University of South Alabama

Biosafety Manual

And

Exposure Control Plan

Revised: March 2017

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INTRODUCTION

INTRODUCTION TO UNIVERSITY OF SOUTH ALABAMA

COLLEGE OF MEDICINE BIOSAFETY PROGRAM

The University of South Alabama College of Medicine (USACOM) is dedicated to maintaining a high quality safety program to protect workers who are performing potentially biohazardous tasks at several sites of operation. The safe handling and proper containment of infectious materials is an essential component of the overall safety program for all research sites. The safe handling of potentially infectious agents and materials is termed Biological Safety or Biosafety.

The University of South Alabama College of Medicine desires that their Biological Safety Program be consistently applied across all work sites. Workers handling similar biohazards must receive uniform biological safety training and guidance. All workers who are at risk of exposure to potentially infectious or biohazardous materials must have ready access to a common Biological Safety Manual and Exposure Control Plan to inform them and prevent or limit accidental exposures to biohazardous materials.

Biological safety regulatory requirements are guided by all applicable Federal, State, and Local laws. Alabama is a member of the “Safe State” alliance in complying with OSHA Standards. This means that the State of Alabama has agreed to comply with OSHA standards or exceed them and in return will be responsible for self-monitoring its agencies and institutions for compliance. For our purposes in managing biological safety in this College, we will follow the OSHA Standards, CDC, NIH, and DOT guidelines specifically.

OSHA/Safe State requires that employees at risk for exposure to biohazardous materials, particularly to human blood, body fluids and tissues, be provided with a well-conceived employer's *Exposure Control Plan* [ECP] which adequately covers the biohazards intrinsic in the work. The ECP has been developed by Office of Research Compliance and Assurance to prevent accidental exposure of workers to human biohazardous materials. Compliance with this ECP has the added benefit of protecting against a broad spectrum of human and animal pathogens. Guidance on the handling of biohazardous material is given in the form of a code of practice entitled "Biosafety in Microbiological and Biomedical Laboratories" (5th Edition) produced by the Centers for Disease Control (CDC) and National Institutes of Health (NIH), in addition to various Federal Standards such as the OSHA Bloodborne Pathogens Standard (29 CFR 1910.1030) and the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules* (revised 2013). The University of South Alabama has pledged to comply with CDC, NIH, and Recombinant DNA guidelines to be eligible to receive funds from the NIH and other federal sources.

This document has been compiled to provide a single source of biosafety information for the employee, student, principal scientist/supervisor, and department chairperson who are planning to initiate research activities with potentially biohazardous materials. According to the NIH, biohazardous materials include certain types of recombinant DNA; organisms and viruses infectious to humans, animals or plants (e.g. parasites, viruses, bacteria, fungi, prions, rickettsia); and biologically active agents (i.e. toxins, allergens, venoms) that may cause disease in other living organisms or cause significant impact to the environment or community. Information is also supplied to help the supervisor or principal investigator prepare a registration document for approval to conduct this work, to contain the work, and to ensure that staff are protected from work-related risks to health.

SCOPE OF THIS DOCUMENT

This Biosafety Manual applies to all RESEARCH laboratories that handle infectious microbes categorized as biohazards by CDC/NIH or to biological materials that may contain such materials. It also describes COM procedures to protect staff from risks to health from human and non-human primate bloodborne pathogens and any body fluids or products. These biohazards require special precautions. Individual work sites may have more detailed Standard Operating Procedures (SOPs) that govern specific details of management of those biohazards. These SOPs as well as general biosafety guidelines described in this manual should be followed for those operations. Each University Hospital and clinic facility where patients are treated has its own separate biosafety requirements and procedures and internally managed biosafety programs

POLICY STATEMENT

I. Purpose

It is the University of South Alabama's policy to establish the process for compliance with the following documents:

NIH Guidelines for Research Involving Recombinant and Synthetic Nucleic Acid Molecules (NIH Guidelines

Biosafety in Microbiological and Biomedical Laboratories (BMBL, 5th edition)

II. Policy

The University of South Alabama is committed to protecting the safety and welfare of its faculty, staff and students, and to protect the environment and community. It is recognized that use of potentially pathogenic microorganisms and organisms containing recombinant DNA (rDNA) is necessary in many academic research and teaching laboratories. To ensure the safe handling of these organisms, the University requires compliance with the *NIH Guidelines* and with the recommendations in the *BMBL*. Compliance with other applicable federal, state, and local regulations is also required.

III. Responsibilities

The Principal Investigator (PI) is accountable for the safe operation of the laboratory. His/her experience and judgment are critical in conducting risk assessments and complying with this manual. Ultimately, safety is a shared responsibility amongst all laboratory staff. Many resources are available to assist the PI with these responsibilities, including the Office of Research Compliance and Assurance (ORCA), the Institutional Biosafety Committee (IBC), and Safety and Environmental Compliance.

OCRA shall:

- Prepare the Biosafety Manual and Exposure Control Plan, with revisions as necessary;
- Review and report to the IBC accidents involving infectious agents;
- Oversee the biological waste program;
- Provide or coordinate biosafety training as requested;
- Monitor and track required biosafety training, and;
- Administer all components of the Biosafety Program, assist with the submission of registrations to the IBC, and maintain registration files.

PIs shall:

- Assess the risks of experimental procedures;
- Ensure the safe operation of their laboratory;
- Train laboratory personnel in safe work practices;
- Comply with all applicable state and federal regulations and guidelines;
- Register the following experiments with the IBC, as required:

  (1) recombinant and synthetic nucleic acid activities;
  (2) work with infectious agents or select agents/toxins;
  (3) experiments involving the use of human blood or other potentially infectious materials, such as unfixed human tissues, human cell lines, and certain body fluids; and animal and plant pathogens.

IBC shall:

- Review recombinant and synthetic nucleic acid research conducted at or sponsored by the University for compliance with the *NIH Guidelines,* and approve those research projects that are found to conform with the *NIH Guidelines* and carries out the functions detailed in Section IV-B-2-b;
- Review research involving potentially infectious agents conducted at or sponsored by the University for compliance with the guidelines in *Biosafety in Microbiological and Biomedical Laboratories (BMBL)*, and approve those research projects that are found to conform with the recommendations in *BMBL*;
- Notify the PI of the IBC's review and approval;
- Report any significant problems with or violations of the *NIH Guidelines* and any significant research-related accidents or illness to the appropriate Institutional official and to the NIH Office of Biotechnology Activities (OBA) within 30 days;
- Follow the guidelines for membership defined by NIH, OBA; and
- Have the authority to implement operational changes and to limit or suspend research that is not in compliance with the USA Biosafety Program.

Biological Safety Officer (BSO) shall:

- Assist the Office of Research Compliance and Assurance in monitoring compliance with Federal, State and University biosafety policies and procedures, including inspections/audits to ensure that laboratory standards are rigorously followed;
- Reporting to the IBC and the institution any significant problems, violations of the *NIH Guidelines*, local or federal laws, or other USA institutional policies, and any significant research-related accidents or illnesses of which the BSO becomes aware;
- Provide advice on laboratory safety and security;
- Assist in the conduct of educational training for biological hazards and policy development/guidelines, as needed;

USA Urgent Health Care Clinic shall:

- Provide medical evaluation; and
- Provide vaccinations, as required.

Research laboratory personnel shall:

- Comply with safety recommendations for approved work being performed; and
- Report accidents or injuries to the PI.

INSTITUTIONAL BIOSAFETY COMMITTEE

The Institutional Biosafety Committee (IBC) meets as required by NIH to discuss and categorize biohazardous work and to formally register such work. The existence of this committee is required as part of compliance with major sections of the NIH Guidelines for Research Involving Recombinant DNA Molecules. This committee is important for carrying out a successful and effective biosafety program. The committee is responsible for inventory, review and approval of biological hazards and safety practices for work involving use of microbial agents, or tissues, body fluids, or wastes that may be contaminated with such microbes that represent a potential danger to personnel, products or the environment. *All potentially biohazardous materials to be used by employees must be registered with and approved for use by the IBC.*

Composition of the Institutional Biosafety Committee shall consist of:

1. Several members with backgrounds in scientific disciplines who are familiar with biohazards, biosafety practices and/or recombinant DNA research;
2. A member of Environmental Safety;
3. Representation from the Office of Research Compliance and Assurance;
4. A member with the D.V.M degree, preferably with management responsibility for animal research activities including non-human primate work;
5. At least two members from the outside community;
6. A senior lab technician/lab supervisor;
7. Biosafety Officer; and
8. There must be at least 7 members serving, but there is no maximum limit.

Committee members must be identified by name to the NIH OBA; members must also provide a recent copy of their curriculum vita/resume to the OBA. The committee's composition is submitted to the NIH OBA annually.

IBC appointments last for a period of three years with the possibility of appointment to consecutive terms. The Biosafety Officer is a permanent member of the IBC.

DEFINITION OF BIOHAZARDOUS MATERIALS

For the purposes of this document, "biohazardous materials" include certain types of recombinant DNA; organisms and viruses infectious to humans, animals or plants (e.g. parasites, viruses, bacteria, fungi, prions, rickettsia); and biologically active agents (i.e. toxins, allergens, venoms) that may cause disease in other living organisms or cause significant impact to the environment or community. Biohazardous materials from animals which can cause documented zoonotic infections produced by pathogenic microbes are considered as biohazardous. Materials that may harbor biohazardous microbes or agents such as human and non-human primate blood, body fluids, tissues, and cells must also be considered a biohazard.

BIOHAZARD CLASSIFICATIONS

Principal Investigators (PI) and Department Chairs must assign all work with biohazardous materials in their department to one of four hazard categories, as outlined by CDC. The Biosafety Officer and the Institutional Biosafety Committee (IBC) will assist the PI in making this assignment, if needed, and will review and validate the Biosafety Level proposed.

I. CDC classifies agents into one of four classes of biohazard:

Biosafety Level 1 agents are well-characterized and are not known to consistently cause disease in immunocompetent adult humans and that present minimal potential hazard to laboratory personnel and the environment.

Biosafety Level 2 agents pose moderate hazards to personnel and the environment. These agents are generally associated with human disease. Routes of transmission include percutaneous injury, ingestion, and mucous membrane exposure.

Biosafety Level 3 agents are indigenous or exotic, and the associated diseases may have serious or lethal consequences. There also exists a potential for aerosol transmission.

Biosafety Level 4 agents are dangerous and exotic and pose a high individual risk for inducing life-threatening disease. BSL-4 agents require the most stringent conditions for their containment because they are extremely hazardous to laboratory personnel or may cause serious epidemic disease with high mortality. Some of these agents often derive from outside the United States and require a federal permit for importation unless they are specified for higher classification. *The U.S. Department of Agriculture has a Class 5 category for "foreign animal pathogens that are excluded from the United States by law".*

Note: All samples from human or non-human primate sources must be handled at a minimum of Biological Safety Level 2 [BSL-2]. Biological Level 3 [BSL-3] containment may be required and considered appropriate for certain operations using these microbes or material infected with them where aerosol or mucous membrane transmission is likely or where the procedure will enrich their number or cause the propagation of the microbe. According to OSHA, this includes human primary explants of tissue in culture, established cell lines, and cell strains. Highly characterized, culturally-protected human cell lines may be used at less than BSL-2 containment but only if certified by a special petition to the IBC and if all OSHA requirements to be free of human pathogenic agents are met.

II. *All biohazardous work must be electronically registered with the Institutional Biosafety Committee* through the completion of the Protocol Form and South Alabama IACUC/IBC Application form found at www.irbnet.org; and a risk assessment undertaken by the PI leading the work. In all cases, the authority of a department chairperson should be obtained when submitting an application.

III. The department chair has the final responsibility in assuring that all biohazardous research is safely planned and approved by the IBC and in assuring that PIs in their charge train staff to safely handle biohazardous material. This is not an assignable responsibility.

IV. An accurate inventory of biohazardous microbes and materials that might contain them at a work site will be maintained, including, if applicable, details of vertebrate animal species that are deliberately exposed to such microbes and materials. Work where animals are to be injected with human or non-human primate materials must be registered. All new work with biohazardous materials work must be filed with

the IBC. Furthermore, any changes in PI, personnel, agents, cell lines, etc. should be filed with the IBC via the Amendment Form found on IRBNet Forms and Templates.

V. Authorized work with recombinant materials (rDNA), synthetic nucleic acid molecules, or transgenic animals must be registered with the IBC via the Protocol Form and South Alabama IACUC/IBC Application form found on IRBNet. Work categorized by NIH or CDC as "exempt" must be reviewed and approved by the IBC Chair/Vice-Chair as Exempt. Exemption criteria are set forth in the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules* (*revised in 2013*). The IBC will assist, if asked, in preparing any necessary synthetic or recombinant DNA applications and will provide advice on and interpretation of the guidelines upon request.

Section I

Facility Standards and Basic Biosafety Requirements

BIOSAFETY LEVEL 1 REQUIREMENTS

Biosafety Level I (BSL-1) is suitable for work with agents in biohazard Biosafety Level 1 or materials that may contain them. These agents and biohazardous materials are regarded as normally non-pathogenic for normal humans or animals and are thus considered only opportunistic pathogens.

1. The laboratory manager or PI may limit or restrict access to the laboratory. Lab entrance doors should remain closed when work is in progress and window screens should be in place and adequate to prevent the entry of flies and insects from the outside. See the CDC, NIH classification book "*Biosafety in Microbiological and Biomedical Laboratories*" (5th Edition) for categorization listings.

2. Laboratory personnel must receive instruction from the PI or supervisor leading the work in relevant biosafety procedures conducted in the laboratory. These are normally the principles of sterile technique and good microbiological practices.

3. Eating, drinking, smoking, handling contact eye lenses, applying cosmetics, or storing food is not permitted in the laboratory.

4. All procedures must be performed to minimize the production of aerosols. Activities known to produce substantial aerosols such as vigorous shaking or mixing, high speed homogenization, or sonication should only be carried out in a biosafety cabinet or using equipment designed to contain aerosols.

5. Mouth pipetting is prohibited; mechanical pipetting devices must be used.

6. Laboratory coats and safety glasses must be worn by all personnel. Goggles or visors should be worn when there is significant risk of splash or droplet generation.

7. Laboratory coats should be removed when leaving the laboratory suite.

8. The laboratory work surfaces should be easy to clean, impervious to water and resistant to acids, alkalis, solvents, disinfectants, and moderate heat. Surfaces must be decontaminated once a day and after any spill of biological material.

9. The use of glassware should be minimized; durable plasticware is preferred and should be used whenever possible. Only glassware free of chips or cracks may be used.

10. Used laboratory glassware and other materials awaiting disinfection must be stored in a safe manner. Glassware, pipettes, etc., if placed in disinfectant, must be totally immersed. All waste material that is not to be incinerated on site should be rendered non-viable before disposal. Materials for disposal must be transported in covered, durable containers without spillage.

11. The use of syringe needles should be minimized and should be avoided for casual dispensing or transfer of material. When the use of syringe needles is essential, then disposable needles/syringes should be used and immediately discarded into a red Stericycle-issued sharps container. Needles must not be re-sheathed after use, bent or cut, but be discarded intact in the sharps container.

12. Blunt-nosed forceps and scissors should be used wherever possible.

13. Personnel must be trained to contain and decontaminate spillage of material. A clearly labeled spill kit containing absorbent material, gloves, biohazard bags, forceps, dust pan, and appropriate disinfectant must be immediately available in the laboratory.

14. Hands must be washed or disinfected after handling biological materials, when contamination is suspected, and before leaving the laboratory. The laboratory must contain a hand basin or sink which can be used for hand washing and handwashing soap and towels must be present at all times.

15. All accidents and significant potential exposure incidents must be recorded and reported to the supervisor and/or department chairperson and to the Office of Research Compliance and Assurance on the appropriate forms.

16. A sign incorporating the universal biohazard symbol must be posted at the entrance to the laboratory *when infectious agents are present*. The sign must include the name of the agent(s) in use and the name and phone number of the laboratory supervisor or other responsible personnel.

BIOSAFETY LEVEL 2 REQUIREMENTS

Biosafety Level 2 (BSL-2) is suitable for work with agents up to and including biohazard Biosafety Level 2 microbes or materials that may contain them. See the CDC, NIH classification book "*Biosafety in Microbiological and Biomedical Laboratories*" (5th Edition) for categorization listings. Laboratory personnel must receive instruction and training in handling pathogenic materials from the PI, be proficient in conducting the safety practices before working alone with the material, and an appropriate standard of supervision by the PI of the work must be maintained. This work must be registered and approved by the IBC.

