorously followed.

**D. Laboratory Facilities (Secondary Barriers)**

- 1. Laboratories should have doors for access control.
- 2. Laboratories must have a sink for hand washing.
- 3. The laboratory should be designed so that it can be easily cleaned. Carpets and rugs in laboratories are not appropriate.
- 4. Laboratory furniture must be capable of supporting anticipated loads and uses. Spaces between benches, cabinets, and equipment should be accessible for cleaning.
  - a. Bench tops must be impervious to water and resistant to heat, organic solvents, acids, alkalis, and other chemicals.
  - b. Chairs used in laboratory work must be covered with a non-porous material that can be easily cleaned and decontaminated with appropriate disinfectant.
- 5. Laboratories windows that open to the exterior should be fitted with screens.

**14.2.2 Biosafety Level 2.** Practices, equipment, and facility design and construction are applicable to clinical, diagnostic, teaching, and other laboratories in which work is done with the broad spectrum of indigenous moderate-risk agents that are present in the community and associated with human disease of varying severity. With good microbiological techniques, these agents can be used safely in activities conducted on the open bench, provided the potential for producing splashes or aerosols is low. Hepatitis B virus (HBV), the salmonellae, and *Toxoplasma* spp. are representative of microorganisms assigned to this containment level. BSL-2 is appropriate when work is done with any human-derived blood, body fluids, tissues, or primary human cell lines where the presence of an infectious agent may be unknown. (Laboratory personnel working with human-derived materials should refer to the Occupational Safety and Health Administration (OSHA) Bloodborne Pathogen Standards <sup>(2)</sup> for specific required precautions.) Primary hazards to personnel working with these agents relate to accidental percutaneous or mucous membrane exposures, or ingestion of infectious materials. Extreme caution should be taken with contaminated needles or sharp instruments. Even though organisms routinely manipulated at BSL-2 are not known to be transmissible by the aerosol route, procedures with aerosol or high splash potential that may increase the risk of such personnel exposure must be conducted in primary containment equipment, or in devices such as a biological safety cabinet or safety centrifuge cups. Other primary barriers should be used as appropriate, such as splash shields, face protection gowns, and gloves. Secondary barriers such as hand washing sinks and waste decontamination facilities must be available to reduce potential environmental contamination.

**Biosafety Level 2** builds upon BSL-1. BSL-2 is suitable for work involving agents that pose moderate hazards to personnel and the environment. It differs from BSL-1 in that 1) laboratory personnel have specific training in handling pathogenic agents and are supervised by scientists competent in handling infectious agents and associated procedures; 2) access to the laboratory is restricted when work is being conducted; and 3) all procedures in which infectious aerosols or splashes may be created are conducted in BSCs or other physical containment equipment. The following standard and special practices, safety equipment, and facility requirements apply to BSL-2:

### **A. Standard Microbiological Practices**

1. The laboratory supervisor must enforce the institutional policies that control access to the laboratory.
2. Persons must wash their hands after working with potentially hazardous materials and before leaving the laboratory.
3. Eating, drinking, smoking, handling contact lenses, applying cosmetics, and storing food for human consumption must not be permitted in laboratory areas. Food must be stored outside the laboratory area in cabinets or refrigerators designated and used for this purpose.
4. Mouth pipetting is prohibited; mechanical pipetting devices must be used.
5. Policies for the safe handling of sharps, such as needles, scalpels, pipettes, and broken glassware must be developed and implemented. Whenever practical, laboratory supervisors should adopt improved engineering and work practice controls that reduce risk of sharps injuries. Precautions, including those listed below, must always be taken with sharp items. These include:
  - a. Careful management of needles and other sharps are of primary importance. Needles must not be bent, sheared, broken, recapped, removed from disposable syringes, or otherwise manipulated by hand before disposal.
  - b. Used disposable needles and syringes must be carefully placed in conveniently located puncture-resistant containers used for sharps disposal.
  - c. Non-disposable sharps must be placed in a hard walled container for transport to a processing area for decontamination, preferably by autoclaving.
  - d. Broken glassware must not be handled directly. Instead, it must be removed using a brush and dustpan, tongs, or forceps. Plasticware should be substituted for glassware whenever possible.
6. Perform all procedures to minimize the creation of splashes and/or aerosols.
7. Decontaminate work surfaces after completion of work and after any spill or splash of potentially infectious material with appropriate disinfectant.
8. Decontaminate all cultures, stocks, and other potentially infectious materials before disposal using an effective method. Depending on where the decontamination will be performed, the following methods should be used prior to transport:
  - a. Materials to be decontaminated outside of the immediate laboratory must be placed in a durable, leak proof container and secured for transport.
  - b. Materials to be removed from the facility for decontamination must be packed in accordance with applicable local, state, and federal regulations.
9. A sign incorporating the universal biohazard symbol must be posted at the entrance to the laboratory when infectious agents are present. Posted information must include: the laboratory's biosafety level, the supervisor's name (or other responsible personnel), telephone number, and required procedures for entering and exiting the laboratory. Agent information should be posted in accordance with the institutional policy.
10. An effective integrated pest management program is required.
11. The laboratory supervisor must ensure that laboratory personnel receive appropriate training regarding their duties, the necessary precautions to prevent exposures, and exposure evaluation procedures. Personnel must receive annual updates or additional training when procedural or policy changes occur. Personal health status may impact an individual's

susceptibility to infection, ability to receive immunizations or prophylactic interventions. Therefore, all laboratory personnel and particularly women of child-bearing age should be provided with information regarding immune competence and conditions that may predispose them to infection. Individuals having these conditions should be encouraged to self-identify to the institution's healthcare provider for appropriate counseling and guidance.

## **B. Special Practices**

1. All persons entering the laboratory must be advised of the potential hazards and meet specific entry/exit requirements.
2. Laboratory personnel must be provided medical surveillance and offered appropriate immunizations for agents handled or potentially present in the laboratory.
3. When appropriate, a baseline serum sample should be stored.
4. A laboratory-specific biosafety manual must be prepared and adopted as policy. The biosafety manual must be available and accessible.
5. The laboratory supervisor must ensure that laboratory personnel demonstrate proficiency in standard and special microbiological practices before working with BSL-2 agents.
6. Potentially infectious materials must be placed in a durable, leak proof container during collection, handling, processing, storage, or transport within a facility.
7. Laboratory equipment should be routinely decontaminated, as well as, after spills, splashes, or other potential contamination.
  - a. Spills involving infectious materials must be contained, decontaminated, and cleaned up by staff properly trained and equipped to work with infectious material.
  - b. Equipment must be decontaminated before repair, maintenance, or removal from the laboratory.
8. Incidents that may result in exposure to infectious materials must be immediately evaluated and treated according to procedures described in the laboratory biosafety safety manual. All such incidents must be reported to the laboratory supervisor. Medical evaluation, surveillance, and treatment should be provided and appropriate records maintained.
9. Animals and plants not associated with the work being performed must not be permitted in the laboratory.
10. All procedures involving the manipulation of infectious materials that may generate an aerosol should be conducted within a BSC or other physical containment devices.

## **C. Safety Equipment (Primary Barriers and Personal Protective Equipment)**

1. Properly maintained BSCs (preferably Class II), other appropriate personal protective equipment, or other physical containment devices must be used whenever:
  - a. Procedures with a potential for creating infectious aerosols or splashes are conducted. These may include pipetting, centrifuging, grinding, blending, shaking, mixing, sonicating, opening containers of infectious materials, inoculating animals intranasally, and harvesting infected tissues from animals or eggs.
  - b. High concentrations or large volumes of infectious agents are used. Such materials may be centrifuged in the open laboratory using sealed rotor heads or centrifuge safety cups.