1. The laboratory must be clearly labeled as a BSL-2 laboratory with an appropriate Biohazard Warning Sign at the entrance. Access should be restricted to authorized personnel. The sign displaying the universal biohazard emblem should list the biological hazard(s) present (e.g., herpes viruses or human blood) with the name and phone number of the laboratory supervisor to be contacted in an emergency. All equipment **directly** used to handle, process, culture, incubate, and store biohazardous materialsmust bear the biohazard emblem. **Examples include biosafety cabinets, incubators, freezers, refrigerators, centrifuges, water baths, thermocycler's, heating blocks, shakers, pipettes', and pipette aids. This equipment must be thoroughly decontaminated using appropriate disinfectants/decontaminants prior to service or removal from the laboratory environment. Ancillary equipment such as computers and other electronic data capture devices need not be labelled; however, care should be taken to avoid contamination by removing or decontaminating gloves prior to use.**

2. Only trained, informed, and approved service personnel may enter to conduct routine work. A clearance to work granted by the PI is required before maintenance and service personnel work in the area. Their activities must be monitored by the laboratory supervisor or an assigned individual with the goal of preventing accidental exposures.

3. Doors must remain closed when work is in progress. All windows must be closed and fitted with insect screens, if necessary, to restrict insect entrance from the outside.

4. Laboratory coats and safety glasses must be worn by all personnel. Goggles, full face visors, or mounted plexiglass screens must be used when there is significant risk of splash or droplet generation. Where the risk assessment shows a possible route of infection via the skin (as is usually the case with BSL-2 or higher classed microbes), gloves must be worn. Work with some viruses like HIV or Hepatitis B viruses may require double gloving. Caution must be exercised to prevent used, contaminated gloves from cross-contaminating laboratory surfaces, laboratory coats, doorknobs, wall switches, phones, computer keyboards, or laboratory notebooks. Contaminated gloves should be removed after each operation and disposed of as biohazardous waste in the red-lined biohazardous waste tubs.

5. Laboratory coats should be the side- or back-fastening type and remain in the laboratory suite after use.

Separate storage pegs must be provided near the entrance in the laboratory suite for this clothing. If front-opening lab coats must be used, they should be buttoned at all times.

6. Eating, drinking, smoking, handling contact eye lenses, applying cosmetics, or storing food is not permitted in the laboratory.

7. Mouth pipetting is prohibited; mechanical pipetting devices must be used.

8. Laboratory work surfaces must be decontaminated on a routine basis and after any biological material spill. Surfaces should be easy to clean, impervious to water, and resistant to acids, alkalis, solvents, and disinfectants.

9. The use of glassware should be minimized; durable plastic ware is preferred and must be used whenever possible. Where there is no substitute, then glassware free of chips or cracks may be used.

10. Hand washing is an absolute requirement for all personnel leaving the laboratory suite. A wrist-operated hand-washing basin with taps that can be operated without being touched by hand must be located near the exit. Soap and towels must be available at the sink.

11. In general, some work may be undertaken on the open bench (e.g., streaking Petri plates with *Streptococcus* or *Pseudomonas* cultures), but care must be taken to minimize the production of aerosols [hold lid in place above the medium surface when picking colonies]. For manipulations such as vigorous shaking or mixing, high speed homogenization, sonication, or vigorous pipetting a biosafety cabinet conforming to National Sanitation Foundation (Standard 49) for BSL-2 work must be used. Cabinet air from such systems must exhaust into the outside air or be recycled internally through two HEPA filters. All such biosafety cabinets should be certified to have annual HEPA filters leaking tested or more frequently if needed to guarantee safe operations. It is the laboratory supervisor's responsibility to see that this re-certification is carried out.

12. An inward airflow into the laboratory should be maintained to ensure that (at least) modest negative pressure is maintained.

13. All biohazardous waste, contaminated labware, and disposable personal protective gear [gloves, shoe covers, etc.] likely to have been contaminated during work must be autoclaved or otherwise decontaminated by a validated method or disposed of as medical waste in biohazard bags. Glassware, pipettes etc., if placed in disinfectant, must be totally immersed. When contaminated materials are removed by service personnel for autoclaving and decontamination/incineration within the same building, they must be transported in lidded containers capable of retaining any spillages. All biohazardous waste material must be disinfected before disposal or carefully disposed of and removed for incineration. Chemical inactivation of some BSL-2 organisms grown in the laboratory may be used, but the process must be validated and recorded.

14. Procedures using needles and/ or sharps while handling BSL-2 microbes should be strictly controlled. Such applications must be performed under approved, written laboratory procedures. Needles and sharps must be placed in durable, puncture resistant, appropriate biohazard “sharps” containers.

15. Blunt-nosed forceps and scissors must be used wherever possible.

16. All personnel handling BSL-2 microbes or materials must know the basic infectious qualities of the material and disease symptoms of the agents or biohazardous material being used in the workplace. They must also understand the biosafety procedures and physical containment necessary to handle them. They must notify their supervisor and the Biosafety Officer, c/o Office of Research Compliance and Assurance of any potential work-related or otherwise unexplained illnesses. The exposed worker should always seek immediate first aid and follow up medical attention.

17. Immunization against specific agents must be offered when a suitable vaccine is available. Hepatitis B vaccine is recommended and must be available at all times to all personnel who are categorized by work task analysis as being at risk for exposure to human bloodborne pathogens according to the OSHA Standard (29 CFR 1910.1030). This includes all workers who may experience accidental contact or significant exposure with **human blood, body fluids or tissues, cultures of microbes derived from these human materials, or animals injected with these human materials**. Accidental exposure to **non-human primate** blood, body fluids, and tissue also require immediate reporting not only to achieve medical attention for the worker but also to insure collection of the offending specimen or animal source for laboratory testing. Baseline serum samples for laboratory and other at risk personnel may be required to be collected and stored based upon the recommendation of IBC.

18. A copy of the USA Biosafety Manual and lab-specific Exposure Control Plan and relevant written procedures must be present in the laboratory where biohazards are handled for quick reference.

19. Personnel must be trained to contain and decontaminate spillages of biohazardous material. A clearly labeled spill kit containing absorbent material, gloves, disposable plastic scoops, tongs, biohazard bags, and appropriate disinfectants must be available in the laboratory.

20. All accidents and significant potential exposure incidents must be recorded and reported to the supervisor and/or department chairperson and to the Office of Research Compliance and Assurance on the appropriate forms

BIOSAFETY LEVEL 3 REQUIREMENTS

Biosafety Level 3 (BSL-3) is suitable for work with microbes up to and including biohazards comprising Biosafety Level 3 microbes or materials containing them. Laboratory personnel must be trained to handle pathogenic and potentially lethal organisms, be proficient in managing the specific biohazardous procedures to be used, work under close supervision, and be properly trained to use safety and protective equipment. All previous requirements for BSL-1 and BSL-2 practices must be met. See the CDC, NIH classification book "*Biosafety in Microbiological and Biomedical Laboratories*" (5th Edition) for categorization listings.

1. The laboratory must not be sited in areas of general circulation and should have two contiguous entry doors with a space between them (ante-room) for donning and doffing PPE. This area should also have automatically-monitored negative air pressure to the adjoining hallways or labs; be large enough for holding a handwashing sink with foot or wrist controls; and should be equipped with medical waste containers, fresh gowns, appropriate bins for holding discarded lab clothing, and other needed items.
    - Access to the laboratory must be strictly limited; only trained, informed and approved personnel may enter to conduct work.
    - A high standard of supervision of work must be maintained.
    - A permit to work from the PI is required before maintenance and service personnel can conduct work in the area. Activities involving biohazardous equipment or space must be reviewed and scrutinized by the laboratory supervisor in concert with the maintenance supervisor to prevent exposure of service and maintenance personnel to BSL-3 agents.

2. The laboratory should contain an un-obscured glass panel so occupants working in the BSL-3 unit can be seen from the outside. Doors must remain closed when work is in progress. When the room is unoccupied, the door must be capable of being locked.

3. The laboratory must be identified with the universal biohazard sign indicating the containment level (BSL-3), the biohazards in use and the name and work contact phone number of the lab supervisor. There

should be adequate space for each worker. All equipment **directly** used to handle, process, culture, incubate,and store biohazardous materials must bear the biohazard emblem, including the biosafety cabinet. Medical waste containers or incineration boxes should bear the biohazard warning emblem. **Examples include biosafety cabinets, incubators, freezers, refrigerators, centrifuges, water baths, thermocyclers, heating blocks, shakers, pipettes, and pipette aids. This equipment must be thoroughly decontaminated using appropriate disinfectants/decontaminants prior to service or removal from the laboratory environment. Ancillary equipment such as computers and other electronic data capture devices need not be labelled; however, care should be taken to avoid contamination by removing or decontaminating gloves prior to use.**

4. A continuous, directional, negative air flow into the BSL-3 laboratory must be maintained during work with agents. More than 15 air changes per hour from a 100% fresh air source should occur in normal operations. Under any operating condition, the air exchange rate [complete fresh air changes per hour] of BSL-3 facilities should be ascertained from engineering and known to the laboratory supervisor. All **exhaust air** should be HEPA filtered prior to entry into independent ducting with proper stack height as required by local and state codes. Location of exhaust stacks on the roof should be positioned to provide maximum dilution of the air in facilities when extracted to the external environment. Supply and extract air controls must be interlocked to prevent positive pressurization of the room in the event of failure of the extraction fan(s). The ventilation system must not be capable of reverse airflows.

5. Eating, drinking, smoking, handling contact eye lenses, applying cosmetics, or storing food is not permitted in the laboratory. Animals and plants not associated with the work being performed are not permitted in the laboratory.

7. Mouth pipetting is prohibited; mechanical pipetting devices must be used.

8. The use of needles and/or sharps is not normally allowed in the BSL-3 laboratory. Where their use is essential, extreme caution must be used. Such procedures requiring use of such instruments must be justified **in writing** in a special exposure control plan that explains their use in association with hand shields or other needle stick preventive devices. The needle and syringe must be promptly placed in a puncture resistant container after use. This waste must be incinerated before disposal.

9. The use of glassware should be minimized; durable plastic ware is preferred and must be used whenever possible. Where there is no substitute possible, glassware free of chips or cracks may be used. Broken glassware must not be handled directly. Instead, it must be removed with a brush, tongs, or forceps.

10. Proper PPE must be donned at all times.
    - Laboratory coats gloves must be worn by all personnel.
    - Goggles, safety glasses, or light weight visors/face shields must be worn in the laboratory when there is risk of splash or droplet generation.
    - Caution must be exercised to prevent used, contaminated gloves from cross-contaminating laboratory surfaces, laboratory coats, door knobs, wall switches, phones, computer keyboards or laboratory notebooks.
    - Contaminated gloves should be removed after each operation. Used gloves and disposable gowning must be handled as biohazardous waste.
    - Eye, face, and respiratory protection must be used in rooms containing infected animals.

11. Side or back fastening gowns must be used in the laboratory and autoclaved before being sent for laundering. These gowns must not be used outside the laboratory suite. Separate storage pegs must be provided in the laboratory suite or ante-room for this clothing.

12. Laboratory work surfaces must be decontaminated daily after use and after any biological material spill.

Surfaces should be easy to clean and impervious to water and resistant to acids, alkalis, solvents, and disinfectants.

13. Hand washing is an absolute requirement for all personnel leaving the BSL-3 laboratory. A wrist-operated hand-washing basin with taps that can be operated without being touched by hand must be located near the exit. Soap and towels must be present.

14. It is advised that laboratory procedures requiring use of potentially infective materials be carried out within a biological safety cabinet conforming to National Sanitation Foundation (Standard 49) and exhausting to the outside air through a HEPA Filter. All procedures should be performed to minimize the creation of splashes and/or aerosols. A safety cabinet recirculating air back into the workroom via two HEPA filters may be used with prior approval of the Biosafety Officer. Biosafety cabinets must be tested and certified every twelve months and must be properly used and maintained.

15. The laboratory should contain its own equipment and storage facilities suitable for the containment of BSL-3 agents. Equipment used should bear the universal biohazard warning emblem.

16. BSL-3 rated organisms must be chemically destroyed by an approved, agent-specific protocol or be autoclaved before leaving the BSL-3 laboratory. An autoclave suitable for this must be located in the suite and its performance must be monitored on each load. Writing materials used in the laboratory should not be used outside the laboratory suite.

17. The PI/Laboratory Director must establish policies and procedures for the laboratory as required by the Exposure Control Plan (ECP). Detailed emergency procedures must be available in the laboratory suite.

18. All personnel must know of the basic infectious qualities and disease symptoms of the agents or biohazardous materials being used in the workplace and the biosafety procedures necessary to safely handle them. Personnel must notify their supervisor and the Biosafety Officer of any unexplained illnesses and of any accidental exposures.

19. Immunization against specific agents must be offered when suitable vaccine is available. Hepatitis B vaccine is recommended for all personnel who work with human bloodborne pathogens and who may come into contact with human blood, body fluids, or tissues. Baseline serum samples for all laboratory and other at-risk personnel should be collected and stored. All BSL-3 workers must be enrolled in an Occupational Health Program.

20. A copy of the USA Biosafety Manual and lab-specific Exposure Control Plan and relevant written procedures must be present in the laboratory.

21. Personnel must be prepared to contain and decontaminate biohazardous spills. A clearly labeled spill kit containing absorbent material, gloves, biohazard bags, tongs and disposable plastic scoops, and appropriate proven disinfectant must be available in the laboratory.

22. All accidents, spills, and exposures to/of infective materials must be recorded by the person responsible for the work. Accidents and incidents must be reported to the laboratory supervisor, department chairperson, and to the Office of Research Compliance and Assurance on the appropriate forms.

23. Isolated vacuum lines should be protected with HEPA filters and liquid disinfectant traps.

24. An insect and rodent control plan must be in effect.

25. Plumbing waste liquids to the sanitary sewer from the BSL-3 suite must be preventable by a treatment-type holding tank or direct disconnect system.

*Note: Enhanced BSL-3 stipulations exist for work with risk group 3 influenza virus. Additional measures can be found Appendix G-II-C-5 of the NIH GUIDELINES FOR RESEARCH INVOLVING RECOMBINANT OR SYNTHETIC NUCLEIC ACID MOLECULES

ANIMAL ROOM CONTAINMENT LEVELS

The following three containment levels are suitable for work with vertebrates which that are deliberately inoculated with organisms of Biosafety Levels 1, 2, and 3 or with materials suspected of containing these organisms. Most work undertaken will be accommodated by the facilities operated at Animal Biosafety Level 1. Where the work involves the use of known pathogens (or material suspected of containing pathogens) of Biosafety Level 2 or 3, then higher rated facilities must be used. No work will be undertaken at animal containment level 4. Prior to beginning a study animal protocols must also be reviewed by the Institutional Animal Care and Use Committee (IACUC) as well as the IBC.

ANIMAL BIOSAFETY LEVEL 1

Animal Biosafety Level 1is suitable for work with vertebrates deliberately inoculated with BSL-1 organisms or materials containing them. The person responsible for the animal experiment in association with vivarial management must ensure those having contact with the animals and waste materials are suitably trained, familiar with the local codes of practice, and are aware of any other precautions and procedures that may be required.

1. The animal room should be easy to clean with washable, durable surfaces, and ceilings.
2. The animal room must be adequately ventilated with exhaust air discharged to the outside without being recirculated to other rooms. There should be an inward airflow into the animal facility.
3. Access to the room must be limited to authorized persons. The Director of the facility must establish a policy whereby only persons who have been advised of the potential hazard and meet specific requirements may enter the animal room.
4. A validated autoclave for sterilizing waste materials should be available on site. Bedding materials must be disposed of in compliance with local requirements. Animal carcasses must be incinerated.
5. Suitable protective clothing, gloves, eye protection, and footwear must be worn in the animal room and cleansed or removed when leaving.
6. Hands must always be disinfected or washed immediately when contamination is suspected and after animals or animal waste is handled.
7. Eating, drinking, smoking, handling contact eye lenses, and applying cosmetics is prohibited. Food for human consumption must be stored in designated areas outside the animal suite.
8. Mouth pipetting is prohibited; mechanical pipetting devices must be used.
9. All procedures should be performed to minimize the production of aerosols.
10. Appropriate disinfectants must be available for immediate use.
11. All waste materials must be disposed of safely.

12. Used animal cages must be rendered non-infective after use. Cages should be using a cage washer with a final rinse temperature of 180°F.

13. Materials for autoclaving or incineration and used animal cages must be transported without spillage.

14. All accidents and incidents, including animal bites and scratches, must be reported to the laboratory supervisor, department chairperson, and the Department of Comparative Medicine on the appropriate forms.

15. An insect and rodent control program must be in operation.

16. If the animal facility has windows that open, they must be fitted with fly screens.

17. A copy of the USA Biosafety Manual and lab-specific Exposure Control Plan must be available in the animal facility.

ANIMAL BIOSAFETY LEVEL 2

Animal Biosafety Level 2 is suitable for work with vertebrates that are deliberately inoculated with microbes in Biosafety Level 2 (or material suspected of containing viable BSL- 2 microbes). Human materials inoculated into animals must be handled at BSL-2. Some species of non-human primates may harbor potentially lethal microbes including *Herpesvirus simiae* (Herpes B virus). Special personnel protections are required for these monkeys. The person responsible for the animal experiment in association with the Department of Comparative Medicine must ensure that all those having contact with the animals and their waste materials are suitably trained, adequately supervised, offered relevant vaccines, and are familiar with the local code of practice and are aware of any other precautions and procedures that may be required. Animal Biosafety Level 1 requirements should be met in addition to the following requirements.

A. Standard Practices

1. Access to the animal facility must be limited or restricted at the discretion of the laboratory or animal facility director.

2. All personnel must wash their hands after handling cultures and animals, after removing gloves, and before leaving the animal facilities.

3. Eating, drinking, smoking, handling contact eye lenses, applying cosmetics, and storing food for human consumption are not permitted in animal rooms. Persons who wear contact lenses in animal rooms should also wear goggles or a face shield.

4. All invasive procedures must be carefully performed to minimize the creation of aerosols.

5. Work surfaces must be decontaminated after use or spill of viable materials.

6. Doors to animal rooms must open inward, be self-closing, and be kept closed when experimental animals are present.

7. All wastes from the animal room must be appropriately decontaminated, preferably by autoclaving, before disposal. Infected animal carcasses must be incinerated after being transported from the animal room in covered leak-proof containers.

8. An insect and rodent control program must be in effect.

B. Special Practices

1. The laboratory or animal facility director should limit access to the animal room(s) to personnel who have been advised of the potential hazard and who need to enter the room for program or service purposes when work is in progress. In general, persons with special medical conditions who may be at increased risk of acquiring infection (skin eczema, severe animal dander allergies, immunosuppressed, etc.) or for whom infection might be unusually hazardous (pregnancy) should not be allowed in the animal rooms. Decisions to permit pregnant workers to handle biohazardous materials must be made by the PI in consultation with the Department of Comparative Medicine.

2. The laboratory or animal facility director must establish policies and procedures whereby only persons who have been advised of the potential hazard and meet all specific requirements (e.g. immunization) may enter the animal room(s).

3. Animal rooms housing BSL-2 work require a biohazard warning sign incorporating the universal biohazard symbol to be posted on the access door to the animal room. The hazard warning sign should identify the infectious agent(s) in use, list the name and telephone number of the animal facility supervisor or other responsible person(s), and indicate the special requirement(s) for entering the animal room.

4. Laboratory personnel, animal handlers, and other animal service personnel must receive appropriate immunizations or tests for the agent(s) handled or potentially present in the laboratory (e.g. Hepatitis B vaccine or TB skin testing).

5. When appropriate, considering the agent(s) handled, baseline serum samples from animal care and other at-risk personnel should be collected and stored. Additional serum samples may be collected periodically depending on the agents handled or the function of the facility. The decision to establish a serologic surveillance program must take into account the availability of methods for the assessment of antibody to the agent(s) of concern.

6. A special biosafety exposure control plan or specific SOPs must be prepared and adopted. Personnel must be advised of special hazards and be required to read and follow instructions on practices and procedures.

7. Laboratory personnel must receive appropriate training from the PI or supervisor on the potential hazards associated with the work involved, necessary precautions to prevent exposures, and exposure evaluation procedures. Personnel must receive annual updates or additional training as necessary for procedural or policy changes.

8. A high degree of precaution must always be taken with any contaminated sharp items, including needles and syringes, slides, glass cover slips, pipettes, capillary tubes, and scalpels. Use of needles and syringes or other sharp instruments should be restricted to *only* when there is no alternative, such as for parenteral injection, blood collection, or aspiration of fluids from laboratory animals and diaphragm bottles. Plastic ware should be substituted for glassware whenever possible.

8.1 Only needle-locking syringes or disposable syringe-needle units (i.e. needle is integral to the syringe) should be used for injection or aspiration of infectious materials. Used disposable needles must not be bent, sheared, broken, recapped, removed from disposable syringes, or other-wise manipulated by hand before disposal; rather, they must be carefully placed in conveniently located puncture-resistant containers used for sharps disposal. Non-disposable sharps must be placed in a hard-walled container for transport to a processing area for decontamination, preferably by autoclaving.

8.2 Needle-less systems and other safe devices should be used when appropriate.

8.3 Broken glassware must not be handled directly by hand but must be removed by mechanical means such as a brush and dustpan, tongs or forceps. Containers of contaminated needles, sharp equipment, and broken glass should be decontaminated before disposal, according to local, state, or federal regulations.

9. Cultures, tissues, or specimens of body fluids must be placed in a container that prevents leakage during collection, handling, processing, storage, transport, or shipping.

10. Cages must be appropriately decontaminated (preferably by autoclaving) before they are cleaned and washed. Equipment and work surfaces should be decontaminated with an appropriate disinfectant on a routine basis, after work with infectious materials is finished, and especially after overt spills, splashes or other contamination by infectious materials. Contaminated equipment must be decontaminated according to local, state, or federal regulations before it is sent for repair or maintenance or packaged for transport in accordance with applicable local, state, or federal regulations before removal from the facility.

11. Spills and accidents that result in overt exposures to infectious materials must be immediately reported to the lab supervisor, Biosafety Officer, and, if appropriate, the animal facility supervision.

12. Animals not involved in the work being performed are not permitted in the lab.

C. Safety Equipment (Primary Barriers)

1. Biological safety cabinets, negative air flow necropsy tables, other physical containment devices, and/or personal protective equipment (e.g., respirators, face shields) are used whenever procedures with a high potential for creating aerosols are conducted. These include necropsy of infected animals, harvesting of tissues or fluids from infected animals or eggs, intranasal inoculation of animals, and manipulations of high concentrations or large volumes of infectious materials.

2. Appropriate face/eye and respiratory protection must be worn by all personnel entering animal rooms housing non-human primates.

3. Laboratory coats, gowns, or uniforms must be worn while in the animal room. The protective clothing must be removed before leaving the animal facility.

4. Special care must be taken to avoid skin contamination with infectious materials; gloves should be worn when handling infected animals and when skin contact with infectious materials is unavoidable.

D. Animal Facilities (Secondary Barriers)

1. The animal facility must be designed and constructed to facilitate cleaning and housekeeping.

2. A hand washing sink must be available in the room where infected animals are housed.

3. If floor drains are provided, the drain traps must always be filled with water or a suitable disinfectant.

4. It is recommended that the direction of airflow in the animal facility is inward.

5. An autoclave, which can be used for decontaminating infections laboratory waste, must be available in the building with the animal facility.

ANIMAL BIOSAFETY LEVEL 3

Animal Biosafety Level 3 is suitable for work with vertebrates that are deliberately inoculated with microbes up to and including hazard BSL- 3 (or material suspected of containing such infectious microbes). Personnel must be experienced in the handling of the animals to be used, and a high standard of supervision of the work must be maintained. The person responsible for the animal experiment in association with vivarial management must ensure all those having contact with the animals and waste materials are familiar with the local codes of practice and are aware of any other precautions and procedures that may be required. Animal Biosafety Level 1 and 2 practices and procedures must be met in addition to the following requirements.

A. Standard Practices

1. Access to the animal facility should be limited or restricted at the discretion of the laboratory or animal facility director.

2. Personnel must wash their hands after handling cultures and animals, after removing gloves, and before leaving the animal facility.

3. Eating, drinking, smoking, handling contact eye lenses, applying cosmetics, and storing food for human use are not permitted in animal rooms. Persons who wear contact lenses in animal rooms should also wear goggles or a face shield.

4. All procedures must be carefully performed to minimize the creation of aerosols.

5. Work surfaces must be decontaminated after use or spill of viable materials.

6. Doors to animal rooms should open inward, be self-closing, and be kept closed when experimental animals are present.

7. All wastes from the animal room must be appropriately decontaminated, preferably by autoclaving, before disposal. Infected animal carcasses must be incinerated after being transported from the animal room in leak proof, covered containers.

8. An insect and rodent control program must be in effect.

B. Special Practices

1. The laboratory director or other responsible person should restrict access to the animal room to personnel who have been advised of the potential hazard and who need to enter the room for program or service purposes when infected animals are present. Persons who are at increased risk of acquiring infection, or for whom infection might be unusually hazardous, should not be allowed in the animal room. Persons at increased risk may include pregnant women and persons who are immunodeficient or immunosuppressed.

2. The laboratory director or other responsible person must establish policies and procedures whereby only persons who have been advised of the potential hazard and meet any specific requirements (e.g., for immunization) may enter the animal room.

3. When the infectious agent(s) in use in the animal room requires special entry provisions (e.g., the need for immunizations and respirators), a biohazard warning sign, incorporating the universal biohazard symbol must be posted on the access door to the animal room. The hazard warning sign should identify the infectious agent(s) in use, list the name and telephone number of the animal facility supervisor or other responsible person(s), and indicate the special requirement(s) for entering the animal room.

4. Laboratory personnel must receive appropriate immunizations or tests for the agent(s) handled or potentially present in the laboratory (e.g., -Hepatitis B vaccine or TB skin testing).

5. Baseline serum samples from all personnel working in the facility and other at-risk personnel may be required to be collected and stored. Additional serum samples may be collected periodically and stored. The serum surveillance program must take in account the availability of methods for the assessment of antibody to the agent(s) of concern.

6. A special biosafety manual and SOPs must be prepared or adopted. Personnel must be advised of special hazards and are required to read and follow instructions on practices and procedures.

7. Laboratory personnel must receive appropriate training on the potential hazards associated with the work involved, necessary precautions to prevent exposures, and exposure evaluation procedures. Personnel must receive annual updates or additional training as necessary for procedural or policy changes.

8. A high degree of precaution must always be taken with any contaminated sharp items, including needles and syringes, slides, pipettes, capillary tubes, and scalpels. Needles and syringes or other sharp instruments should be restricted in the laboratory for use only when there is no alternative, such as for parenteral injection, blood collection, or aspiration of fluids from laboratory animals and diaphragm bottles. Plastic ware should be substituted for glassware whenever possible.

   8.1 Only needle-locking syringes or disposable syringe-needle units (i.e. needle is integral to the syringe) must be used for injection or aspiration of infectious materials. Used disposable needles must not be bent, sheared, broken, recapped, removed from disposable syringes, or other-wise manipulated by hand before disposal; rather, they must be carefully placed in conveniently located puncture resistant containers used for sharps disposal. Non-disposable sharps must be placed in a hard-walled container, preferably containing a suitable disinfectant, for transport to a processing area for decontamination, preferably by autoclaving.

   8.2 Needle-less systems and other safe devices should be used when appropriate.

8.3 Broken glassware must not be touched directly by hand but should be removed by mechanical means such as a brush and dustpan, tongs, or forceps. Containers of contaminated needles, sharp equipment, and broken glass should be decontaminated before disposal, according to local, state, or federal regulations.

9. Cultures, tissues, or specimens of body fluids must be placed in a container that prevents leakage during collection, handling, processing, storage, transport, or shipping.

10. Cages must be autoclaved or thoroughly decontaminated before bedding is removed or before they are cleaned and washed. Equipment and work surfaces should be decontaminated with an appropriate disinfectant on a routine basis, after work with infectious materials is finished, and especially after overt spills, splashes, or other contamination by infectious materials. Contaminated equipment must be decontaminated before it is sent for repair or maintenance, or packaged for transport in accordance with applicable local, state, or federal regulations, before removal from the facility.

11. Spills and accidents which result in overt exposures to infectious materials or animals must be immediately reported to the lab supervisor, Biosafety Officer, and if appropriate, the animal facility supervision. Medical evaluation, surveillance, and treatment should be provided as appropriate and written records maintained.

12. All wastes from the animal room must be autoclaved before disposal. All animal carcasses must be incinerated. Dead animals must be transported from the animal room to the incinerator in covered leak-proof containers.

13. Animals not involved in the work being performed are not permitted in the lab.

C. Safety Equipment (Primary Barriers)

1. Personal protective equipment must be used for all activities involving infected animals or manipulations of infectious materials.

1.1 Wrap-around or solid-front gowns or uniforms must be worn by personnel entering the animal room. Front-button laboratory coats are unsuitable. Used protective gowns should be appropriately contained until decontamination or disposal.

1.2 Personnel must wear gloves when handling infected animals. Gloves should be aseptically removed and autoclaved with other animal room wastes before disposal.

1.3 Appropriate face/eye and respiratory protection should be worn by all personnel entering animal rooms housing non-human primates.

1.4 Boots, shoe covers, or other protective footwear, and disinfectant footbath are available and must be used when indicated.

2. Physical containment devices and equipment appropriate for the animal species must be used for all procedures and manipulations of infectious materials or infected animals.

3. The risk of infectious aerosols from infected animals or their bedding also can be reduced if animals are housed in partial containment caging systems, such as open cages placed in ventilated enclosures (e.g., laminar flow cabinets), solid wall and bottom cages covered with filter bonnets, or other equivalent primary containment systems.

D. Animal Facilities (Secondary Barriers)

1. The animal facility must be designed and constructed to facilitate cleaning and housekeeping and must be separated from areas that are open to unrestricted personnel traffic within the building. Passage through two sets of doors is the basic requirement for entry into the animal room from access corridors or other contiguous areas. Physical separation of the animal room from access corridors or other activities must be provided by a double-doored clothes change room (showers may be included), airlock, or other access facility that requires passage through two sets of doors before entering the animal room.

2. The interior surfaces or walls, floors, and ceilings must be water resistant so they can easily be cleaned. Penetrations of these surfaces are sealed to facilitate fumigation or space decontamination.

3. A foot, elbow, or automatically operated hand washing sink must be provided in each animal room near the exit door.

4. If vacuum service (i.e., central or local) is provided, each service connection should be fitted with liquid disinfectant traps and a HEPA filter.

5. If floor drains are provided, they must be protected with liquid traps that are always filled with water or disinfectant.

6. Animal room doors must be self-closing and be kept closed when infected animals are present.

7. An autoclave for decontaminating wastes must be available, preferably within the animal facility. Materials must be transferred to the autoclave in a covered, leak-proof container whose outer surface has been decontaminated.

8. A non-recirculating ventilation system must be provided. The supply and exhaust components of the system must be balanced to provide for directional flow of air into the animal room. The exhaust air must be discharged directly to the outside and clear of occupied areas and air intakes.

9. The HEPA filtered exhaust air from Class I or Class II biological safety cabinets or other primary containment devices must be discharged directly to the outside or through the building exhaust system.

PHYSICAL CONTAINMENT FOR LARGE SCALE WORK WITH BIOHAZARDOUS ORGANISMS

The use of biohazardous organisms on a scale above that which is routinely encountered in laboratories requires a different standard of work practice and conditions. This work is termed "Large Scale biohazard work". The conditions are laid down in guidance issued by NIH in 1986, 1987 and in 1992 by the Organization for Economic Cooperation and Development (OECD). Large scale work with biohazardous materials is a specialized activity which can only be undertaken in dedicated facilities. The systems of work are very different from laboratory scale and detailed codes of practice/ standard operating procedures are detailed in Appendix K of NIH rDNA Guidelines.

Categorization of Work

For the purposes of large-scale research or production on a scale greater than ten liters, three physical containment levels have been established by NIH. These are referred to as BSL1-LS, BSL2-LS, and BSL3-LS. The BSL-LS level of physical containment is required for large scale research with viable microbes or with the

production of viable organisms containing recombinant DNA molecules (rDNA) that require BSL-1 containment at the smaller laboratory scale. For the purposes of this document, the CDC categorization of pathogens should be used as a guide to establish the correct containment level for work with hazardous organisms.