2. Protective laboratory coats, gowns, smocks, or uniforms designated for laboratory use must be worn while working with hazardous materials. Remove protective clothing before leaving for non-laboratory areas (e.g., cafeteria, library, administrative offices). Dispose of protective clothing appropriately, or deposit it for laundering by the institution. It is recommended that laboratory clothing not be taken home.
3. Eye and face protection (goggles, mask, face shield or other splatter guard) is used for anticipated splashes or sprays of infectious or other hazardous materials when the microorganisms must be handled outside the BSC or containment device. Eye and face protection must be disposed of with other contaminated laboratory waste or decontaminated before reuse. Persons who wear contact lenses in laboratories should also wear eye protection.
4. Gloves must be worn to protect hands from exposure to hazardous materials. Glove selection should be based on an appropriate risk assessment. Alternatives to latex gloves should be available. Gloves must not be worn outside the laboratory. In addition, BSL-2 laboratory workers should:
  - a. Change gloves when contaminated, integrity has been compromised, or when otherwise necessary. Wear two pairs of gloves when appropriate.
  - b. Remove gloves and wash hands when work with hazardous materials has been completed and before leaving the laboratory.
  - c. Do not wash or reuse disposable gloves. Dispose of used gloves with other contaminated laboratory waste. Hand washing protocols must be rigorously followed.
5. Eye, face and respiratory protection should be used in rooms containing infected animals as determined by the risk assessment.

**D. Laboratory Facilities (Secondary Barriers)**

1. Laboratory doors should be self-closing and have locks in accordance with the institutional policies.
2. Laboratories must have a sink for hand washing. The sink may be manually, hands-free, or automatically operated. It should be located near the exit door.
3. The laboratory should be designed so that it can be easily cleaned and decontaminated. Carpets and rugs in laboratories are not permitted.
4. Laboratory furniture must be capable of supporting anticipated loads and uses. Spaces between benches, cabinets, and equipment should be accessible for cleaning.
  - a. Bench tops must be impervious to water and resistant to heat, organic solvents, acids, alkalis, and other chemicals.
  - b. Chairs used in laboratory work must be covered with a non-porous material that can be easily cleaned and decontaminated with appropriate disinfectant.
5. Laboratory windows that open to the exterior are not recommended. However, if a laboratory does have windows that open to the exterior, they must be fitted with screens.
6. BSCs must be installed so that fluctuations of the room air supply and exhaust do not interfere with proper operations. BSCs should be located away from doors, windows that can be opened, heavily traveled laboratory areas, and other possible airflow disruptions.
7. Vacuum lines should be protected with High Efficiency Particulate Air (HEPA) filters, or their equivalent. Filters must be replaced as needed. Liquid disinfectant traps may be required.
8. An eyewash station must be readily available.

9. There are no specific requirements on ventilation systems. However, planning of new facilities should consider mechanical ventilation systems that provide an inward flow of air without recirculation to spaces outside of the laboratory.
10. HEPA filtered exhaust air from a Class II BSC can be safely re-circulated back into the laboratory environment if the cabinet is tested and certified at least annually and operated according to manufacturer's recommendations. BSCs can also be connected to the laboratory exhaust system by either a thimble (canopy) connection or a direct (hard) connection. Provisions to assure proper safety cabinet performance and air system operation must be verified.
11. A method for decontaminating all laboratory wastes should be available in the facility (e.g., autoclave, chemical disinfection, incineration, or other validated decontamination method).

**14.2.3** Biosafety Level 3 is applicable to clinical, diagnostic, teaching, research, or production facilities where work is performed with indigenous or exotic agents that may cause serious or potentially lethal disease through inhalation route exposure. Laboratory personnel must receive specific training in handling pathogenic and potentially lethal agents, and must be supervised by scientists competent in handling infectious agents and associated procedures. All procedures involving the manipulation of infectious materials must be conducted within BSCs, other physical containment devices, or by personnel wearing appropriate personal protective equipment. A BSL-3 laboratory has special engineering and design features. The following standard and special safety practices, equipment, and facility requirements apply to BSL-3:

*A. Standard Microbiological Practices*

1. The laboratory supervisor must enforce the institutional policies that control access to the laboratory.
2. Persons must wash their hands after working with potentially hazardous materials and before leaving the laboratory.
3. Eating, drinking, smoking, handling contact lenses, applying cosmetics, and storing food for human consumption must not be permitted in laboratory areas. Food must be stored outside the laboratory area in cabinets or refrigerators designated and used for this purpose.
4. Mouth pipetting is prohibited; mechanical pipetting devices must be used.
5. Policies for the safe handling of sharps, such as needles, scalpels, pipettes, and broken glassware must be developed and implemented. Whenever practical, laboratory supervisors should adopt improved engineering and work practice controls that reduce risk of sharps injuries.

Precautions, including those listed below, must always be taken with sharp items. These include:

- a. Careful management of needles and other sharps are of primary importance. Needles must not be bent, sheared, broken, recapped, removed from disposable syringes, or otherwise manipulated by hand before disposal.
  - b. Used disposable needles and syringes must be carefully placed in conveniently located puncture-resistant containers used for sharps disposal.
  - c. Non-disposable sharps must be placed in a hard walled container for transport to a processing area for decontamination, preferably by autoclaving.
  - d. Broken glassware must not be handled directly. Instead, it must be removed using a brush and dustpan, tongs, or forceps. Plasticware should be substituted for glassware whenever possible.
6. Perform all procedures to minimize the creation of splashes and/or aerosols.

7. Decontaminate work surfaces after completion of work and after any spill or splash of potentially infectious material with appropriate disinfectant.
8. Decontaminate all cultures, stocks, and other potentially infectious materials before disposal using an effective method. A method for decontaminating all laboratory wastes should be available in the facility, preferably within the laboratory (e.g., autoclave, chemical disinfection, incineration, or other validated decontamination method). Depending on where the decontamination will be performed, the following methods should be used prior to transport:
  - a. Materials to be decontaminated outside of the immediate laboratory must be placed in a durable, leak proof container and secured for transport.
  - b. Materials to be removed from the facility for decontamination must be packed in accordance with applicable local, state, and federal regulations.
9. A sign incorporating the universal biohazard symbol must be posted at the entrance to the laboratory when infectious agents are present. Posted information must include the laboratory's biosafety level, the supervisor's name (or other responsible personnel), telephone number, and required procedures for entering and exiting the laboratory. Agent information should be posted in accordance with the institutional policy.
10. An effective integrated pest management program is required.
11. The laboratory supervisor must ensure that laboratory personnel receive appropriate training regarding their duties, the necessary precautions to prevent exposures, and exposure evaluation procedures. Personnel must receive annual updates or additional training when procedural or policy changes occur. Personal health status may impact an individual's susceptibility to infection, ability to receive immunizations or prophylactic interventions. Therefore, all laboratory personnel and particularly women of child-bearing age should be provided with information regarding immune competence and conditions that may predispose them to infection. Individuals having these conditions should be encouraged to self-identify to the institution's healthcare provider for appropriate counseling and guidance.

#### B. *Special Practices*

1. All persons entering the laboratory must be advised of the potential hazards and meet specific entry/exit requirements.
2. Laboratory personnel must be provided medical surveillance and offered appropriate immunizations for agents handled or potentially present in the laboratory.
3. Each institution should consider the need for collection and storage of serum samples from at-risk personnel.
4. A laboratory-specific biosafety manual must be prepared and adopted as policy. The biosafety manual must be available and accessible.
5. The laboratory supervisor must ensure that laboratory personnel demonstrate proficiency in standard and special microbiological practices before working with BSL-3 agents.
6. Potentially infectious materials must be placed in a durable, leak proof container during collection, handling, processing, storage, or transport within a facility.
7. Laboratory equipment should be routinely decontaminated, as well as, after spills, splashes, or other potential contamination.
  - a. Spills involving infectious materials must be contained, decontaminated, and cleaned up by staff properly trained and equipped to work with infectious material.
  - b. Equipment must be decontaminated before repair, maintenance, or removal from the laboratory.
8. Incidents that may result in exposure to infectious materials must be immediately evaluated and treated according to procedures described in the laboratory biosafety safety manual. All such incidents must be reported to the laboratory supervisor. Medical evaluation, surveillance, and treatment should be provided and appropriate records maintained.

9. Animals and plants not associated with the work being performed must not be permitted in the laboratory.

10. All procedures involving the manipulation of infectious materials must be conducted within a BSC, or other physical containment devices. No work with open vessels is conducted on the bench. When a procedure cannot be performed within a BSC, a combination of personal protective equipment and other containment devices, such as a centrifuge safety cup or sealed rotor, must be used.

#### C. *Safety Equipment (Primary Barriers and Personal Protective Equipment)*

1. All procedures involving the manipulation of infectious materials must be conducted within a BSC (preferably Class II or Class III), or other physical containment devices.

2. Protective laboratory clothing with a solid-front such as tie-back or wraparound gowns, scrub suits, or coveralls are worn by workers when in the laboratory. Protective clothing is not worn outside of the laboratory. Reusable clothing is decontaminated with appropriate disinfectant before being laundered. Clothing is changed when contaminated.

3. Eye and face protection (goggles, mask, face shield or other splatter guard) is used for anticipated splashes or sprays of infectious or other hazardous materials. Eye and face protection must be disposed of with other contaminated laboratory waste or decontaminated before reuse. Persons who wear contact lenses in laboratories must also wear eye protection.

4. Gloves must be worn to protect hands from exposure to hazardous materials. Glove selection should be based on an appropriate risk assessment. Alternatives to latex gloves should be available. Gloves must not be worn outside the laboratory. In addition, BSL-3 laboratory workers should:

a. Change gloves when contaminated, integrity has been compromised, or when otherwise necessary. Wear two pairs of gloves when appropriate.

b. Remove gloves and wash hands when work with hazardous materials has been completed and before leaving the laboratory.

c. Do not wash or reuse disposable gloves. Dispose of used gloves with other contaminated laboratory waste. Hand washing protocols must be rigorously followed.

5. Eye, face, and respiratory protection must be used in rooms containing infected animals.

#### D. *Laboratory Facilities (Secondary Barriers)*

1. Laboratory doors must be self closing and have locks in accordance with the institutional policies. The laboratory must be separated from areas that are open to unrestricted traffic flow within the building. Access to the laboratory is restricted to entry by a series of two self-closing doors. A clothing change room (anteroom) may be included in the passageway between the two self-closing doors.

2. Laboratories must have a sink for hand washing. The sink must be hands-free or automatically operated. It should be located near the exit door. If the laboratory is segregated into different laboratories, a sink must also be available for hand washing in each zone. Additional sinks may be required as determined by the risk assessment.

3. The laboratory must be designed so that it can be easily cleaned and decontaminated. Carpets and rugs are not permitted. Seams, floors, walls, and ceiling surfaces should be sealed. Spaces around doors and ventilation openings should be capable of being sealed to facilitate space decontamination.

a. Floors must be slip resistant, impervious to liquids, and resistant to chemicals. Consideration should be given to the installation of seamless, sealed, resilient or poured floors, with integral cove bases.

b. Walls should be constructed to produce a sealed smooth finish that can be easily cleaned and decontaminated.

c. Ceilings should be constructed, sealed, and finished in the same general manner as walls. Decontamination of the entire laboratory should be considered when there

- has been gross contamination of the space, significant changes in laboratory usage, for major renovations, or maintenance shut downs. Selection of the appropriate materials and methods used to decontaminate the laboratory must be based on the risk assessment of the biological agents in use.
4. Laboratory furniture must be capable of supporting anticipated loads and uses. Spaces between benches, cabinets, and equipment must be accessible for cleaning.
    - a. Bench tops must be impervious to water and resistant to heat, organic solvents, acids, alkalis, and other chemicals.
    - b. Chairs used in laboratory work must be covered with a non-porous material that can be easily cleaned and decontaminated with appropriate disinfectant.
  5. All windows in the laboratory must be sealed.
  6. BSCs must be installed so that fluctuations of the room air supply and exhaust do not interfere with proper operations. BSCs should be located away from doors, heavily traveled laboratory areas, and other possible airflow disruptions.
  7. Vacuum lines must be protected with HEPA filters, or their equivalent. Filters must be replaced as needed. Liquid disinfectant traps may be required.
  8. An eyewash station must be readily available in the laboratory.
  9. A ducted air ventilation system is required. This system must provide sustained directional airflow by drawing air into the laboratory from "clean" areas toward "potentially contaminated" areas. The laboratory shall be designed such that under failure conditions the airflow will not be reversed.
    - a. Laboratory personnel must be able to verify directional air flow. A visual monitoring device which confirms directional air flow must be provided at the laboratory entry. Audible alarms should be considered to notify personnel of air flow disruption.
    - b. The laboratory exhaust air must not re-circulate to any other area of the building.
    - c. The laboratory building exhaust air should be dispersed away from occupied areas and from building air intake locations or the exhaust air must be HEPA filtered.
  10. HEPA filtered exhaust air from a Class II BSC can be safely re-circulated into the laboratory environment if the cabinet is tested and certified at least annually and operated according to manufacturer's recommendations. BSCs can also be connected to the laboratory exhaust system by either a thimble (canopy) connection or a direct (hard) connection. Provisions to assure proper safety cabinet performance and air system operation must be verified. BSCs should be certified at least annually to assure correct performance. Class III BSCs must be directly (hard) connected up through the second exhaust HEPA filter of the cabinet. Supply air must be provided in such a manner that prevents positive pressurization of the cabinet.
  11. A method for decontaminating all laboratory wastes should be available in the facility, preferably within the laboratory (e.g., autoclave, chemical disinfection, incineration, or other validated decontamination method).
  12. Equipment that may produce infectious aerosols must be contained in devices that exhaust air through HEPA filtration or other equivalent technology before being discharged into the laboratory. These HEPA filters should be tested and/or replaced at least annually.
  13. Facility design consideration should be given to means of decontaminating large pieces of equipment before removal from the laboratory.
  14. Enhanced environmental and personal protection may be required by the agent summary statement, risk assessment, or applicable local, state, or federal regulations. These laboratory enhancements may include, for example, one or more of the following; an anteroom for clean storage of equipment and supplies with dress-in, shower-out capabilities; gas tight dampers to facilitate laboratory isolation; final HEPA filtration of the laboratory exhaust air; laboratory effluent decontamination; and advanced access control devices such as biometrics. HEPA filter housings should have gas-tight isolation

dampers; decontamination ports; and/or bag-in/bag-out (with appropriate decontamination procedures) capability. The HEPA filter housing should allow for leak testing of each filter and assembly. The filters and the housing should be certified at least annually.

15. The BSL-3 facility design, operational parameters, and procedures must be verified and documented prior to operation. Facilities must be re-verified and documented at least annually.

### **14.3 Occupational Safety and Health Standards - Toxic and Hazardous Substances**

Although safety hazards related to the physical characteristics of a chemical can be objectively defined in terms of testing requirements (e.g. flammability), health hazard definitions are less precise and more subjective. Health hazards may cause measurable changes in the body - such as decreased pulmonary function. These changes are generally indicated by the occurrence of signs and symptoms in the exposed employees - such as shortness of breath, a non-measurable, subjective feeling. Employees exposed to such hazards must be apprised of both the change in body function and the signs and symptoms that may occur to signal that change.

The determination of occupational health hazards is complicated by the fact that many of the effects or signs and symptoms occur commonly in non-occupationally exposed populations, so that effects of exposure are difficult to separate from normally occurring illnesses. Occasionally, a substance causes an effect that is rarely seen in the population at large, such as angiosarcomas caused by vinyl chloride exposure, thus making it easier to ascertain that the occupational exposure was the primary causative factor. More often, however, the effects are common, such as lung cancer. The situation is further complicated by the fact that most chemicals have not been adequately tested to determine their health hazard potential, and data do not exist to substantiate these effects.

There have been many attempts to categorize effects and to define them in various ways. Generally, the terms "acute" and "chronic" are used to delineate between effects on the basis of severity or duration. "Acute" effects usually occur rapidly as a result of short-term exposures, and are of short duration. "Chronic" effects generally occur as a result of long-term exposure, and are of long duration.