For work with Genetically Modified Organisms (GMO's) or rDNA recombinants, the risk assessment approved by the IBC will determine the level of containment necessary. Work with rDNA may be undertaken at Good Large Scale Practice (GLSP) only if the criteria shown in Table 1 are met.

Containment Levels

For microbes classified by CDC as Risk Group1 or regarded as only involving opportunistic pathogens, work may be undertaken under conditions of GLSP.

Materials that may be infectious to healthy humans should be handled at BSL-2-LS through BSL-3-LS as appropriate. BSL-4-LS work can only be attempted with special arrangement within the highest level of containment and the approval by the IBC.

Good Large Scale Practice (GLSP)

For CDC Risk Group 1 / GLSP "harmless" organisms, the following standards should be adopted:

1. Local codes of practice for handling biological materials must be prepared.

2. The work place should be kept clean and hygienic.

3. Good occupational hygiene measures should be followed. Exposure to biological/chemical agents must be prevented.

4. Suitable protective clothing must be provided. Overalls, gloves, protective footwear, and eye protection should be worn.

5. Changing and hand washing facilities must be provided.

6. Eating, drinking, smoking, handling contact eye lenses, applying cosmetics, or storing food are not permitted in the laboratory.

BSL1-LS Level

1. Cultures of viable organisms containing recombinant DNA molecules must be handled in a closed system (e.g., closed vessel used for the propagation and growth of cultures) or other primary containment equipment (e.g. biological safety cabinet containing a centrifuge used to process culture fluids) that is designed to reduce the potential for escape of viable organisms. Volumes less than 10 liters may be handled outside of a closed system or other primary containment equipment provided all physical containing requirements specified in Appendix G-II-A of the *NIH Recombinant or Synthetic Nucleic Acid Molecules Guidelines* are met. The large scale facility must be separated by a suitable physical barrier (walls, closed screened windows and doors) from the outside environment or from other non-BSL-1-LS operations.

2. Culture fluids must not be removed and discarded from a closed system or other primary containment equipment unless the viable organisms or recombinant organisms have been inactivated by a validated inactivation procedure. A validated inactivation procedure is one that has been demonstrated to be effective against the organism or recombinant host.

3. Sample collection from a closed system, addition of materials to a closed system, and transfer of culture fluids from one closed system to another must be undertaken in a manner that minimizes the release of aerosols or contamination of exposed surfaces.

4. Exhaust gases removed from a closed system or other primary containment equipment must be HEPA filtered to minimize the release of viable organisms or recombinant into the environment.

5. A closed system or other primary containment equipment that has contained viable organisms or the recombinant must not be opened for maintenance or other purposes unless it has been sterilized by a validated sterilization procedure. If floor drains in the BSL-1 facility empty into the sanitary sewer, they should be fitted with gas tight closures or stand pipes adequate to retain all liquid waste during LS operations. Ideally, a reservoir or holding sump that could allow chemical disinfection and holding of escaped liquids should separate the area from the sanitary sewer.

6. Emergency plans must be prepared to include methods and procedures defined and practiced for inactivating and handling large losses of culture on an emergency basis.

BL2-LS Level

1. Cultures of viable BSL-2 organisms or BSL-2 rated recombinant microbes must be handled in a closed system (e.g., closed vessel used for the propagation and growth of cultures) or other primary containment equipment (e.g. Class II A or B biological safety cabinet containing a centrifuge used to process culture fluids) that is designed to prevent the escape of viable organisms. Volumes of less than 1.0 liters may be handled outside of a closed system or other primary containment equipment provided that physical containment requirements specified in Appendix G-II-B of the *NIH Recombinant or Synthetic Nucleic Acid Molecules Guidelines* are met.

2. Culture fluids shall not be removed from a closed system or other primary containment equipment unless the viable organisms or BL-2 recombinant have been inactivated by a validated inactivation procedure. A validated inactivation procedure is one that has been demonstrated to be effective using the BSL-2 organism or recombinant.

3. Sample collection from a closed system, the addition of materials to a closed system, and the transfer of cultures fluids from one closed system to another must be undertaken in a manner that prevents the release of aerosols or contamination of exposed surfaces.

4. Exhaust gases removed from a closed system or other primary containment equipment must be HEPA filtered to prevent the release of viable BSL-2 organisms or recombinant to the environment.

5. A closed system or other primary containment equipment that has contained viable, BSL-2 organisms or recombinants must not be opened for maintenance or other purposes unless it has been sterilized by a validated sterilization procedure. In the event of major containment vessel or service line failure, the facility should have diked confinement capability to retain the spill or accidental release. Emergency breathing apparatus (e.g., Scott or other brand) should be located at the entrance to enable workers to don the positive pressure breathing apparatus before entry to effect clean up of released material.

6. Rotating seals and other mechanical devices directly associated with a closed system used for the propagation and growth of viable BSL-2 organisms or recombinants must be designed to prevent leakage or be fully enclosed in ventilated housings exhausted through HEPA filters.

7. The closed system used to contain operations involving viable BSL-2 organisms or recombinants must include monitoring or sensing devices that monitor the integrity of containment during operations.

8. The closed system must be tested for integrity of the containment features using the organisms or recombinants. Testing must be accomplished prior to the introduction of viable organisms and following modification or replacement of essential containment features. Procedures and methods used in the testing must be appropriate for the equipment design and for recovery and demonstration of the test organism. Records of tests and results must be maintained on file.

9. The closed system must be permanently identified. This identification should be used in all records reflecting testing, operation, and maintenance and in all documentation relating to use of this equipment for research or production activities involving viable BSL-2 organisms or recombinants. If floor drains in the BSL-2 facility empty into the sanitary sewer, they should be fitted with gas tight closures or stand pipes adequate to retain all liquid waste during LS operations. Ideally, a reservoir or holding sump that could allow chemical disinfection and holding of escaped liquids should separate the area from the sanitary sewer.

10. The universal biohazard sign must be posted at the entrance and on each closed system and primary containment equipment when used to contain viable BSL-2 organisms or recombinants.

11. Emergency plans must include methods and procedures for handling large losses of culture on an emergency basis.

BSL3-LS Level

1. All practices and emergency breathing equipment and procedures specified for BSL-2-LS above should be in place in BSL-3-LS facilities. Cultures of viable BSL-3 organisms or recombinants must be handled in a closed system (e.g. closed vessels used for the propagation and growth of cultures) or other primary containment equipment (e.g. Class III biological safety cabinet vented externally, containing a centrifuge used to process culture fluids) designed to prevent the escape of viable organisms. Volumes less than 10 liters may be handled outside of a closed system provided all physical containment requirements specified in Appendix G-II-C of the *NIH Recombinant or Synthetic Nucleic Acid Molecules Guidelines* are met.

2. Culture fluids (except as allowed in Appendix K-V-C of the *NIH Recombinant or Synthetic Nucleic Acid Molecules Guidelines*) must not be removed from a closed system or other primary containment equipment unless the viable BSL-3 organisms or recombinants have been inactivated by a validated inactivation procedure.

3. Sample collection from a closed system, the addition of materials to a closed system, and the transfer of culture fluids from one closed system to another must be done in a manner that prevents the release of aerosols or contamination of exposed surfaces.

4. Exhaust gases removed from a closed system or other primary containment equipment must be HEPA filtered to prevent the release of viable BSL-3 organisms or recombinants to the environment.

5. A closed system or other primary containment equipment that has contained viable BSL-3 organisms or recombinants must not be opened for maintenance or other purposes unless it has been sterilized by a validated sterilization procedure.

6. A closed system used for the propagation and growth of viable BSL-3 organisms or recombinants must be operated so the space above the culture level will be maintained at a pressure as low as possible consistent with equipment design in order to maintain the integrity of containment features.

7. Rotating seals and other mechanical devices directly associated with a closed system used to contain viable BSL-3 organisms or recombinants must be designed to prevent leakage or shall be fully enclosed in ventilated housings exhausted through HEPA filters.

8. The closed system used for the propagation and growth of viable BSL-3 organisms or recombinants and other primary containment equipment used to contain operations involving viable BSL-3 organisms or recombinants must include monitoring or sensing devices that monitor the integrity of containment during operations.

9. The closed system must be tested for integrity of the containment features using the organisms that will serve as the host for propagating the BSL-3 pathogen or recombinant. Testing must be accomplished prior to the introduction of viable organisms and following modification or replacement of essential containment features. Procedures and methods used in the testing must be appropriate for the equipment design and for recovery and demonstration of the test organism. Records of tests and results must be maintained on file.

10. The closed system must be permanently identified. This identification must be used in all records reflecting testing, operation, and maintenance and in all documentation relating to the use of this equipment for research production activities involving BSL-3 pathogens or recombinants. If floor drains in the BSL-3 facility empty into the sanitary sewer, they should be fitted with gas tight closures adequate to retain all liquid waste produced during LS operations. Stand pipes are not permitted. Ideally, a reservoir or holding sump that could allow chemical disinfection and holding of escaped liquids should separate the area from the sanitary sewer.

11. The universal biohazard sign must be posted on each closed system and on primary containment equipment when used to contain viable BSL-3 organisms or recombinants.

12. Emergency plans must include methods and procedures for handling large losses of culture on an emergency basis.

13. Closed systems and other primary containment equipment used in handling cultures of viable BSL-3 organisms or recombinants must be located within a controlled area that meets the following requirements:

    13.1 The controlled area must have a separate entry area. The entry area must be a double-doored space such as an air lock, anteroom, or change room that separates the controlled area from the balance of the facility.

    13.2 The surfaces of walls, ceiling, and floors in the controlled area must permit ready cleaning and decontamination.

    13.3 Penetrations into the controlled area must be sealed to permit liquid or vapor phase space decontamination.

13.4 All utilities and service or process piping and wiring entering the controlled area must be protected against contamination and be externally adequate to resist chemical sterilization.

13.5 Hand-washing facilities equipped with foot, elbow, or automatically operated valves must be located at each major work area and near each primary exit.

13.6 A shower facility must be provided and located in close proximity to the controlled area.

13.7 The controlled area must be designed to preclude release of culture fluids outside the controlled area in the event of an accidental spill or release from the closed systems or other primary containment equipment.

13.8 The controlled area must have a ventilation system capable of controlling air movement. The movement of air must be from areas of lower contamination potential to areas of higher contamination potential and the environment always kept under negative pressure. If the ventilation system provides positive pressure supply air, the system must operate in a manner that prevents the reversal of the direction of air movement or be equipped with an alarm that would be actuated in the event that reversal in the direction of air movement were to occur. The exhaust air from the controlled area shall not be recirculated to other areas of the facility. The exhaust air from the controlled area may be discharged to the outdoors without filtration or other means for effectively reducing an accidental aerosol burden provided it can be dispersed clear of occupied buildings and air intakes.

14. The following personnel and operational practices shall be required:

14.1 Personnel entry into the controlled area shall be through the entry area specified above.

14.2 Persons entering the controlled area must exchange or cover their personal clothing with work garments such as jumpsuits, laboratory coats, pants and shirts, head covers, and shoes or shoe covers. At the controlled area exit, the work clothes may be stored in a locker separate from the one used for personal clothing or discarded for laundering as biohazardous laundry. Clothing must be decontaminated before laundering.

14.3 Entry into the controlled area during periods when work is in progress must be restricted to those persons required to meet program or support needs. Prior to entry, all persons must be informed of all operating practices, emergency procedures, and the nature of the work conducted.

14.4 Persons under 18 years of age are not permitted to enter the controlled area.

14.5 The universal biohazard sign must be posted on entry doors to the controlled area and all internal doors when any work involving the organism is in progress. This includes periods when decontamination procedures are in progress. The sign posted on the entry doors to the controlled area must include a statement of agents in use and personnel authorized to enter the controlled area.

14.6 The controlled area must be kept neat and hygienic.

14.7 Eating, drinking, smoking, handling contact lenses, applying cosmetics, or storing food are not permitted in the controlled area.

14.8 Animals and plants must be excluded from the controlled area.

14.9 An effective insect and rodent control program must be maintained.

14.10 Access doors to the controlled area must be kept closed, except as necessary for access, while work is in progress. Serve doors leading directly outdoors must be sealed and locked while work is in progress.

14.11 Persons must wash their hands when leaving the controlled area.

14.12 Persons working in the controlled area must be trained in emergency procedures.

14.13 Equipment and materials required for the management of accidents involving viable BSL-3 organisms or recombinants must be available in the controlled area.

14.14 The controlled area must be decontaminated in accordance with established procedures following spills or other accidental release of viable BSL-3 organisms or recombinants.

TABLE I

Comparison of Laboratory and large-scale Biosafety Requirements[a]

	Laboratory scale				***Large scale***			
Biosafety level criteria	***BSL 1***	***BSL 2***	***BSL 3***	***BSL 4***	***GLSP***	***BSL 1 LS***	***BSL 2 LS***	***BSL 3 LS***
Biosafety Procedures:								
Implement institutional safety code	+	+	+	+	+	+	+	+
Written instructions and training	+	+	+	+	+	+	+	+
Biosafety manual	-	+	+	+	-	-	+	+
Good occupational hygiene	+	+	+	+	+	+	+	+
Compulsory shower out	-	-	-	+	-	-	-	-
Provision and use of appropriate PPE	+	+	+	+	+	+	+	+
Good microbiological techniques	+	+	+	+	+	+	+	+
Surfaces disinfected daily and after spills	+	+	+	+	+	+	+	+
Mouth-pipetting prohibited	+	+	+	+	+	+	+	+
Eating, drinking, smoking prohibited	+	+	+	+	+	+	+	+
Undocumented use of sharps (needles) restricted	-	+	+	+	-	+	+	+
Bench-top work prohibited	-	+/-	+	+	-	+/-	+	+

Internal accident reporting	+	+	+	+	+	+	+	+
Medical surveillance	-	+	+	+	+	+	+	+
Operational and Equipment Requirements:								
Biohazard sign	-	+	+	+	-	-	+	+
Restricted access	-	+	+	+	-	+	+	+
Children under 12 not allowed	-	+	+	+	-	+	+	+
No animals allowed except as part of experiment or process	-	+	+	+	+	+	+	+
No plants allowed except as part of experiment or process	-	-	+	+	+	+	+	+
Control aerosols	-	+	+	+	+/-	+	+	+
Laboratory doors closed when agent is in use	+	+	+	+	+	+	+	+
Insect and rodent control program	+/-	+	+	+	+	+	+	+
Bio-Safety Cabinet (BSC) required	-	+	+	+	-	+	+	+
Vacuum line protected by overflow flask (F) and/or filter (f)	F	F/Ff	Ff	Ff	F	Ff	Ff	Ff
Special Equipment and Facilities:								
Handwashing facility	+	+	+	+	+	+	+	+
Changing facility	-	-	+	+	-	-	+	+
Special engineering design, esp. 100% fresh air	-	-	+	+	-	+	+	+

	Laboratory scale				***Large scale***			
Biosafety level criteria	***BSL 1***	***BSL 2***	***BSL 3***	***BSL 4***	***GLSP***	***BSL 1 LS***	***BSL 2 LS***	***BSL 3 LS***
Laboratory separated from general traffic	-	+	+	+	-	-	+	+
Airlock	-	-	-	+	-	-	-	+
Effluent from sinks and showers collected and treated	-	-	-	+	-	-	-	-
Effluents from process decontaminated	-	-	-	+	-	+	+	+
Solid waste decontaminated or packaged	+/-	+	+	+	-	+	+	+
Liquid waste decontaminated	-	+	+	+	-	+	+	+
Site negative pressure controlled	-	-	+	+	-	-	-	+
HEPA filters in air ducts	-	-	+	+	-	-	-	+
Area hermetically sealable for decontamination	-	-	+	+	-	-	-	+
Site designed to contain large spills	-	-	+	+	-	+	+	+

[a] ***+, Required; -, not required; +/-, required when appropriate; GLSP, Good Large Scale Practices***

Packaging and Shipment of Biological Substances

In the course of conducting research, it may become necessary to transport and ship biological material that could be hazardous to the population at large. Such necessities are acknowledged by freight forwarders and government regulations. For the most dangerous substances that are known to cause harm to humans and animals, formal training is required for individuals responsible for safely packing and shipping the substances.

Introduction

In the normal course of transportation, packages are likely to be subjected to extreme temperature shifts, changes in humidity and pressure, shocks, and vibrations from loading, unloading, and accidental drops. Any of these can compromise the integrity of the package and/or safety of those around it if the package is breached. The completed package must be designed, constructed, maintained, filled, its contents limited, and closed. The intent is that under conditions normally encountered in transportation, there will be no release of hazardous material into the environment. The regulations dictate that it is the shipper's responsibility, not the courier's or the recipient's, to assure that the contents are properly packaged to meet this objective. When the classification "Infectious Substance" is used, there is the understanding that the substance being shipped has crossed the line from unregulated or minimally regulated materials into Hazardous Materials when shipped over the U.S. highways or airways.

Common Terminology

DOT: United States Department of Transportation. These regulations cover all items to be shipped over land.

IATA: International Air Transport Association. IATA is the trade association of the world's international airline industry. It currently groups together close to 300 airlines, which cover 95% of all international air traffic. The regulations for shipping hazardous material in the air are more stringent than those for shipping over land.

Category A Infectious Substance: An infectious substance in a form that is capable of causing permanent disability, life-threatening, or fatal disease in otherwise healthy humans or animals when exposure occurs. A Category A infectious substance must be described as "infectious substance affecting humans" assigned to identification number UN 2814 based on the known medical history or symptoms of a source patient or animal, endemic local conditions, or professional judgment concerning the individual circumstances of the source human or animal. [49CFR173.134(a)(1)(i)]

Category B Infectious Substance: An infectious substance that is not in a form generally capable of causing permanent disability or life-threatening or fatal disease in otherwise healthy humans or animal when exposure occurs. This includes infectious substances transported for diagnostic or investigational purposes. Category B infectious substances must be described as "biological substances" and assigned identification number UN 3373. This does not include regulated medical waste. [49CFR173.134(a)(1)(ii)]

Training

IATA regulations are the more stringent set of rules for shipping biohazardous substances. By being trained and following IATA guidelines, shippers can be confident of conforming to all national regulations. Formal training for shipping Category B substance is not required as long as an ethical and good faith effort is made to educate a shipper as to the best practices of packing and labeling specimens. Conversely, training for shipping Category A substances is highly regulated and requires a passing test score at the conclusion of training to be certified to ship.

Instructions for shipping Category B materials can be found on the University of South Alabama Biosafety website at: http://www.southalabama.edu/researchcompliance/biosafety.html. The module must be completed before testing is allowed. At the conclusion of the exam, the score sheet can be printed and returned to Office of Research Compliance and Assurance. Upon completion of the module, individuals shipping such

substances are qualified to do so. Training must be updated every three years [49 CFR 172.704(c)(2)]. At that same location, information is available for those shipping Category A substances. The University requires Saf-T-Pak training for select agent shipping. The Office of Research Compliance and Assurance oversees distribution of the Saf-T-Pak training program.

Section II

Biosafety Program Administration

REGISTRATION OF WORK IN BIOLOGICAL CONTAINMENT LABORATORIES

Responsibilities

The use of biohazardous materials for purposes of research must be registered and approved with the Institutional Biosafety Committee (IBC). The Principal Investigator (PI) is responsible for the initiation and supervision of all potentially biohazardous work and responsible for preparing and submitting a Protocol Application and IACUC/IBC Application form (available at www.irbnet.org) to the IBC.

The Department Chairperson supervising the PI carries the final responsibility of ensuring all departmental activities involving work with potentially biohazardous material and the agents they might contain are registered. All required record keeping, especially for the OSHA Bloodborne Pathogen Standard, must be retained via electronic copy for inspection by the IBC or other authorities.

The IBC Administrator is responsible for reviewing and routing the biohazardous, rDNA, or the synthetic nucleic acids registration form(s) to the IBC, as appropriate. Initial review of these registration forms will be performed by the Committee Administrator to ensure completeness of information provided by the PI, correct assignment of the requested biosafety level as specified in "*Biosafety in Microbiological and Biomedical Laboratories*", OSHA Bloodborne Pathogen Standard (29 CFR 1910.1030), and/or *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules* and the evaluation of the need for the preparation of a special, written Exposure Control Plan (ECP) by the PI. A laboratory specific ECP is necessary giving that every research environment utilizes different layouts, facilities, personnel, procedures, etc. A template for such a plan is available.

The IBC is responsible for:

- Review and approval of biological hazards and safety practices
- Formal approval of registrations by the committee
- Conducting annual inspections of registered research laboratories
- Overseeing responsibility for biosafety training practices
- Reporting any significant problems with or violations of the *NIH Guidelines* and any significant research-related accidents or illness to the appropriate Institutional official and to the NIH Office of Biotechnology Activities (OBA) within 30 days; and
- Following the guidelines for membership defined by NIH with the additional requirement of one representative from the Department of Comparative Medicine.

Registration of Work with Biohazardous Materials

Protocol Submission Process for Biohazardous Materials, rDNA, & Synthetic Nucleic Molecules in IRBNet

All work with biohazardous materials must be registered with the IBC using the Protocol Form and USA IACUC/IBC Application form found at www.irbnet.org. All forms must be fully completed by the PI, co-signed by the Department Chairperson involved, and submitted to the Office of Research Compliance and Assurance via IRBnet.

All applications will be reviewed for completeness, including the PI's signature, Departmental Chairperson's signature, and all other required information / documentation as listed above. Training of the PI and all key personnel can be uploaded into the system. Applications are considered complete once they have training, the IBC Protocol Application, and the On-line wizard form linked or attached. If a more detailed ECP is required, the PI will be contacted. A more detailed ECP is generally required on all large-scale productions (> 10 liters)

of rDNA organisms and for the handling of human pathogens under any special circumstances or in any significant volume.

All registration forms will be presented to the IBC prior to the next scheduled meeting. This will permit time for reflection, group discussion, and final recording of the action taken regarding the protocol application. A decision may be made to route biohazardous agent registrations (not to include rDNA work) for electronic review and vote via IRBNet if the risks of the research are relatively low. These reviews are recorded on the next IBC meeting agenda as having been electronically reviewed by a full committee. The Committee Administrator communicates IBC review outcomes with the PI via electronic notification in IRBNet. If warranted, clarifications and revisions must be addressed and verified prior to project approval. The IBC, at a future date, may review the status of the approved research already approved and, after deliberations, may require additional conditions. Based on changing safety considerations, modifications of the ECP may be deemed necessary. In this event, a memorandum will be written stating any necessary changes.

The PI responsible for the proposed research may be requested to attend the scheduled meeting of the IBC to clarify any problems or to brief the committee on the proposed research. The PI may meet with the Committee or the Chairperson of the IBC to ask for special reconsideration or explanation of committee action.

And changes in PI, personnel, agent, cell line, location modifications, etc. should be filed with the IBC via the Amendment Form in IRBNet.

Registering Work with rDNA Organisms, Synthetic Nucleic Acid Molecules, or Related Activities.

The handling of genetically modified organisms, transgenic animal work, or recombinant DNA work in the U.S. is regulated by guidelines updated by NIH in 2013 titled, "*NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*".

The NIH Guidelines specify practices for constructing and handling:
- Recombinant DNA molecules;
- Organisms and viruses containing recombinant DNA molecules; and
- Synthetic Nucleic Acid Molecules

Any amendment to said guidelines takes immediate precedence over older guidelines.

Scope of rDNA & Synthetic Nucleic Acid Molecules Guidelines

The purpose of the *Guidelines* (section I-A) is to specify the practices for constructing and handling:

- Recombinant nucleic acid molecules
- Synthetic nucleic acid molecules, including those that are chemically or otherwise modified but can base pair with naturally occurring acid molecules, and
- Cells, organisms, and viruses containing such molecules

Small DNA molecules such as oligonucleotides and PCR primers are not included in these categories.

The guidelines define recombinant and synthetic DNA is defined as:

- Molecules that:
    - Are constructed by joining nucleic acid molecules, and
    - Can replicate in a living cell (i.e., recombinant nucleic acids)
- Nucleic acid molecules that are chemically or by other means synthesized or amplified, including those that are chemically or otherwise modified but can base pair with naturally occurring nucleic acid molecules (i.e., synthetic nucleic acids)
- Molecules that result from the replication of those described

The amended *NIH Guidelines* apply to research with synthetic nucleic acids that present biosafety risk equivalent to rDNA research that is subject to NIH Guidelines (described in the next section). Importantly, the *NIH Guidelines* do not cover the chemical synthesis of nucleic acids; research with nucleic acids that are not contained in cells, organisms, or viruses is exempted. The *NIH Guidelines* only apply to synthetic nucleic acids once they have been placed in a biologic system.

Impacts

Laboratory Research

Lab research that meets any of the following criteria must register with the IBC:

- The synthetic nucleic acid molecules you are working with can replicate
- They can generate nucleic acids that can replicate in a living cell
- They can integrate into a host cell's DNA
- They produce a toxin that is lethal for vertebrates at an LD50 of less than 100 nanograms/kilogram body weight
- They synthesize an organism that doesn't naturally occur outside of a laboratory setting (i.e., 1918 H1N1 influenza, wild-type polio virus, etc.)

Clinical Research

Human Gene Transfer is now defined as the deliberate transfer into human research participants of either:

- Recombinant nucleic acid molecules, or DNA, or RNA derived from recombinant nucleic acid molecules, or
- Synthetic nucleic acid molecules, or DNA, or RNA derived from synthetic nucleic acid molecules that meet any one of the following guidelines:
    - Contains more than 100 nucleotides; or
    - Possesses biological properties that enable integration into the genome (e.g., *cis* elements involved in integration); or
    - Have the potential to replicate in a cell; or
    - Can be translated or transcribed

Modified Select Agent Regulations Pertinent to Synthetic Nucleic Acids and Synthetic Organisms (*42 CFR 73*)

Genetic elements, recombinant and / or synthetic nucleic acids, and recombinant and / or synthetic organisms:

i. Nucleic acids that can produce infectious forms of any of the select agent viruses listed at [73.3(b)] or the overlap select agent viruses listed at [73.4(b)]

ii. Recombinant and / or synthetic nucleic acids that encode for the functional form(s) of any of the toxins listed at [73.3(b)] or [73.4(b)] if the nucleic acids:
    a. Can be expressed *in vivo* or *in vitro*, or
    b. Are in a vector or recombinant host genome and can be expressed *in vivo* or *in vitro*

iii. Select agents and toxins listed at [73.3(b)] or [73.4(b)] that have been genetically modified.

Exemptions

Exemptions for rDNA molecules in Section III-F of the *Guidelines* will be maintained. Certain synthetic nucleic acid molecules are exempt because:

- Their introduction into a biological system is not expected to present a biosafety risk that requires IBC review, or
- The introduction of these nucleic acid molecules into biological systems would be akin to the processes of nucleic acid transfer that already occur in nature, so that the appropriate biosafety practices would be the same as those used for the natural organism.

Synthetic nucleic acids meeting the following criteria will be exempt:

i. They can neither replicate nor generate nucleic acids that can replicate in any living cell (e.g., oligonucleotides or other synthetic nucleic acids that do not contain an origin of replication or contain elements known to interact with either DNA or RNA polymerase), and
ii. They are not designed to integrate into DNA, and
iii. They do not produce a toxin that is lethal for vertebrates at an LD50 of less than 100 nanograms per kilogram body weight.

The amended NIH Guidelines *do not cover the chemical synthesis of nucleic acids. Research not contained in cells, organisms, and viruses is exempted*, *thus the chemical synthesis of nucleic acids is exempt*.
Further information regarding exemptions can be located at: NIH FAQs (question 8, re: exemptions and 10, re: chemical synthesis)

Dual Use Research of Concern (DURC)

As per the NIH Office of Biotechnology Activities (OBA) and National Science Advisory Board for Biosecurity (NSABB), Dual Use Research of Concern (DURC) is research that could possibly provide knowledge, products, or technologies that when used inappropriately compromises public health and safety, agricultural crops, and other plans, animals, environments, or materials. To summarize, DURC is research that can be used for benevolent and simultaneously malevolent purposes.

The seven categories outlined by NSABB that might qualify as DURC and should be further scrutinized during design, conduct, and publication are research that might:

- Enhance the harmful consequences of a biological agent or toxin
- Disrupt immunity or the effectiveness of an immunization without clinical and/or agricultural justification
- Confer to a biological agent or toxin resistance to clinically and/or agriculturally useful prophylactic or therapeutic interventions against that agent or toxin or facilitate their ability to evade detection methodologies
- Increase the stability, transmissibility, or the ability to disseminate a biological agent or toxin
- Alter the host range or tropism of a biological agent or toxin
- Enhance the susceptibility of a host population
- Generate a novel pathogenic agent or toxin or reconstitute an eradicated or extinct biological agent

Thus, it is the PI's responsibility to:

- Be aware of the concept of DURC and aware of the risks of such research
- Be knowledgeable about federal oversight policies
- Be forthcoming about their potential DURC
- Ensure all lab staff, students, and other research personnel are trained in DURC issues and mitigation of such issues
- Assess research on an ongoing basis for potential DURC within the research design as well as publication of the research's results

The IBC enforces the oversight of life sciences DURC by including screening questions on the IBC Application form that must be addressed by PIs.

When completing a new protocol application, the PI should respond to the questions to the best of his or her abilities; the IBC review process will determine if the questions were responded to appropriately and follow-up with the PI if need be. The IBC may also recommend additional training to enhance awareness of potential issues and to enhance a culture of responsibility as it relates to those issues.

DURC Training is intended to enhance the knowledge and awareness of PIs, students, and laboratory personnel on recognizing and mitigating risks relative to DURC. The Office of Research Compliance and

Assurance has implemented a 5-step training program for DURC. Training packets can be procured by contacting ORCA.

Training includes:

1. Viewed the NIH's Office of Science Policy Office of Biotechnology Activities video titled "Dual Use Research: A Dialogue" at http://oba.od.nih.gov/biosecurity/biosecurity.html.
2. Thoroughly read the slide presentation developed by Boston University and adopted by the University of South Alabama titled, "Dual Use Research of Concern."
3. Completed the NIH case study PDF titled "The Cases: Objectives for Learning and Discussion" and documented my responses in the space provided below.
4. Printed, read, and retained the NIH OBA document, "United States Government Policy for Oversight of Life Sciences Dual Use Research of Concern."
5. Signed the Dual Use Research of Concern Training Certification document, retained a copy for personal records, and returned a copy to ORCA.

Guidelines for Covered Experiments

The guidelines classify work with rDNA into six main types of experiments:

1. *Experiments that require IBC approval, RAC review, and NIH approval before initiation.*

   Experiments in this category are considered Major Actions and cannot be initiated without the submission of relevant information to the Office of Recombinant DNA Activities (ORCA) and specific approval by NIH. Experiments that involve the deliberate release of rDNA organisms to environment and/or the deliberate transfer of a drug resistance traits or the deliberate transfer of rDNA into humans are strictly controlled and require the authorization of the RAC before work can commence. All relevant information must be submitted to NIH. Details of the proposal will then be published in the Federal Register for 15 days, with review by RAC and specific approval by NIH.

2. *Experiments that require NIH/ORDA and IBC Approval before initiation.*

   These experiments include the deliberate formation of recombinant DNA containing genes for the biosynthesis of toxin molecules lethal for vertebrates at an LD_{50} of < 100 ng, and minor modifications in human gene transfer protocols.

3. *Experiments that require IBC approval before initiation of experiment.*

   Some experiments require approval by the IBC before work commences. These experiments are those using human or animal pathogens (class 2, 3, 4) as host vector systems, experiments where DNA from human or animal pathogens is cloned into nonpathogenic prokaryotic or lower eukaryotic host vector systems, and experiments involving the use of infectious animal or plant DNA etc. in presence of helper virus in tissue culture systems. Experiments involving whole animals or plants or experiments involving more than 10 liters of culture must also be approved by the IBC before initiation of the work.

   Prior to the initiation of the experiment, a registration document must be submitted to the IBC by the PI containing a description of:

   a. Source of DNA.

b. Nature of inserted DNA sequences.
c. Hosts and vectors used.
d. Whether deliberate attempt made to obtain expression of foreign gene, and if so the protein to be produced.
e. Containment conditions specified by NIH.

The IBC will review and approve the experiment before work is initiated.