The acute effects referred to most frequently are those defined by the American National Standards Institute (ANSI) standard for Precautionary Labeling of Hazardous Industrial Chemicals (Z129.1-1988) - irritation, corrosivity, sensitization and lethal dose. Although these are important health effects, they do not adequately cover the considerable range of acute effects which may occur as a result of occupational exposure, such as, for example, narcosis.

Similarly, the term chronic effect is often used to cover only carcinogenicity, teratogenicity, and mutagenicity. These effects are obviously a concern in the workplace, but again, do not adequately cover the area of chronic effects, excluding, for example, blood dyscrasias (such as anemia), chronic bronchitis and liver atrophy.

The goal of defining precisely, in measurable terms, every possible health effect that may occur in the workplace as a result of chemical exposures cannot realistically be accomplished. This does not negate the need for employees to be informed of such effects and protected from them. Appendix B, which is also mandatory, outlines the principles and procedures of hazard assessment.

For purposes of this section, any chemicals which meet any of the following definitions, as determined by the criteria set forth in Appendix B are health hazards. However, this is not intended to be an exclusive categorization scheme. If there are available scientific data that involve other animal species or test methods, they must also be evaluated to determine the applicability of the HCS.

1. **"Carcinogen:"** A chemical is considered to be a carcinogen if:
  - (a) It has been evaluated by the International Agency for Research on Cancer (IARC), and found to be a carcinogen or potential carcinogen;  
or
  - (b) It is listed as a carcinogen or potential carcinogen in the Annual Report on Carcinogens published by the National Toxicology Program (NTP) (latest edition); or,
  - (c) It is regulated by DEHSA as a carcinogen.
  
2. **"Corrosive:"** A chemical that causes visible destruction of, or irreversible alterations in, living tissue by chemical action at the site of contact. For example, a chemical is considered to be corrosive if, when tested on the intact skin of albino rabbits by the method described by the U.S. Department of Transportation in appendix A to 49 CFR part 173, it destroys or changes irreversibly the structure of the tissue at the site of contact following an exposure period of four hours. This term shall not refer to action on inanimate surfaces.
  
3. **"Highly toxic:"** A chemical falling within any of the following categories:
  - (a) A chemical that has a median lethal dose (LD (50)) of 50 milligrams or less per kilogram of body weight when administered orally to albino rats weighing between 200 and 300 grams each.
  
  - (b) A chemical that has a median lethal dose (LD(50)) of 200 milligrams or less per kilogram of body weight when administered by continuous contact for 24 hours (or less if death occurs within 24 hours) with the bare skin of albino rabbits weighing between two and three kilograms each.
  
  - (c) A chemical that has a median lethal concentration (LC(50)) in air of 200 parts per million by volume or less of gas or vapor, or 2 milligrams per liter or less of mist, fume, or dust, when administered by continuous inhalation for one hour (or less if death occurs within one hour) to albino rats weighing between 200 and 300 grams each.
  
4. **"Irritant:"** A chemical, which is not corrosive, but which causes a reversible inflammatory effect on living tissue by chemical action at the site of contact. A chemical is a skin irritant if, when tested on the intact skin of albino rabbits by the methods of 16 CFR 1500.41 for four hours exposure or by other appropriate techniques, it results in an empirical score of five or more. A chemical is an eye irritant if so determined under the procedure listed in 16 CFR 1500.42 or other appropriate techniques.

5. **"Sensitizer:"** A chemical that causes a substantial proportion of exposed people or animals to develop an allergic reaction in normal tissue after repeated exposure to the chemical.

6. **"Toxic."** A chemical falling within any of the following categories:

- (a) A chemical that has a median lethal dose (LD(50)) of more than 50 milligrams per kilogram but not more than 500 milligrams per kilogram of body weight when administered orally to albino rats weighing between 200 and 300 grams each.
- (b) A chemical that has a median lethal dose (LD(50)) of more than 200 milligrams per kilogram but not more than 1,000 milligrams per kilogram of body weight when administered by continuous contact for 24 hours (or less if death occurs within 24 hours) with the bare skin of albino rabbits weighing between two and three kilograms each.
- (c) A chemical that has a median lethal concentration (LC(50)) in air of more than 200 parts per million but not more than 2,000 parts per million by volume of gas or vapor, or more than two milligrams per liter but not more than 20 milligrams per liter of mist, fume, or dust, when administered by continuous inhalation for one hour (or less if death occurs within one hour) to albino rats weighing between 200 and 300 grams each.

7. **"Target organ effects."**

The following is a target organ categorization of effects which may occur, including examples of signs and symptoms and chemicals which have been found to cause such effects. These examples are presented to illustrate the range and diversity of effects and hazards found in the workplace, and the broad scope employers must consider in this area, but are not intended to be all-inclusive.

- a. **Hepatotoxins:** Chemicals which produce liver damage  
Signs & Symptoms: Jaundice; liver enlargement  
Chemicals: Carbon tetrachloride; nitrosamines
- b. **Nephrotoxins:** Chemicals which produce kidney damage  
Signs & symptoms: Edema; proteinuria  
Chemicals: Halogenated hydrocarbons; uranium
- c. **Neurotoxins:** Chemicals which produce their primary toxic effects on the nervous system  
Signs & Symptoms: Narcosis; behavioral changes; decrease in motor functions  
Chemicals: Mercury; carbon disulfide
- d. **Agents which act on the blood or hemato-poietic system:** Decrease hemoglobin function; deprive the body tissues of oxygen  
Signs & Symptoms: Cyanosis; loss of consciousness  
Chemicals: Carbon monoxide; cyanides
- e. **Agents which damage the lung:** Chemicals which irritate or damage pulmonary tissue  
Signs & Symptoms: Cough; tightness in chest; shortness of breath

- Chemicals: Silica; asbestos
- f. **Reproductive toxins:** Chemicals which affect the reproductive capabilities including chromosomal damage (mutations) and effects on fetuses (teratogenesis)  
Signs & Symptoms: Birth defects; sterility  
Chemicals: Lead; DBCP
  - g. **Cutaneous hazards:** Chemicals which affect the dermal layer of the body  
Signs & Symptoms: Defatting of the skin; rashes; irritation  
Chemicals: Ketones; chlorinated compounds
  - h. **Eye hazards:** Chemicals which affect the eye or visual capacity  
Signs & Symptoms: Conjunctivitis; corneal damage  
Chemicals: Organic solvents; acids

#### 14.4 Handling Toxins

In recognition of the growing number of microbiological and biomedical laboratories working with toxins of biological origin, the following is provided as a guideline for working with these toxins.

The material below is adapted from the Biological Defense Safety Program, Technical Safety Requirements (DA Pamphlet 385-69)<sup>(1)</sup> and Appendix A of the United States Department of Labor Occupational Safety and Health Association rule "Occupational Exposure to Hazardous Chemicals in Laboratories"<sup>(2)</sup>.

Laboratory managers and facility safety officials should use the references listed below and to consult with the Department of Safety and Health before purchasing or using any toxin, to ensure that appropriate facilities, containment equipment, policies and procedures, personnel training programs and medical surveillance protocols specific to the toxin and the laboratory are in place.

##### **A. General**

The laboratory facilities, equipment, and procedures appropriate for work with toxins of biological origin must reflect the intrinsic level of hazard posed by a particular toxin as well as the potential risks inherent in the operations performed. If both toxins and infectious agents are used, both must be considered when containment equipment is selected and policies and procedures are written. If animals are used, animal safety practices must also be considered.

##### **B. Standard Practices**

Standard practices listed under BSL 2 and BSL 3 (pages 20 and 27) should be reviewed and incorporated as appropriate into protocols for work with toxins.

##### **C. Special Practices**

Special practices listed under BSL 2 and BSL 3 (see sections 13.1-13.3 above) should be reviewed and incorporated as appropriate into protocols for work with toxins.

- i. Each laboratory should develop a chemical hygiene plan specific to the toxin(s) used in that laboratory. The chemical hygiene plan should
  - 1) identify the hazards that will be encountered in normal use of the toxin, and those that could be encountered in case of a spill or other accident, and
  - 2) specify the policies and practices to be used to minimize risks (e.g., containment and personal protective equipment, management of spills, management of accidental exposures, medical surveillance).<sup>(3)</sup>

- ii. Training specific to the toxin(s) used should be required and documented for all laboratory personnel working with toxins, before starting work with the toxin and at intervals thereafter.
- iii. An inventory control system should be in place.
- iv. Toxins should be stored in locked storage rooms, cabinets, or freezers when not in use.
- v. Access to areas containing toxins should be restricted to those whose work assignments require access.
- vi. Preparation of primary containers of toxin stock solutions and manipulations of primary containers of dry forms of toxins should be conducted in a chemical fume hood, a glove box, or a biological safety cabinet or equivalent containment system approved by the safety officer. HEPA and/or charcoal filtration of the exhaust air may be required, depending on the toxin.
- vii. The user should verify inward airflow of the hood or biological safety cabinet before initiating work.
- viii. All work should be done within the operationally effective zone of the hood or biological safety cabinet.
- ix. When toxins are in use, the room should be posted to indicate "Toxins in Use Authorized Personnel Only." Any special entry requirements should be posted on the entrance(s) to the room. Only personnel whose presence is required should be permitted in the room while toxins are in use.
- x. All high risk operations should be conducted with two knowledgeable individuals present. Each must be familiar with the applicable procedures, maintain visual contact with the other, and be ready to assist in the event of an accident.
- xi. Before containers are removed from the hood, cabinet, or glove box, the exterior of the closed primary container should be decontaminated and placed in a clean secondary container. Toxins should be transported only in leak/spill-proof secondary containers.
- xii. Contaminated and potentially contaminated protective clothing and equipment should be decontaminated using methods known to be effective against the toxin before removal from the laboratory for disposal, cleaning or repair. If decontamination is not possible/practical, materials (e.g., used gloves) should be disposed of as toxic waste. Materials contaminated with infectious agents as well as toxins should also be autoclaved or otherwise rendered non-infectious before leaving the laboratory.
- xiii. The interior of the hood, glove box, or cabinet should be decontaminated periodically, for example, at the end of a series of related experiments. Until decontaminated, the hood, box, or cabinet should be posted to indicate that toxins are in use, and access to the equipment and apparatus restricted to necessary, authorized personnel.

#### ***D. Safety Equipment***

The safety equipment guidelines listed under BSL 2 and BSL 3 (see Section III) should be reviewed and incorporated as appropriate into protocols for work with toxins.

- i. When using an open-fronted fume hood or biological safety cabinet, protective clothing, including gloves and a disposable long-sleeved body covering (gown, laboratory coat, smock, coverall, or similar garment) should be worn so that hands and arms are completely covered.
- ii. Eye protection should be worn if an open-fronted containment system is used.
- iii. Other protective equipment may be required, depending on the characteristics of the toxin and the containment system. For example, use additional respiratory

- protection if aerosols may be generated and it is not possible to use containment equipment or other engineering controls.
- iv. When handling dry forms of toxins that are electrostatic:
    - a. Do not wear gloves (such as latex) that help to generate static electricity
    - b. Use glove bag within a hood or biological safety cabinet, a glove box, or a class biological safety cabinet.
  - v. When handling toxins that are percutaneous hazards (irritants, necrotic to tissue, or extremely toxic from dermal exposure), select gloves that are known to be impervious to the toxin.
  - vi. Consider both toxin and diluent when selecting gloves and other protective clothing.
  - vii. If infectious agents and toxins are used together in an experimental system, consider both when selecting protective clothing and equipment.

#### **E. Laboratory Facilities**

Laboratory facility recommendations listed under BSL 2 and BSL 3 (See Section III) and DEHSA standards<sup>(4)</sup> should be reviewed and incorporated as appropriate into protocols for work with toxins.

When vacuum lines are used with systems containing toxins, they should be protected with a HEPA filter to prevent entry of toxins into the lines. Sink drains should be similarly protected when water aspirators are used.

#### **F. References**

1. Department of the Army, DOD. 32 CFR Parts 626, 627 Biological Defense Safety Program.
2. United States Department of Labor, Occupational Safety and Health Administration. 29 CFR Part 1910 - Occupational Safety and Health Standards.
3. United States Department of Labor, Occupational Safety and Health Administration. 29 CFR Part 1910. (2)
4. United States Department Occupational Safety and Health Administration. 29 CFR Part 1910. (2)
5. American Industrial Hygiene Association - Biosafety Reference Manual. Heinsohn P.A.; Jacobs R.R.; Concoy B.A. (eds.). American Industrial Hygiene Association, Fairfax. 1995.
6. National Research Council. Prudent Practices in the Laboratory: Handling and Disposal of Chemicals. National Academy Press, Washington D.C. 1995.
7. CRC handbook of Toxicology. Derelanko M.J., Hollinger M.A. (eds.). CRC Press, Boca Raton 1995.
8. Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning. Ellenhorn M.J., Schonwald S., Ordog G., Wasserberger J., Williams and Wilkins, Baltimore 1997.

#### **G. Research Involving Genetic Elements, Recombinant Nucleic Acids and Recombinant Organisms**

The institution considers the requirement for handling genetic elements, recombinant nucleic acids and recombinant organisms as outlined in the "NIH Guidelines for Research Involving Recombinant DNA Molecules." The guidelines can be downloaded from the following website:

[http://oba.od.nih.gov/rdna/nih\\_guidelines\\_oba.html](http://oba.od.nih.gov/rdna/nih_guidelines_oba.html). They are also available in Appendix A.

These guidelines include among other things, provisions regarding security assessments, physical containments, and local review.

## **15. SECURITY**

The provisions of § 73.11 require the institution to subject to the provisions of the part 73 regulations to develop and implement a security plan establishing policy and procedures that ensure the security of areas containing select agents and toxins. The provisions of § 73.11 are designed to meet these objectives and the Act's mandate to establish security requirements for the purpose of protecting the public health and safety (42 U.S.C.262a (e)). The security of areas containing select agents and toxins is provided below.

### **15.1 Physical Security Systems**

This section has set forth policies to:

- i. Establish appropriate levels of protection against unauthorized access, theft, diversion, or loss of custody of BSL-2/3 pathogens and other select agents;
- ii. loss or theft of information related to BSL-2/3 pathogens and other acts that may cause unacceptable adverse impacts on national security or on the health and safety of USDA employees, the public, or the environment;
- iii. Provide levels of protection in a graded manner in accordance with the potential consequences and
- iv. Implement effective planning of graded protection levels and prudent application of resources.

BSL-2/3 pathogens are ubiquitous, existing both in nature and in laboratories around the world. However, it is prudent to limit access to BSL-2/3 pathogens and information related to BSL-2/3 pathogens to authorized individuals, and to deter and detect unauthorized access.

#### **a. Risk Assessment.**

The physical security system has been designed according to a site-specific risk assessment, which will evaluate targets, adversary capabilities, consequences, and vulnerabilities. The risk assessment was developed by Drexel University's Executive Director of Public Safety who has the expertise in physical security. The objectives and performance of the physical security system shall be reviewed regularly, but no less than every 5 years, by qualified individuals who have expertise in physical and biological security.

#### **b. Site-Specific Considerations.**

The physical security systems has been tailored to address site-specific characteristics and requirements, ongoing programs, and operational needs, and to achieve acceptable protection levels using current technology in a cost-effective manner. The protection strategy has been tailored to address varying circumstances and may range from prevention to pursuit. Any questions regarding the Bio-Safety Level-3 (BSL-2/3) Access Control Procedure must be directed to the lab manager.

The Security system for the Bio-Safety Level-3 (BSL-2/3) will consist of a card reader located on the main entrance to the lab, two cameras viewed remotely, one focus on the lab entrance, and second internal camera focused on the doorway, two duress alarms are strategically located in the lab, and the locking mechanism to the main door will consist of an electronic strike.

#### **c. Graded Protection.**

Physical security systems provide graded protection in accordance with the importance of the asset. That is, the University intends that the highest level of protection be given to security interests whose loss, theft, compromise, and/or unauthorized use will seriously affect the national security, and/or the health and

safety of our personnel, the public, the environment and the University's research programs. Therefore, protection of BSL-2/3 pathogens and other select agents will be given the highest level of protection. Protection of other interests will have lower levels of protection.