4. *Experiments that require IBC notification simultaneous with initiation.*

Certain types of work do not meet the criteria specified above. In these cases, work registration documents must be filed with the IBC and reviewed, but approval is not required before the commencement of work. All experiments not included in A, B, C or E can be carried out at BSL- 1. For experiments in this category, a registration document must be dated and signed by the Principal Investigator and filed with the IBC. For example, experiments in which all components are derived from non-pathogenic prokaryotes and non-pathogenic lower eukaryotes and fall under this section may be conducted at BSL- 1. Experiments involving whole plants, and those involving the formation of recombinant DNA molecules containing no more than 2/3 of the genome of any Eukaryotic virus may be propagated at BSL- 1. The Biosafety Officer or the IBC Chair can be contacted for assistance in making this decision.

5. *Experiments that are exempt from the procedures of the guidelines.*

Some work with rDNA is classified as "Exempt" under the guidelines provided certain basic requirements are satisfied. In these cases, no notification or registration with the IBC is necessary, but the PI must keep a list of the specific work that is exempt in a departmental file available for inspection.

The following rDNA molecules are considered to be exempt:

a. Those that are not in organisms or viruses.
b. Those consisting entirely of DNA segments from a single non-chromosomal or viral DNA source (though one or more of the segments may be a synthetic equivalent).
c. Those consisting entirely of DNA from a prokaryotic host including its indigenous plasmids or viruses when propagated only in that host (or a closely related strain of the same species) or when transferred to another host by well-established physiological means.
d. Those that consist entirely of DNA from an eukaryotic host including its chloroplasts mitochondria, or plasmids (but excluding viruses) when propagated only in that host (or a closely related strain of the same species).
e. Certain specified rDNA molecules consisting entirely of DNA segments from different species that exchange DNA by known physiological processes.
f. Other classes of rDNA molecules that NlH finds do not present a significant risk to health or the environment (See Attachment 7).

6. *Experiments that Require Institutional Biosafety Committee and Institutional Review Board Approvals and RAC Review before Research Participant Enrollment*

For an experiment involving the deliberate transfer of recombinant DNA, or DNA or RNA derived from recombinant DNA, into human research participants (human gene transfer), no research participant shall be enrolled) until the RAC review process has been completed).

For a clinical trial site that is added after the RAC review process, no research participant shall be enrolled at the clinical trial site until the following documentation has been submitted to NIH OBA: (1) Institutional Biosafety Committee approval (from the clinical trial site); (2) Institutional Review Board approval; (3) Institutional Review Board-approved informed consent document; (4) curriculum vitae of the principal investigator(s) (no more than two pages in biographical sketch format); and (5) NIH grant number(s) if applicable.

Roles and Responsibilities

To comply with these guidelines, USA must have in place and implement policies for work with rDNA. To oversee this work, the Office of Research Compliance and Assurance has responsibility to ensure compliance with these guidelines. The members of the IBC must be trained in the requirements of the guidelines, and report to HHS Office of Biotechnology Activities if any significant problems with the program. The IBC is also responsible for determining the necessity for health surveillance for those staff who work with rDNA.

HHS and USDA Select Agents and Toxins
7 CFR Part 331, 9 CFR Part 121, and 42 CFR Part 73
Updated: 12-14-2012

HHS SELECT AGENTS AND TOXINS

Abrin
Botulinum neurotoxins*
Botulinum neurotoxin producing species of *Clostridium*
Conotoxins (Short, paralytic alpha conotoxins containing the following amino acid sequence $X_1CCX_2PACGX_3X_4X_5X_6CX_7$)
Coxiella burnetii
Crimean-Congo haemorrhagic fever virus
Diacetoxyscirpenol
Eastern Equine Encephalitis virus[1]
Ebola virus
Francisella tularensis
Lassa fever virus
Marburg virus*
Monkeypox virus[1]
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
Saxitoxin
South American Haemorrhagic Fever viruses:
- Chapare
- Guanarito
- Junin
- Machupo
- Sabia

Staphylococcal enterotoxins A, B, C, D, E subtypes
T-2 toxin
Tetrodotoxin
Tick-borne encephalitis complex (flavi) viruses:
- Far Eastern subtype
- Siberian subtype
- Kyasanur Forest disease virus
- Omsk hemorrhagic fever virus
- Variola major virus (Smallpox virus)* Variola minor virus (Alastrim)* *Yersinia pestis**

OVERLAP SELECT AGENTS AND TOXINS

*Bacillus anthracis**
Bacillus anthracis Pasteur strain
Brucella abortus
Brucella melitensis
*Brucella suis Burkholderia mallei** *Burkholderia pseudomallei** Hendra virus
Nipah virus
Rift Valley fever virus
Venezuelan Equine Encephalitis virus[1]

USDA Select Agents and Toxins

African horse sickness virus
African swine fever virus
Avian influenza virus[1]
Classical swine fever virus
Foot-and mouth disease virus*
Goat pox virus
Lumpy skin disease virus
Mycoplasma capricolum[1]
Mycoplasma mycoides[1]
Newcastle disease virus[1], [2]
Peste des petits ruminants virus
Rinderpest virus*
Sheep pox virus
Swine vesicular disease virus

USDA PLANT PROTECTION AND QUARANTINE (PPQ) SELECT AGENTS AND TOXINS

Peronosclerospora philippinensis (*Peronosclerospora sacchari*)
Phoma glycinicola (formerly *Pyrenochaeta glycines*)
Ralstonia solanacearum
Rathayibacter toxicus
Sclerophthora rayssiae
Synchytrium endobioticum
Xanthomonas oryzae

**Denotes Tier 1 Agent*

[1] Select agents that meet any of the following criteria are excluded from the requirements of this part: Any low pathogenic strains of avian influenza virus, South American genotype of eastern equine encephalitis virus , west African clade of Monkeypox viruses, any strain of Newcastle disease virus which does not meet the criteria for virulent Newcastle disease virus, all subspecies Mycoplasma capricolum except subspecies capripneumoniae (contagious caprine pleuropneumonia), all subspecies Mycoplasma mycoides except subspecies mycoides small colony (Mmm SC) (contagious bovine pleuropneumonia), any subtypes of Venezuelan equine encephalitis virus except for Subtypes IAB or IC, and Vesicular stomatitis virus (exotic): Indiana subtypes VSV-IN2, VSV-IN3, provided that the individual or entity can verify that the agent is within the exclusion category.

[2] A virulent Newcastle disease virus (avian paramyxovirus serotype 1) has an intracerebral pathogenicity index in day-old chicks (Gallus gallus) of 0.7 or greater or has an amino acid sequence at the fusion (F) protein cleavage site that is consistent with virulent strains of Newcastle disease virus. A failure to detect a cleavage site that is consistent with virulent strains does not confirm the absence of a virulent virus.

OSHA BLOODBORNE PATHOGENS STANDARD (29 CFR 1910.1030)

The OSHA Bloodborne Pathogen Standard was proposed to reduce occupational exposure to Hepatitis B virus (HBV), Human Immunodeficiency Virus (HIV), and other bloodborne pathogens. The aim of this standard is to minimize or eliminate risks using a combination of engineering and work practice controls, personal protective clothing and equipment, training, medical follow up of exposure, vaccination, and other provisions.

Exposure Control Plan

The key requirement of the OSHA Standard is to establish a written Exposure Control Plan (ECP) designed to eliminate or minimize employee exposure. The ECP describes how USA will comply with the standard, including aspects of vaccination, communication of information to employees, and record keeping. A copy of the ECP is kept in each laboratory by all Principal Investigators and is accessible to and should be reviewed by all employees. The ECP will be updated annually if required by new tasks or activities related to the PI's research or by changes in regulations. A laboratory specific ECP is necessary giving that every research environment utilizes different layouts, facilities, personnel, procedures, etc. A template for such a plan is available in the USA Biosafety Manual and on the Office of Research Compliance and Assurance web page.

Exposure Determination

OSHA requires employers to make an exposure determination for all employees. This is done by assessing exposure risks for standard and emergency tasks employees are required to undertake in their respective work assignments. This biohazardous task evaluation is completed and is reviewed annually for significant changes. To deal safely with these tasks, USACOM has adopted a system recommended by the CDC/OSHA/DHHS Joint Advisory Notice of Oct. 19, 1987, and 29 CFR 1910.1030, which places employees into one of three categories:

Category I: Job classifications where job tasks necessitate routine occupational exposure to human blood, body fluids and tissues and other potentially infectious materials.

*Category II**:* Job classifications where job tasks necessitate occasional occupational exposure to human blood, body fluids of tissues or other potentially infectious materials.

Category III: Job classifications where job tasks involve no exposure to human blood, body fluids or tissues or work with HIV or HBV, and employment does not require performance of Category I or II tasks.

** Note that OSHA recommended this type of categorization in the initial recommendations for the Bloodborne Pathogen Standard of 1991 but dropped Category II and changed Category III [no exposure] to Category II. Many employers, including USA, have elected to retain the categorization into three subgroups to distinguish those who occasionally work with human material [Category II] from those who regularly are at risk of exposure [Category I].

An Exposure Determination is conducted by the PI to facilitate the classification of each new employee by the Supervisor. For the purposes of this standard, any position where an employee performs any task outlined in Attachments 4 and 5 is classified as Category I, II, or III.

It is the responsibility of the principal investigator or the Departmental Chair to ensure all employees are categorized into one of the three categories.

Requirements for Categories

Category I and Category II

Category I and II employees must be provided with biosafety training prior to a potential occupational exposure and annually thereafter. Employees must understand the modes of germ or pathogen transmission, types of protective equipment available, how to handle spills and emergencies, as well as the different categories of pathogens [germs] and review of biohazardous tasks. All notifications, training, and monitoring programs must be documented. USA's biosafety training is available through www.CITIprogram.org.

All category I and II employees must be offered a Hepatitis B vaccination [HBV] within 10 working days of being assigned to a job where an occupational exposure may occur. An employee declining the vaccine must sign a declination form provided by the IBC. The HBV offer stands open to any Category I or II employee at any time free of charge, even if the employee has previously refused the vaccine. USACOM encourages all such employees to take this safe and effective vaccine.

Category I and II employees must follow Universal Precautions when handling blood and body fluids and comply with all aspects of the USA Exposure Control Plan to prevent and restrict accidental exposures to biohazards.

It is the responsibility of the PI or supervisor to ensure that each employee has updated training, has been offered suggested vaccinations, and is familiar with the lab-specific ECP.

Category III.

Category III employees must be aware of their employee biohazard classification category, the Exposure Control Plan (ECP), the meaning of the Universal Biohazard Symbol, and understand that biohazards are handled on site in areas marked with these biohazard emblems. If one's job description is changed to involve tasks where exposure to human materials may occur, the Category III employee's supervisor should change the employee to Category I or II.

Section III

Procedural Controls

INTRODUCTION

This section describes some important safe working practices that should be followed in biohazard areas. Emergency procedures are to be followed in the event of biohazard spills, health surveillance following incidents, and safety tips in conducting phlebotomy and intravenous therapy. The PI or lab supervisor is responsible for providing information to non-scientific staff entering biohazard areas for performing maintenance and repairs.

BIOHAZARD SPILL PROCEDURES

Biosafety Level 1

1. Biohazardous material must be transported between labs in a splash-proof container on a stable cart. If a considerable distance is to be covered, the cart should be equipped with a spill kit containing dry chlorine shock and absorbent material.
2. Appropriate disinfectants in well-marked spill kits must be ready to use in containment areas at all times. Kits are best located near the sink in each lab.
3. Equipment and clothing in areas where a spill has occurred should be decontaminated as appropriate.
4. Waste should be disposed of as outlined within this manual.
5. Wash hands thoroughly.

Biosafety Level 2

Lab scale spills involving BSL-2 and BSL-3 biohazardous agents require a different management philosophy than chemical or radiation spills. Microbiologists who normally handle the infectious agents or materials are most knowledgeable in killing the released material and managing its removal, provided they have know-how, proper personal protective equipment in the area, and an appropriate "spill kit".

For small or medium sized spills with little personnel contamination using BSL-2 agents and some BSL-3 agents, calling in a spill team of specialists like those used to manage radiation or chemical spills is unnecessary. In BSL-2 laboratories, the agent is less likely to be aerosol transmitted, so the best action is to add a sterilant chemical immediately after the spill and confine the spill while the chemical disinfectant is working. Hence, for medium to small spills, those lab personnel who are not contaminated are best informed to clean up these spills.

In the event of a spill, non-contaminated personnel should:

- Don protective gear available in the area, which must include gloves and face protection and may include HEPA masks or positive pressure breathing apparatus depending upon the agent [e.g., Rabies virus requires BSL-2 for routine operations, but BSL-3 where droplet transmission is likely]
- Immediately add bleach or other appropriate disinfectant to the spill
- Limit the spill’s spread with absorbent material.

After waiting for the sterilant to kill most of the microbes, proceed with the clean-up. The guidelines to be used are:

1. Biohazardous material must be transported in a splash-resistant container, fitted with a lid. The lab should be equipped with a spill kit containing dry chlorine shock and absorbent material.
2. Appropriate disinfectants must be ready to use in containment laboratory areas and when materials are being transported on site. The spill kit must be well marked, stocked, and located near the sink or on the transport cart if possible.
3. For small spills absorb and disinfect as appropriate using bleach in the spill kits. Leave the spill covered with disinfectant for 10 minutes or more depending on its volume before cleaning attempting to clean up the waste.
4. If a major spill occurs [liters], notify all workers in the immediate area and evacuate all non-contaminated persons to a clean area. An appropriate spill kit should be used to inactivate and clean up the spill as soon as possible thereafter. Care to avoid further personal exposure with the spill should be taken.
5. Waste should be disposed of as outlined in this manual.
6. Contaminated persons should remain in the BSL-2 lab area and must immediately:

Remove any contaminated clothing and safely store in biohazard bags.

   a. Remove any contaminated clothing and safely store in biohazard bags.
   b. Decontaminate skin areas with appropriate disinfectant.
   c. Wash contaminated skin thoroughly with soap and rinse with large amounts of tap water.
   d. Notify the Biosafety Officer.
   e. Place waste in appropriate biohazard disposal bags for removal; clean and disinfect the surrounding area thoroughly.
7. Report the spill to the laboratory supervisor (who must make a record of it and any subsequent action and send a copy to the Biosafety Officer, c/o Office of Research Compliance and Assurance).

Biosafety Level 3

In all spills or accidental releases involving BSL-3 agents or materials containing these agents, one must immediately don protective breathing apparatus (HEPA mask or positive pressure air pack) and then proceed with the clean-up if not directly exposed. All non-essential, non-exposed personnel should leave the BSL-3 area immediately. Only one or two workers should remain to inactivate the spill when properly equipped to do so. BSL-3 labs have negative pressure air control to provide time for proper and safe disinfection.

1. Biohazardous material should be transported in an approved, closed, splash-proof container.
2. Appropriate disinfectants (e.g., fresh household bleach) must be ready to use in containment areas and when materials are being transported on site. Disinfectants should be freshly prepared and be appropriate for the materials being handled. Dry bleach "shock" is ideal for clean-up of larger spills.

3. Immediately evacuate to the laboratory ante-room if a major spill occurs, and you are not directly contaminated.
4. Remove contaminated gowns, gloves, underclothing, etc. **in the containment room** away from the spill area and near the entrance. Wipe exposed skin with soap and disinfectant. Wash contaminated skin thoroughly with biocide, and then flush the area with tap water. Report the spill to the Biosafety Officer by phone (460-6509) as back up and proceed with the decontamination phase of the clean-up. Persons seriously exposed should not attempt the spill clean-up but should report to the dispensary for medical attention after personal decontamination and delivery of required first aid. Those who will clean-up should then move into the ante-room and don new protective gear and respirator.
5. When properly protected, re-enter the contaminated laboratory, dispense sterilant, limit the area of the spill with absorbent material, cover the spill if possible with absorbent material and again exit the lab, disposing of contaminated gloves and foot protection as medical waste.
6. Immediately report the incident to the supervisor and to the Biosafety Office, c/o Office of Research Compliance.
7. Leave the laboratory sealed for at least 1 hour to allow disinfection time and the aerosols to settle.
8. Wearing appropriate protective clothing and respirator, re-enter the laboratory. Leave all switches "on" to the room ventilation system and in the biosafety cabinets to discharge contaminated air via the HEPA filters.
9. Pick up all contaminated absorbent material with tongs and place in double biohazard bags. Clean up broken glassware with dust pan and disposable scoops or brooms. Dispose of all these items in biohazard waste bags and handle as sharps. Re-treat freshly-diked contaminated areas with fresh bleach. Leave for 8 hours, then enter to fumigate the laboratory.
10. Ensure all contaminated lab coats etc. are autoclaved prior to laundering.
11. Ensure the incident is recorded with the Biosafety Officer.

Biosafety Cabinets

In the event of a biohazardous spill in a biosafety cabinet (Class I or Class II):

1. Keep the extract fan running
2. Start decontamination using a spill kit and disinfectant
3. Leave disinfectant to act for at least 10 minutes or preferably longer
4. Clean and disinfect hands or clothing if necessary
5. After disinfection remove any waste taking care not to spread any further contamination
6. Repeat disinfection of the spill area (including any catch trays used or built into the cabinet)

Centrifuges

Wherever possible, centrifuges should be operated using sealed rotors or buckets which should be opened in a biosafety cabinet.

In the event of a breakage in a centrifuge:

1. Leave the centrifuge with the lid closed for at least 30 minutes to allow aerosols to settle
2. Open the lid and carefully remove any broken glass, plastic, etc., using forceps
   Immerse contaminated tubes, caps, etc., in disinfectant for at least 1 hour
3. Swab down all surfaces with an appropriate disinfectant
4. Remove the rotor or buckets and thoroughly decontaminate
5. Where the breakage is in a sealed rotor, remove it to a microbiological safety cabinet before opening

Accident Reporting

Immediately following an occupational exposure incident involving the use of biohazards, report the potential exposure incident by completing the University's "Report of Accident/Incident" form and provide to the PI or lab supervisor for review, signature, and processing. A copy must be provided to the Office of Research Compliance and Assurance and, if medical evaluation is sought, the health care provider. The Urgent Health Care Clinic is the designated healthcare provider for the University's biosafety program. A supplemental incident report form for BSL-3 workers must be completed to assist in the medical evaluation. This information is obtained from the individual with the potential exposure, the individual's supervisor, the PI and biosafety personnel. The individual's supervisor should be notified as soon as possible following the initial evaluation of the potential exposure. The supervisor will provide appropriate updates to the Office of Research Compliance and Assurance.

ACCIDENTAL EXPOSURE TO HUMAN BLOOD, SERUM, BODY FLUIDS OR TISSUES OR HUMAN IMMUNODEFICIENCY VIRUSES (HIV)

Responsibilities

1. Contaminated employees, with the help of fellow co-workers present, should perform immediate first-aid with the goal of decontaminating the wound or exposure area. If no direct worker-exposure has occurred, disinfecting the spill without further personnel exposures becomes the primary goal.
2. Assuming personal injury has occurred and a real exposure to these biohazards has resulted, the PI or lab supervisor is responsible for ensuring any others (co-workers, cleaning staff, etc.) in the area or in the surrounding area who were contaminated as a result of the accident are treated as per this Standard Operating Procedure. The PI must ensure the emergency procedures are followed. The PI must also secure the offending biohazardous samples for future testing.
3. Security is responsible for responding to the immediate area, notifying the Office of Research Compliance and Assurance (460-6509), and assisting in moving an injured individual to the Dispensary after the appropriate decontamination procedures listed above are completed.

4. The PI or highest supervisor present, if uninvolved in the exposure, is responsible for minimizing the spread of contamination, directing and assisting in appropriate decontamination/disinfection of affected areas and personnel, and assisting the Biosafety Officer, Security, and/or Environmental Safety personnel as required.

Procedure

1. Punctures or cuts by sharps should be cleansed with iodinated surgical soap and/or diluted Clorox bleach (0.5%) or another approved disinfectant as vigorously as possible without causing significant additional tissue injury. The time between the exposure to disinfecting is important, but the injury should be rinsed and retreated with soap and/or bleach at least once. If you are injured from to being splashed to in face, the eyes, nose, mouth, and facial skin should first be rinsed with copious amounts of water; the unbroken skin can then be washed with surgical soap and rinsed; the eyes should not be treated soap or bleach; they should be thoroughly rinsed in an approved eye wash. Immediately seek medical aid from the USAMC emergency room following rinsing procedure. Care should be taken not to worsen the damage to the eyes.
2. The offending sample should be identified and secured to completely contain its biohazardous content to allow for testing. If necessary, the sample should be stored at 4C to prevent its deterioration. If the material is human or non-human primate blood, body fluids or tissues, the sample should be tested immediately for HIV and Hepatitis viruses or Herpes B as appropriate.
3. All personal injuries involving biohazardous materials should be reported to the Biosafety Officer and to the supervisor.
4. The occupational physician should immediately counsel the injured party and attempt to obtain permission to collect a blood sample for antibody and virus testing (Hepatitis viruses, HIV or the specific virus involved, if known.) This will be an acute post-accident sample.
5. A blood sample (15 ml) should be collected and tested as requested by the occupational physician with due consideration for confidentiality of the result(s) and in compliance with established OSHA specified procedures. All test results will remain confidential and will not be released to outside sources without the permission of the employee or unless such is required by applicable law. Permission for the release of test results should be documented or witnessed. Two ml of the serum from the sample should be saved and frozen (-70 C).
6. If permission is not given for testing, a blood sample should still be collected, secured, and stored for future reference in compliance with OSHA guidelines for containment management in work with Class 2 or higher biohazardous agents. The employee's refusal to submit the sample for testing should be documented.
7. If the source sample causing the exposure risk is positive for HIV and/or HBV or other known viruses, the patient should be informed and counseled. If the patient agrees to testing, the worker should be evaluated clinically for evidence of infection with Hepatitis viruses or HIV per the OSHA B.B.P. standard. The required "opinion letter" from the

treating physician must be obtained by the supervisor according to the OSHA BBP standard and filed in the employee accident report.

8. T4(CD4) / T8(CD8) blood lymphocyte profile and blood work-up should be conducted as early as possible post-exposure to human biohazardous material and again at any point following a report of illness.
9. A patient exposed to bloodborne pathogens or who acquired a laboratory infection with these pathogens should receive adequate medical counseling and medical follow-up.
10. Exposed patients who do not show evidence of infection and/ or sero-conversion in twelve weeks should be retested at twelve weeks and at six months post-exposure. These persons should also be given psychological and medical follow-up as needed by the College of Medicine.

BIOSAFETY PRACTICES IN PHLEBOTOMY AND INTRAVENOUS THERAPY

1. Employees must know the Universal Precautions for handling blood, body fluids, and tissues from humans and other primates.
2. While performing phlebotomy, iv therapy, and clean-up, latex gloves, eye protection, and protective lab clothing must be worn at all times. Whenever a potential exists for splashing or aerosolization of blood or body fluids, a face shield, or goggles and mask for basic eye / mucous membrane protection must be worn. Contaminated gloves must be disposed as biohazardous waste.
3. Used needles must not be resheathed, recapped or clipped. Used or contaminated needles or sharps must be disposed in an approved sharp-proof, autoclavable container as biohazardous waste. Broken or contaminated glassware, sharps, or used finger lancets should not be handled.
4. Any spilled blood and body fluids should be removed from the surrounding area with appropriate disinfectant (bleach diluted 1:10; ethanol is not sufficient). Gloves must be worn to clean up spilled blood.
5. All tubes containing human/ primate body fluids, blood smears, and blood must be handled as if contaminated with HIV and HBV. Collection tubes must be placed in approved holders or racks marked with the universal biohazard sign. Filled blood tubes or vacutanors must not be placed in pockets or left loose on desks, trays, tables or trolleys.
6. Hands must be thoroughly washed with soap and water after gloves are removed; fresh gloves must be used for each patient / donor.
7. Employees must understand the exposure control plan and be familiar with the appropriate standard operating procedures for accidental exposure to human/primate materials. The specimens involved must be identified and tested for HIV and HBV or other pathogens as the attending physician requires, and the relevant procedures followed. In the event of an accidental needle stick, the wound should be washed immediately with surgical soap or 1:10 diluted bleach and the source material should be

saved for testing. Such accidents must be reported to the laboratory supervisor and Biosafety Officer as soon as possible.

8. All waste human/primate blood, body fluids, and tissues must be disposed of as biohazardous waste in properly marked biohazard containers. Materials which become contaminated (e.g., paper towels, gloves, etc.) should be disposed as hazardous waste.

INSTRUCTIONS FOR LABORATORY ATTENDANTS AND CONTRACT CLEANERS WORKING IN BIOHAZARD CONTAINMENT LABORATORIES

Contract Cleaners

1. Cleaners are not permitted to enter containment level 3 laboratories.
2. No cleaners may work in containment level 2 areas until work has stopped and all infectious material has been put away. They must receive detailed instructions from their managers prior to commencing work, including procedures to be followed and the person to contact in the event of spillages. If they clean laboratories using human blood, body fluids or tissues or handle medical laundry, they must be classed as Category I risks and trained appropriately by their employer and offered immunization against HBV. Special care should be given to train these workers to recognize the universal biohazard emblem and honor its warning.
3. Suitable protective clothing and durable utility gloves must be provided for use and worn by cleaners at all times in the laboratories.
4. Eating, drinking, smoking, handling contact eye lenses, applying cosmetics are not permitted in the laboratory.
5. Hands must be washed before leaving the laboratory.
6. If clothing is contaminated, they should be removed, suitably packaged and arrangements made by laboratory staff for them to be autoclaved prior to being collected and sent to laundry.
7. All accidents and incidents must be reported to the supervisor who should notify the Office of Research Compliance and Assurance.
8. Only non-biohazardous containers will be emptied by cleaning staff.

Glassware Washing Operations

1. Glassware operations staff are not permitted to work in containment level 3 laboratories. All biohazardous materials removed from BSL-2 and BSL-3 areas must be sterilized or disposed for incineration as medical waste by service personnel specially trained to carry out safe decontamination of the glassware or recycled items to be cleaned.
2. All materials must be made safe by the user or by trained service personnel prior to handing over to glassware operations personnel. All glassware must have been decontaminated before washing is begun.
3. Requests for any other work should be directed to the glassware operations supervisor for approval.

Security

1. In the event of an emergency, security officers may be required to enter containment laboratories. Access may be permitted to BSL-1 and BSL-2 laboratories provided work areas are left undisturbed. Security staff should not touch any equipment or work surfaces. In the event specialist help is required, the laboratory supervisor or Biosafety Officer should be contacted.
2. Security staff must not enter BSL-3 laboratories. In the event of an emergency, the laboratory supervisor or PI should be contacted as well as the Biosafety Officer.

AUTOCLAVE SAFETY CAUTION - AUTOCLAVES MAY CAUSE SERIOUS BURNS
TO PREVENT INJURY:

- Loosen screw caps on bottles and tubes of liquids before autoclaving.
- Check that chamber pressure has returned to zero before opening door.
- Wear eye and face protection.
- Stand behind door when opening it.
- Slowly open door only a crack. Beware rush of steam.
- Keep face away from door as it opens. Escaping steam may burn face.
- Wait 5 minutes after opening door before removing liquids.
- Liquids removed too soon may boil up and out of container, burning operator.

INSTRUCTIONS FOR FACILITIES ENGINEERING PERSONNEL WORKING IN BIOSAFETY LABORATORIES

Access during Normal Working Hours

1. No access is allowed to BSL-3 laboratories unless they have been previously decontaminated.
2. No unsupervised access to BSL-1 and BSL-2 laboratories is allowed during working hours. All biosafety cabinets must be decontaminated by approved CDC procedures before working on them.
3. The laboratory supervisor must ensure the work area has been decontaminated, as well as cleared, and confirm this in writing. The laboratory supervisor must provide warning of any other hazard and detail precautions to be taken.
4. The laboratory supervisor will provide appropriate protective clothing (lab coats, gloves, mask, etc.) and suitable disinfectant as required.
5. On completion of work, the engineer must clean and disinfect his hands and any tools that have become contaminated.
6. Protective clothing must be removed before leaving the laboratory for disposal or decontamination by laboratory staff.

Access Out of Working Hours

1. For BSL-2 and BSL-3 laboratories, as for any other hazardous area, the laboratory supervisor/line manager must be contacted for approval prior to work in the laboratory and the above precautions must be observed.
2. For BSL-1 areas, the laboratory supervisor must approve access and to ensure any relevant safety information is given before commencing work. Hands must be washed before leaving the laboratory.

Section IV

Exposure Control Plan
(Compliance Document for OSHA BBP Standard 29 CFR 1910.1030)

Exposure Control Plan [ECP]
Employer: University of South Alabama
Laboratory Location:
Location Supervisor Name:
Location Manager Name:
Date Modified and Posted in Location Work Area:

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I. Introduction

The University of South Alabama has mandated that each work site develop an independent Exposure Control Plan (ECP) and implement the plan to ensure the safety and health of all personnel determined to have occupational exposure to human blood, body fluids, tissues, and other potentially infectious materials in their job assignments.

The University of South Alabama requires that this Exposure Control Plan (ECP) be updated to identify the job classification and category assignment for this work site and all personal at risk of infections with human bloodborne pathogens. The ECP must identify the duties, task and procedures associated with each job classification and category assignment where occupational exposure to bloodborne pathogens is most likely to occur. Employees performing these biohazardous tasks must comply with this work site ECP and the OSHA Standard.

The University of South Alabama requires that all personnel have access to a hard copy of the updated Exposure Control Plan for review before and after work assignments where the training will be addressed. The ECP must be updated at least annually and whenever necessary to reflect new or modified tasks and procedures that affect occupational exposure to reflect new or revised employee positions with occupational exposure and to review the exposure incidents that occurred since the previous update.

II. Responsible Persons and Their Duties

Responsible Person(s)	Duties
Institutional Biosafety Committee	Develop and maintain ECP (except Appendix A)
Departments/Lab locations	Develop and maintain Appendix A (site specific plan)
Supervisors, Managers, Department Chairs, Directors	Ensure employees comply with this ECP and with the provisions of the OSHA BBP Standard

III. Exposure Determination

This ECP plan covers all employees who may reasonably be anticipated to be at risk for exposure to human blood, or other potentially infectious materials (OPIM). Principal Investigators must determine whether an employee has the potential for exposure without considering the use of personal protective equipment (PPE). Employees determined to be at risk for exposure must be offered the Hepatitis B vaccine at no charge to the employee and must receive annual Bloodborne Pathogens training.

Check the job classifications in the lab with potential for exposure to human blood/OPIM:

- ☐ Laboratory/ Research Instructor
- ☐ Laboratory/ Research Technician
- ☐ Laboratory Manager
- ☐ Post-Doctoral Fellow
- ☐ Professor
- ☐ Research Associate
- ☐ Other (specify): _____
- ☐ Student (specify): _____

Check the tasks and procedures performed by the employees listed above in which occupational exposure occurs:

- ☐ Handling and manipulating human blood or OPIM
- ☐ Other (specify): _____

IV. Methods of Compliance

Principal Investigators and all staff will comply with the OSHA Bloodborne Pathogens Standard 29 CFR 1910.1030 using the following methods:

A. Universal Precautions

All human blood and Other Potentially Infectious Material (OPIM) are considered contaminated with bloodborne and other pathogens. Employees must avoid direct contact with human blood, and OPIM to avoid exposure to bloodborne and other human pathogens.

B. Engineering and Work Practice Controls

Engineering controls and safe work practices will be used to minimize exposure to human blood, and OPIM by altering the physical manner in which specific tasks are performed (e.g., prohibiting recapping of needles, limiting the use of needles, eliminating glassware from lab operations and placing it with plastic ware, requiring hand washing after working with biohazardous materials, etc.). Safe work practices are reviewed by the Institutional Biosafety Committee (IBC).

1. **Personal protective equipment.**
   If the potential for exposure remains in spite of work practice and engineering controls, personal protective equipment (PPE) must be used. The University of South Alabama will provide, clean, and dispose of PPE at no cost to the employee. PPE must be worn during procedures in which human blood or OPIM exposure to skin, eyes, nose or mouth is reasonably anticipated. PPE must be selected based on the type of exposure anticipated. PPE must cover all body parts and street clothes that may be exposed and must prevent soak through. Non-latex gloves should be available for employees with latex sensitivity or allergy. PPE and personal clothing must be removed if they become contaminated. Disposable PPE that is contaminated must be discarded as biomedical waste. Reusable PPE such as goggles and lab coats that have become contaminated must be placed in a specified container for decontamination and reprocessing.