It should be recognized that risks must be accepted (i.e., that actions cannot be taken to reduce the probability or consequences of all malevolent events to zero); however, an acceptable level of risk should be determined based on evaluation of a variety of facility-specific goals and considerations. Protection-related plans shall describe, justify, and document the graded protection provided to BSL-2/3 pathogens and information related to BSL-2/3 pathogens. The Principal Investigator is responsible for ensuring that these plans are reviewed and updated annually. The Principal Investigators will be trained to perform this function.

The nature of the threat, the vulnerability of the asset, and the potential consequences of an adversarial act shall be considered in determining the appropriate level of protection against risk. Accordingly, physical security systems shall provide graded protection in accordance with the importance of the asset.

Consequently, facilities shall consolidate BSL-2/3 pathogens and select agents, concentrate intrusion detection and assessment systems at the remaining locations where the BSL-2/3 pathogens are kept, and control access to these locations. To maintain the continuity of operation, the protection strategy shall be to mitigate the severity of the event through response and recovery option planning.

**d. Security and Restricted Access Areas.**

Unescorted access shall be limited to authorized individuals. Any unauthorized individual will be escorted at all times by an authorized individual. All unauthorized individuals will read and sign a Visitor's Training Form before entering the labs (see appendix for a copy of the Visitor's Training Form). The PI shall establish appropriate escort-to-visitor ratios.

Unauthorized lab guests, such as visiting scientists, rotating graduate students, other Drexel Med employees or staff, housekeeping or maintenance personnel, and others must be approved by the PI or laboratory director and must follow all laboratory rules and regulations, and must be accompanied at ***all times*** by an authorized user. As they enter the labs all guests will don fully buttoned disposable lab coats with elastic cuffs, gloves and booties. Before they enter the labs, guests will read and sign a Visitor Training Form (see Appendix). The local authorized host will review the Visitor Training Form with all visitors, assure the form is signed and copied, and assure the visitor retains a copy for his/her records. When prudent and appropriate, guests will don hair nets, booties and N95 masks, as instructed by the authorized host. Personnel, especially maintenance or repair personnel, must bring in to the lab only the minimum number of tools, ladders, etc to perform the job. Coats, jackets, brief cases, computers, etc that won't be used for the job, cannot be brought into the lab. Once inside the labs, all tools will be placed on disposable lab mats or unopened (flat) trash bags so that at no time will tools, ladders, etc, touch the lab floor, lab benches, or other lab surfaces.

Controls shall be established to detect, assess, and deter unauthorized access to security areas. Access control requirements may be layered as appropriate for the situation. At succeeding boundaries, access controls may be increased. Means shall be provided to deter and detect unauthorized intrusion into limited and exclusion areas as defined below. Means include: use of intrusion detection sensors and alarm systems, random patrols, and/or visual observation. The protection program shall include suitable means to assess alarms.

- i. **Procedure:** The purpose of the Access Control Procedure is to provide a guideline for controlling access to laboratories containing select agents. Any questions regarding the Access Control Procedure must be directed to the Principal Investigator.
- ii. **Access:** Only authorized individuals, approved by Office of Research (Office of Research) and/or Office of Research Designee, are permitted access to the designated Bio-safety Laboratories. Individuals entering the laboratories must use their assigned ID card to gain access to the laboratories. Under no circumstance is anyone permitted to use an ID card other than the one assigned. Lost ID card must immediately be report to the Lab Manager, the RO and the ARO and the Department of Public Safety. Once entrance to the laboratory has been gained the individual is responsible for signing the Access Control Log noting date and time of the entry. Any problems must immediately be reported to the RO (via email), facility security personnel (by phone or in person), and the Principal Investigator (in person, if possible, or cell phone and email).
- iii. **Egress:** When exiting the laboratory individuals must log out in the Access Control Log. If no one is in the laboratory, check that the doors are locked. Any problems must immediately be reported to the RO and ARO (via email), Principal Investigator and the facility security personnel.
- iv. **Guest:** All select agents must be secured before any guest is allowed to enter a laboratory containing such material. When entering the facility guests are required to adhere to the access control procedures established for the main facility. The Public Safety Officer will contact the host employee and inform them of the guest's arrival. The host employee must escort the guest to the laboratory and remain with the quest at all times. When entering the laboratory, the guest is responsible for signing the Access Control Log noting date and time of the entry. In addition, the host staff member will train the guest/visitor on proper protocol while in the laboratory. The guest will read and sign the Visitor Training Form. A copy of the signed form will be given to the visitor. When exiting the laboratory guest must log out in the Access Control Log. The host employee is responsible for escorting the guest back to the Lobby and signs the guest out. Any problems must immediately be reported to the RO and ARO (via email), Principal Investigator and facility security personnel.

**e. Access Control and Entry/Exit Inspections.**

Access control points shall be designed to provide positive control over pedestrian traffic. The access control points shall provide a barrier to personnel entering limited areas and exclusion areas until such time as entry is requested and/or authorized.

Automated access control systems shall read data entered by the person requesting access, and if the data are successfully validated, the portal shall be

electrically unlocked. All individuals will wear a university photo identification badge.

The access authorization list shall be updated when an individual's access authorization has changed or when an individual is transferred or reassigned. Badge readers shall be equipped with anti-pass back protection.

Door locks opened by badge readers shall be designed to relock immediately after the door has closed to deter another person from opening the door without following procedures.

The system shall record all transactions--authorized access (for tracking purposes) and attempted unauthorized access.

If in use, keypad devices shall have a visual shielding device mounted so that an unauthorized person in the immediate vicinity cannot observe the numbers entered.

## **15.2 Personnel Security Level (PSL).**

Designation assigned to positions that are located at BSL-2/3 facilities and/or facilities using or storing select agents/toxins. The designations are commensurate with low, moderate, and high-risk levels of public trust and have similar investigative requirements.

**PSL-1:** Personnel assigned to positions within a BSL-2/3 facility/center/complex, but whose duties do not involve access to BSL-2/3 pathogens or select agents shall, at a minimum, be determined to encumber low risk public trust positions.

**PSL-2:** Personnel assigned to positions that have access to or work with BSL-2/3 facilities or that have access to or work with BSL-2/3 pathogens or select agents shall, at a minimum, be determined to encumber moderate risk public trust positions.

**PSL-3:** Personnel who are assigned to leadership/supervisory positions and who plan, report, and control research and access to BSL-2/3 facilities and/or BSL-2/3 pathogens or select agents shall be determined to encumber high risk public trust positions.

**Responsibilities:** All University personnel working at BSL-2/3 facilities or facilities using/storing select agents are responsible for security of University assets. The University Department of Public Safety is responsible for implementing and managing biosecurity programs with direct oversight assigned to researchers and diagnosticians. The biosecurity program will outline individual responsibility to deter, detect, and respond to any security threat to ensure that pathogens are not removed illegally from the bio-containment facilities. All security threats and breaches must be reported immediately to the RO, ARO, Director of Security and the laboratory manager. The following agency positions have responsibility for ensuring biosecurity procedures and policies are implemented: Researchers must ensure that all pathogens and toxins (select agents) used in their laboratories are entered in the DSH's database and that repository records are current and reflect the materials on hand.

## **15.3 Cybersecurity systems**

### **a. Overview**

Drexel University (DU) and Drexel University College of Medicine (DUCoM) operate research facilities that may work with agents held at Biosafety Level 2 and 3 (BSL-2/3). Any breach in the security of the computing systems or networks in such facility could disrupt the University and/or allow such confidential information to be transmitted quickly, silently and without geographic or constituency limits.

Recognizing these vulnerabilities and the need for institutions to limit access to such information, the Federal Government has passed numerous laws concerning personal information. Failure to comply with legislation can have significant adverse consequences on the University, its academic program, research funding and reputation.

### **b. Statement of Purpose**

In order to ensure the continued availability, confidentiality, and integrity of University research information, to protect critical networks and systems, and to comply with federal law, the Office of Information Resources & Technology ("IRT") and DUCoM-IT has established a number of policies and practices, including the BSL-2/3 Information Systems and Security Plan ("Plan"). The goal of the Plan is to assure ongoing compliance with federal

statutes and regulations related to the Plan and to position the University for likely future privacy and security regulations.

The Plan outlines requirements for all BSL-2/3 facilities and the individuals who work in them. Accordingly, all handheld, laptop and desktop computers, servers, and other computing systems operated by or for the University in such a facility are governed by this policy.

Each person who accesses such facilities or uses or manages a computer by or for the University in such a facility must abide by the Plan. All levels of management must ensure that, for their areas of responsibility, each individual knows his responsibilities as outlined in the Plan.

The College of Medicine operates a private network, connected to the public internet. It is protected using a layered methodology. The layers are as follows: Perimeter, Network, Host, Application and Data. The ultimate goal of the layered approach is to protect data. There are five core methodologies implemented: authentication, traffic shaping, encryption, application management and analysis. Please refer to "Security Technologies Deployed" graphic for detailed information.

At the perimeter is located Cisco based firewalls with 3Com Tippingpoint as an intrusion protection system. Two weeks of activity is logged for both diagnostic and forensic purposes. Remote access is controlled via IPSec VPN and authenticated against Microsoft Windows Active Directory. Password complexity is in place.

At the host layer, patch management is in place, anti-virus has been deployed to the enterprise and authentication is tied to Microsoft Windows Active Directory. Group policies enforce screen locks with password to unlock screens. Desktop firewalls are also managed by group policies.

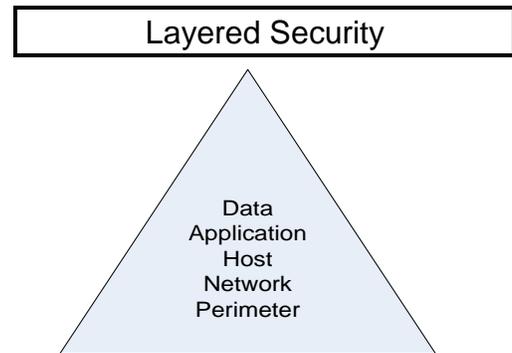
IT services are provided by a centralized IT Department know as Drexel University College of Medicine IT (DUCoM-IT). Centralized managed servers are backed up and housed in an enterprise class data center.

There are wireless networks providing access to the internal and public networks. Internal access is encrypted and authenticated against Microsoft Windows Active Directory. Guest access is encrypted and only permits access to public (Internet) destinations and printers. Systems activity is logged via Kiwi syslog server and Windows system logs. Network activity is managed with Netflows.

## Drexel University College of Medicine CoM IT

Security Technologies Deployed				
	Technology	Manufacturer	Description	Protection Provided
1	PIX	Cisco	Perimeter firewall	Private network isolated from Internet
2	VPN	Cisco	Secure remote access to private network	Remote users and business partners
3	TippingPoint	3COM	IPS (intrusion prevention)	Actively blocks known network attacks from Internet
4	Wireless (802.11)	Cisco	Encrypted and authenticated wireless	Wireless network traffic
5	MXLogic	MXLogic	SPAM/eMail AV scanning service	Exchange mailboxes
6	Backup for Workgroups	Lockstep	System/Data backup	Devices with backup client installed
7	Antivirus	Symantec	Scans files for virus/malware	Desktops and Servers
9	WSUS (system update service)	Microsoft	Centralized/Automatic patch distribution	Desktops and Servers
10	Group Policies	Microsoft	Centralized system setting management	Desktops and Servers
11	Desktop Firewall	Microsoft	Centralized client based firewall	Desktops
12	MRTG	MRTG	Traffic analysis	Private network
13	Syslog	Kiwi	Traffic analysis	Private network
14	Netflow	Cisco	Traffic analysis	Private network

Security Methodology
Authentication, 2, 4, 5, 9, 10
Traffic shaping 1, 2, 3, 4, 5
Encryption 2, 4
Application management 9, 10, 11
Analysis 12, 13, 14



#### **15.4 Personnel Suitability**

**Purpose:** This section sets policy on suitability requirements for University and non-University personnel requiring access to BSL-2/3 facilities OR LABORATORIES WHERE SELECT AGENTS ARE USED.

**Background Investigations.** All individuals who are employees of the institution will have gone thru DOJ background checks. There will be pre-employment records check requiring documentation when necessary. Non-University Personnel such as personnel from other universities, cooperators, contractors, students, visiting scientists, laboratory visitors, seminar attendees, etc. will be escorted all times by staff members who have a completed background investigation and appropriate facility authorization.

#### **15.5 Biosecurity Incident Response Plan**

**Purpose:** A policy for responses to specific types of incidents in order to protect personnel and secure pathogen holdings.

**The biosecurity plan includes responses to the following types of incident:**

- i. Bio-containment breach
- ii Bio-containment security breach
- iii. Inventory violation
- v. Non-biological incident such as violence
- vi Cybersecurity breach

**The plan addresses the following issues:**

- i. Personnel safety and health
- ii. Containment
- iii. Inventory control
- iv. Notification of managers and responders

Each Principal investigator shall immediately submit a biosecurity incident response plan to the RO, DSH and CDC/USDA in accordance with Federal Regulations.

#### **16. EMERGENCY RESPONSE PLAN**

The select agent use in this institution is approved for a single laboratory and use of a single select agent. Additional investigators, laboratories and use of select agents may be added to the existing registration, but require approval from the HHS secretary. All applications to the HHS Secretary to amend the registration must be reviewed, approved and submitted by the RO through the Office of Research Compliance. The provisions of § 73.12 state that entities required to register under the part 73 regulations must develop and implement an emergency response plan for the possession and use of each of the select agents. The requirements for the plan are designed to ensure that all investigators and laboratories to plan ahead to ready to take appropriate action to deal with any hazard that could arise. Thus the institution has prepared an Anthrax Emergency Plan (see Appendix B) making sure that the other Federal, State, or local emergency response planning laws as well as Drexel University's DEHS's Hazardous Waste Operations and Hazardous Material Emergency Response Plans) are included under this plan. The Anthrax Emergency Response Plan is largely geared towards the protection of human health and the environment incase of accidental release, exposure, medical emergency or fire. Other areas of concern such as severe weather emergencies, natural disasters, workplace violence, bomb threats, suspicious package reports, power failures, gas leaks and fires or explosion, etc. are also referenced in the Drexel University's Emergency Preparedness Plan that was developed by the Drexel University Department of Public Safety. An overview of the plan, including a listing of its contents, can be found at the following link:

## **17. TRAINING**

The institution is required to provide information and training on safety and security for working with select agents or toxins on a timely basis to each individual approved for access under § 73.8 and each unapproved individual working in, or visiting, areas where select agents and toxins are handled or stored. This is to ensure that individuals understand the hazards and how to deal with them. Details of the training program are provided in Appendix C. The program also requires that individual records are kept for those who have been trained and periodic updates are made to the training program and to update and inform those approved to work or visiting areas where select agents are used. The Center for Disease Control (CDC) has also posted a training program. This program can be accessed through the website <http://www.cdc.gov/od/sap/training.htm>. The CDC program is for educational purposes only. Individuals within the institution are required to complete the Institution's training program. When training is completed, individuals will receive a certificate to document that they have received the appropriate training for the possession and handling of select agents and toxins.

## **18. TRANSFER OF SELECT AGENTS**

The transfer provisions in § 73.14, state that a select agent or toxin may not be transferred from one entity to another entity within the United States (regardless of whether the transfer is interstate or intrastate), or received by an entity in the United States from an entity outside the United States, unless the transfer meets specified requirements. The transfer provisions are designed to ensure that select agents and toxins are shipped only to recipients that have authority to use or possess them. Also, the transfer provisions are designed to ensure that HHS and the participants monitor the shipments and that any problems are quickly reported to HHS so that any required action could be taken.

The transfer of a select agent or toxin requires filing of a specific form with the CDC or APHIS. HHS and the participants (institution and investigators) must monitor the shipments and any problems with the shipment, transfer or receipt must be quickly reported to the CDC/APHIS through the respective ROs.

The purpose of this form is to provide a method for the documentation of the transfer of a select agent or toxin. The form must be completed by the ROs of the transferring and receiving institution for each transfer of select agents. Investigators are not authorized to submit these forms to the CDC/APHIS. The process for transferring select agents or toxins is as follows:

**Prior to transferring a select agent**, the recipient's RO fills out blocks 1 and 2 of the form and submits it to the sender. The sender's RO fills out block 3 and transmits the form via facsimile to CDC (FAX: 404-498-2265) or APHIS (for animal agents and toxins send FAX to 301-734-3652; for plant agents and toxins send FAX to 301-734-8700), as appropriate. CDC or APHIS will then FAX the form back to the sender with an approval confirmation number after verification of the information on the form. If the sender has a suspicion that the agent may not be used for the requested purpose, or there are any other concerns, then the sender should consult with CDC or APHIS prior to the transfer. **Please contact the Office of Research Compliance at 215-255-7857 if you are planning to transfer or receiving select agents or toxins. Please plan your studies in such a way to allow the approval process to be completed before select agents or toxins are received.**

The process for transfer of the agent is as follows:

**(a) Shipment of the select biological agent or toxin to the recipient.** If you are the sender, you should ship the material to the receiver only after the institution and you have received a verification number from CDC or APHIS regarding the information in blocks 1 and 2 of the form. As the sender, you will complete Block 4, including the date the agent was shipped. Characterization of agent should include data such as strain designation, GenBank Accession number, publication citation with additional molecular characterization data, etc.; provide additional information on attached sheet, if needed. Select biological agents and toxins must be packaged, labeled, and shipped in accordance with all federal regulations (e.g., 42 CFR 72, 49 CFR 100-180, 9 CFR 121, and 7 CFR 331) and international (IATA) regulations. Please contact the Office of Safety and Health for assistance regarding packaging and shipping select agents and toxins. Utilize a method for tracking the movement of the select biological agents and toxins being shipped. Return receipt is required by law for some select biological agents and toxins listed in 42 CFR 72.3(f) and 9 CFR 121.

**(b) Transmittal of the form to the CDC or APHIS.** The RO from the recipient's entity must fill out Block 4 of the form with the date received and FAX or mail the form to both the Sender's RO and the CDC or APHIS within 2 business days of receipt.

**(c) Destruction or depletion of a select agent.** The RO of the recipient's entity should complete the appropriate boxes of Block 4 within 5 business days when the select agent is to be depleted or destroyed. A copy of the form must be mailed or faxed to the CDC or APHIS.

Records must be kept in the laboratory for all transfers and receipt of shipments and any problems that may have occurred during shipment and how those problems were resolved.

## **19. RECORDS**

### **19.1 Inventory Control Procedures**

The purpose of this section is to set policy on the handling, storage, shipping, disposal, record keeping, and monitoring of all biological agents. The intent of this section is also to ensure proper chain of custody procedures is utilized.

**1. Accountability Records.** Three types of accountability records are required: (a) a summary; b) a detailed inventory of repository materials to be kept at the research or diagnostic facility; and (c) materials accountability for experimental or working samples. Records in the first two systems must be maintained electronically and backed up on a separate system. The objective of maintaining such records is to ensure that the agency knows which pathogens or other select agents are present, or have been present in its facilities, to ensure the accountability of scientists for the pathogens they store and use, and to know the final disposition of pathogens, including destruction or shipping to another facility. The database will enable the DESH to rapidly identify the facilities at which particular agents are in use. The format for each is described below:

(a) The DESH will maintain a summary inventory database, consisting of the limited fields listed below, to provide management with the capability to rapidly determine pathogens in use at each facility.

Inventory records must include:

1. Agent name
2. Agency/Location/Laboratory
3. Person responsible for pathogenic material (laboratory supervisor)

#### 4. Contact information

**2. Facility Inventory of Repository Materials.** The DSH shall maintain a current detailed inventory as outlined below. The information shall be maintained in a standard database format. The database will not only serve as a record of current inventory but will also serve as a historical record of pathogens use at the facility. Placing records no longer in use in an inactive file rather than deleting them will accomplish this. Inactive records will be kept for at least 5 years.

Information to be included in the database is as follows:

1. Agent (scientific and common name and strain where applicable);
2. Amount (number of vials or contains inventoried);
3. Biosafety Level, Agent Type (bacteria, virus, etc.);
4. Storage location (building, room number, freezer number);
5. Storage conditions (refrigerator, freezer, -70°C, -20°C, liquid N<sub>2</sub>, etc.);
6. Date of change of status, i.e., removal, change of custody, etc.;
7. Site of usage (pinpoint to discrete locations such as building numbers and possibly room numbers);
8. Disposition including shipping when removed from inventory, including method of destruction, when applicable and
9. Scientist with contact information (telephone number and address of researcher or diagnostician).

Any working cultures that become new repository stocks must be added to the inventory. New pathogens (not already in inventory) identified in diagnostic or experimental samples or generated through recombinant technologies must be added to the repository and inventory database.

#### **3. Material Accountability of Experimental or Working Samples.**

Experimental samples and repository stock aliquots used for working stocks or experimental purposes are tracked by laboratory records (laboratory notebooks, electronic systems, etc.). The location of material use must be included. At the conclusion of each experiment, the disposition of the infectious material, including the means of disposal, must be verified by the signature of the researcher or diagnostician, or their designee.

#### **1. Packaging and Shipping of Infectious Material.**

Packing and shipping of pathogens will meet current national and international regulations and guidelines. Shipping and receiving of pathogens will meet applicable guidelines and will be tracked. Shipping and receiving of select agents requires permission from CDC. Researchers at Drexel University employ a small number of agents designated by the CDC as select agents. Shipping and tracking of these agents will be done in accordance with CDC regulations found in 42 CFR Part 72.

The DOC (Department of Commerce) regulations, including requirements for export permits, must be met for the export of pathogenic materials. The Biosafety Officer will review shipping records in the database on at least an annual basis to ensure compliance.

## **2. Physical Review of Accountability Records.**

Scientists working with pathogens are responsible for the accuracy of electronic databases and laboratory notebook records, which are subject to review by the Principal Investigator or his/her designee. Physical review will be at least annually. Methods used during physical review or reconciliation may include counts of entire inventory and repository materials. The Principal Investigator is responsible for ensuring the physical reviews are accomplished. Random reviews shall be conducted on an annual basis by the agency Biosafety Officer to ensure compliance at the locations.

## **3. Pathogen and Select Agents Security.**

All pathogens and select agents shall be stored in secure freezers or other secure cabinets within the facility. BSL-2/3 pathogens must be secured within the high containment facility. Only personnel with the appropriate PSL will have access to freezer keys and codes. The biosafety level risk group or biosafety category of the storage unit will be determined by the highest risk pathogen within the storage unit.

## **4. Sample Labeling.**

All sample vials in the inventory shall be labeled in a permanent manner so that all information is readable.

## **5. Inactivation and Disposal of Pathogens.**

Procedures must be in place at each location for this purpose and must include, as appropriate, autoclaving, other thermal inactivation technology, chemical treatment, or an equally effective comparable process. All pathogens and contaminated supplies will be treated.

## **6. Internal Transfer:**

Internal transfer of select agents also utilize the same rules as transferring select agents to an external site. The receiving investigator must be approved by the CDC/APHIS, has passed the security checks and completed all necessary training enumerated in this manual.

## **20. INSPECTIONS AND AUDITS**

The University and the HHS Secretary (CDC/APHIS) reserves the rights to, without prior notification and with or without cause, to inspect any site any laboratory at which activities regulated by part 73 are conducted and inspect and copy records relating to the activities covered by this part.

## **21. NOTICE OF THEFT OR LOSS**

Good inventory control is key to discovering inadvertent loss or theft of select agents. They must be reported immediately to the RO, ARO, Laboratory Manager and Department of Security as soon as the problem is discovered so that timely responses can be made.