2. **Lab coats and gowns**. Laboratory coats are to be worn by all faculty, staff, students, or visitors when handling biologicals in open bench laboratories and secure laboratory suites. Laboratory coat use outside of these areas should be minimized, unless transportation of materials to and from other laboratories requires PPE. Laboratory coats **are not allowed** to be worn in public, patient or administration areas. Laboratory coats **are not allowed** to be worn in kitchens, break rooms, areas where food is store and prepared. Laboratory coats **are not allowed** in the elevators, conference room areas, or the bathrooms.

   a. **Gloves.** Gloves must be worn when hands may come in contact with **biohazards,** human blood, or OPIM, contaminated items or surfaces. Gloves must be worn when handling animals. Gloves must be replaced as soon as feasible if they are torn or contaminated. Disposable (single use) gloves cannot be reused. Utility gloves may be decontaminated for reuse, but must be discarded if they are cracking, peeling or show other signs of deterioration. Wearing of gloves outside the laboratory should be minimized. If gloves are required to transport biohazards between labs, fresh or decontaminated gloves should be used.

   b. **Protection for eyes, nose and mouth**. Work must be performed in a certified Biological Safety Cabinet; masks and eye protection (goggles or face shields) must be worn whenever splash or spray of human blood, or OPIM to the face is anticipated.

3. **Hand washing**. Hands must be washed with soap and water after contact with specimens, as soon as possible after removing PPE and whenever they become contaminated with human blood, or OPIM. Antiseptic hand cleaner may be used if soap and water are not available, but hands must be washed with soap and water as soon as feasible.

4. **Personal hygiene**. Eating, drinking, smoking, applying cosmetics or lip balm, or handling contact lenses in the lab is not permitted.

5. **Food**. Food and drink must not be stored in labs where human blood or OPIM are present.

6. **Pipetting**. Mouth pipetting is not permitted.**Minimization of aerosols**. Splash, spray, spatter, or generation of droplets must be minimizedduring any procedure that involves human blood, or OPIM. If spattering or generating aerosolsis reasonably anticipated, work should be performed in a certified Biological Safety Cabinet, oreye protection plus a mask or face shield must be worn to prevent an exposure to the mucus membranes of the eyes, nose, and mouth.

7. **Sharps handling**. Bending, recapping, or removing needles is prohibited, except under specific, infrequent circumstances. If recapping, bending, or removing needles or other sharps are required by a specific procedure and no alternative is feasible, then a one-handed scoop technique, mechanical device, or forceps must be used. Written justification supported by reliable evidence must be included as an addendum to this Exposure Control Plan. This justification must state the basis for the Principal Investigator's determination that no alternative is feasible and must describe the specific procedure that requires the recapping, bending, or breaking of needles or other sharps. Disposable sharps must be placed in a plastic sharps container as soon after use as possible. Sharps containers must be easily accessible, with the opening visible, as close as possible to the area where sharps are used and maintained upright during use. Sharps containers must be promptly closed, removed, and replaced when they are ¾ full and placed in a red biohazard bag and placed in the medical waste container. Reusable sharps, such as surgical instruments and large bore reusable needles pose the same exposure hazard as disposable sharps and must be handled in a manner similar to disposable sharps until they are reprocessed. The container used for temporary storage of contaminated reusable sharps must be puncture resistant, and labeled as Biohazard.

8. **Safe Medical Devices**. Safe medical devices are used to prevent percutaneous injuries (examples may include needleless devices, shielded needle devices or plastic capillary tubes). The Principal Investigator is responsible for involving employees in the selection of effective engineering controls and implementing the use of items that would eliminate or minimize exposures.

9. **Specimen Transport on Grounds**. For transport to sites within the grounds of University of South Alabama, specimens of human blood and OPIM must be placed in a secondary leak proof carrier that can contain the contents if the primary container were to leak or break. Carriers must have the biohazard label affixed to the outer surface of the transport container.

10. **Servicing contaminated equipment.** Before servicing or shipping, contaminated equipment **used directly to handle, process, culture, incubate, and store biohazardous materials must be decontaminated,** if possible. If it is not possible to decontaminate equipment, it must bemarked with a biohazard label describing what parts remain contaminated.

11. **Central reprocessing of contaminated reusable supplies equipment**. Supplies and equipmentreturned to a central facility (e.g. department washroom or autoclave room) for

decontamination and reprocessing must be put in a plastic bag or closeable container and marked with a biohazard label.

12. **Housekeeping.** The workplace must be maintained in a clean and sanitary condition. Human blood, or OPIM spills must be cleaned up immediately with a freshly made 1:10 bleach solution or other approved disinfectant using appropriate established spill clean-up procedures.

13. **Equipment and Working Surfaces**. Contaminated work surfaces must be disinfected with 1:10 freshly made dilution of bleach or an alternative approved disinfectant. The decontamination of work surfaces must be done as soon as possible when contaminated with human blood, or OPIM, after completing procedures or at the end of the work shift if the surface may have become contaminated since the last cleaning. Temporary coverings (plastic backed paper, plastic wrap, etc.) over bench tops, equipment and other surfaces must be removed and replaced as soon as possible when contaminated or at the end of the work shift if the surface may have become contaminated since the last cleaning.

14. **Regulated Medical Waste**. Regulated Medical Waste is disposed of by University of South Alabama in accordance with the Alabama Department of Environmental Management (ADEM) regulations. See biomedical waste policy located on the Biosafety website at: http://www.southalabama.edu/com/research/biosafety.shtml

V. Communication of Hazards to Employees

1. **Labels.** Biohazard warning labels must be affixed to refrigerators, freezers, incubators, and other vessels used for storing human blood, or OPIM. Containers used for transporting human specimens beyond the immediate work area must have the biohazard label affixed to the outer surface of the transport container. **Biohazard labels are required on areas and equipment used to directly handle, process, culture, incubate, and store human blood or OPIM.**

VI. Hepatitis B Vaccination Policy

Employees identified as having potential for exposure to human blood or OPIM must be offered the Hepatitis B vaccine at no charge to the employee. The vaccination is a series of three injections given at approximately 0, 1, and 6 months. A routine booster dose is not recommended, but will be given at no charge if the U.S. Public Health Service (PHS) recommends it in the future.

- *The vaccine must be offered within 10 working days of initial assignment to a job category where exposure may occur.*

- *Employees who decline the Hepatitis B vaccine must sign a statement of declination. Principal Investigators must keep a copy of this declination statement on file.*

- *The Urgent Health Care Clinic serves as the healthcare provider and scheduler of the vaccination series.*

VII. Procedures for Exposure Incidents

An exposure is defined as: blood or OPIM contact with broken skin, eyes, nose, mouth, other mucous membranes, a percutaneous injury with a contaminated sharp, or contact with blood or OPIM over a large area of apparently intact skin.

In the event of exposure:

1. Wash the area with soap and water or flush eyes, nose or mouth with large amounts of water for 15 minutes.
2. All exposures must be reported to the immediate supervisor. The Supervisor/Manager will review the report to determine if any additional information is required before; (i) closing the report; or (ii) if medical treatment is required submitting the incident to the Healthcare provider electronically. The report is copied to the Supervisor/Manager, Urgent Health Care Clinic (Healthcare provider), and the Office of Research Compliance and Assurance. Medical personnel will advise exposed employee as to when they should report to the clinic for a post-exposure follow up evaluation if needed.
3. All reported incidents are documented in the annual Institutional Biosafety Committee (IBC) inspection report. If there are any noted trends in reported incidents, these may be used as topics for educational sessions.

A. Evaluation and Treatment of Exposures

The evaluation and treatment of an exposure is confidential and will be given by or under the supervision of a licensed physician and will follow an established protocol in compliance with OSHA standard 29 CFR 1910.1030, U.S. Public Health Service and CDC guidelines. Evaluation and treatment of exposures are managed by Urgent Health Care Clinic.

If the infectivity status of the source individual is unknown and blood is available, it will be tested for HIV, hepatitis B and C in accordance with state law. The exposed employee will be told what the test results are and what they mean.

If the employee consents, his or her blood will be tested as soon as possible after exposure to provide baseline hepatitis B, C and HIV status. If the employee does not consent to HIV testing, the sample will be stored for 90 days and tested if the employee consents in that time period.

Post-exposure prophylaxis will be offered to exposed employees when medically indicated and as recommended by the US Public Health Service. Counseling and medical evaluation will be offered for any reported illnesses the employee develops as a result of the exposure.

B. Documentation of Circumstances

Documentation of the circumstances surrounding the exposure incident is required and allows for the identification and correction of occupational hazards.

VIII. Employee Training

All employees who may have the potential for occupational exposure to human blood, or OPIM must complete Bloodborne Pathogens training when occupational exposure may take place and annually thereafter. Annual retraining is completed via an online program through the Collaborative Institute Training Initiative located at https://www.citiprogram.org .

IX. Recordkeeping Procedures

Medical records required by the OHSA Bloodborne Pathogen Standard includes the employee name, job title, and classification for work with potentially infectious materials, and Hepatitis B vaccination status for all employees at risk for occupational exposure to human blood or other potentially infectious materials. When an exposure incident occurs, the results of all post-exposure testing, information that is provided to Urgent Health Care Clinic and the post exposure opinion letter confirming that all requirements of the OSHA Standard for exposed patients has been done must be documented and filed. All of these records must be retained for duration of the employee's employment plus 30 years. The Office of Research Compliance and Assurance will track all employees who complete bloodborne pathogen training via IRBNet. All PIs and employees must load and link completed training in to IRBNet. Training records will be maintained for at least 3 year in IRBNet.

APPENDIX A
Site Specific Information

Outline for customizing the Exposure Control Plan:

1. Determining occupations at risks of exposure
   (i.e., outlining jobs and tasks performed in the lab that pose potential employee exposure)
2. Identification of biohazard(s) and containment level
3. Documenting site specific engineering controls
4. Documenting site specific work practices
5. Development of clean-up and exposure response procedures *(i.e., chemical disinfectants)*

Section V

Select Agents and Toxins

CDC: 42 CFR Part 73 Possession, Use, and Transfer of Select Agents and Toxins
USDA: 7 CFR Part 331, 9 CFR Part 121 Agricultural Bioterrorism Protection Act of 2002; Possession, Use and Transfer of Biological Agents and Toxins

Safety, Security, and Compliance

The Centers for Disease Control and Prevention is required to regulate the possession of biological agents and toxins that have the potential to pose a severe threat to public health and safety. Laboratories with select agents must comply with University of South Alabama policies and federal regulations and is managed through the Biosafety Office. This regulation addresses the security of select infectious agents, toxins, and genetic elements.

This information has been created to assist with new safety, security and compliance measures. **Use the list of select agents and their exemptions to determine if you fall under the new application requirements.** Most notably, new regulations require:

- Registration for possession of agents
- Application to the Department of Justice for individuals working with agents
- Additional security requirements as referenced in the newly published "Laboratory Security and Emergency Response Guidance for Laboratories Working with Select Agents"

➢ Why is There a Select Agents Law?

This law focuses on the possession of materials that are not uncommon in biomedical research labs, and calls for the Department of Health and Human Services to be more aggressive in tracking individuals who have them. "The Antiterrorism and Effective Death Penalty Act of 1996," which became effective on April 15, 1997, and the "Uniting and Strengthening America by Providing Appropriate Tools Required to Intercept and Obstruct Terrorism Act (USA PATRIOT Act) of 2001" establish provisions that regulate the possession, usage, or transfer of hazardous agents The law was designed to (1) establish a system of safeguards to be followed when specific agents are transported; (2) collect and provide information concerning the location where certain potentially-hazardous agents are transferred (3) track the acquisition and transfer of these specific agents; and (4) establish a process for alerting appropriate authorities if an unauthorized attempt is made to acquire these agents. The directive also places additional shipping and handling requirements on facilities that transfer or receive select infectious agents.

➢ Management of Select Agents

USA facilities that use, handle, transfer, receive, or store select agents must:

- Register and receive approval of research project with the Institutional Biosafety Committee.
- ORCA evaluates registration and determines if CDC or USDA registration is required. Some Select Agents are exempt from the standard. *See Attachment 11 for USA's exempt agent SOPs*. Compliance with USA's Laboratory Security and Emergency Response Procedures for Select Agents and all CDC approved procedural plans.

- Ensure laboratory has a Chemical Hygiene Plan that addresses personal protection, training and safe practices in place when working with select agents/toxins.

➢ **Destruction and Disposal of Select Agents:**

Disposal of any Select Agent must be in accordance with 42 CFR Part 72 titled "Additional Requirements for Facilities Transferring or Receiving Select Agents". The University of South Alabama's guidelines for destruction of select agents/toxins are as follows:

Safety Precautions:
Destruction procedures should be performed in a laboratory hood or a biological safety cabinet. Personal protective equipment for all procedures should include at a minimum the following: a) disposable long sleeved protective lab coat or gown; b) gloves; and c) eye protection

Bacteria and Viruses:
Please refer to USA's Biomedical Waste Policy and Disposal Chart for destruction of bacteria and viruses located in Attachment 9.

Toxins:
The toxins listed below may be destroyed in varying concentrations of sodium hypochlorite and sodium hydroxide. Please consult with the Office of Safety and Environmental Compliance (SEC) at 460-7070 for inactivation.

T-2 Mycotoxin	Saxitoxin
Ricin	Botulinum neurotoxin
Microcystin	Staphylococcal enterotoxin B (SEB)
Tetrodotoxin	Palytoxin
Brevetoxin (PbTx-2)	

Use of a fume hood may be utilized with lower sash to lowest possible sash height for safe and effective work. The hood should not be used for any other purpose during this procedure.

- In fume hood, place plastic backed absorbent paper on bottom of hood.
- The Select Agent Toxin should be in a solution in primary container.
- Arrange primary container in secondary container (e.g., beaker).
- Dispense the same volume of sodium hypochlorite or sodium hypochlorite/sodium hydroxide solution depending on toxin to destroy. Do not put cap on primary container.
- Allow 30 minutes exposure time.
- After destruction, seal the top to the primary container and put into a zip-lock plastic bag. Label as inactivated with toxin name included. Contact SEC (460-7070) for disposal as hazardous waste.
- Upon destruction of the select agent toxin, the investigator and the Responsible Facility Official (RFO) must document its secure storage, depletion, or destruction.

- Inactivation must occur on-site.

Additional Recommendations –

- Exposure for 30 minutes to 1.0% sodium hypochlorite is an effective procedure for laboratory working solutions, equipment, animal cages, and working areas for inactivation of saxitoxin, tetrodotoxin, microcystin, palytoxin, ricin, botulinum neurotoxin, palytoxin, and staphylococcal enterotoxins (SEB).
- Autoclaving can be used with protein toxins (ricin, botulinum toxin, and SEB), but should NOT be used with any of the low molecular toxins.

Ricin, Botulinum toxin, and SEB (Autoclave Option):

Use autoclave for heat destruction. As stated above, autoclaving can be used with protein toxins.

- In a fume hood or biological safety cabinet, unfasten cap of primary container
- Place primary container into secondary container
- Place container into biohazard autoclavable bag
- Autoclave at 121 C for 45 minutes on liquid cycle
- Following autoclaving, allow time for materials to cool
- Discard as infectious waste (Consult SEC at 460-7070 for additional information)
- Upon destruction of the select agent, the investigator and the Responsible Facility Official (RFO) must document its secure storage, depletion or destruction. Inactivation must occur on-site.

Additional Information:

- Contact the Office of Safety and Environmental Compliance at 460-7070 for additional information on procedures for the destruction of select agents and toxins.

Sources:

University of Pennsylvania

Morin, R.S., and Kozlovac, J.P. 2000. Biological Select Agents, p. 261-272. In D.O. Fleming and D.L. Hunt (ed.), Biological Safety, Principles and Practices. ASM Press, Washington, D.C.

Guidance Documents:

http://www.selectagents.gov/ (CDC Select Agent Program site)
http://www.cdc.gov/od/sap/addres.htm (CDC Select Agent –Additional Resources)
http://www.cdc.gov/od/eaipp/ (Importation Permits for Etiologic Agents)

Laboratory Security and Emergency Response Procedures for Select Agents

CONTACTS:

Samuel J. Strada, Ph.D.
Responsible Facility Official
251-460-6041

Dusty Layton
Director, Research Compliance and Assurance
Alternate Facility Official
251-460-6625

Mr. Bill Guess
Director, Safety and Environmental Compliance
251-460-7070

The Laboratory Security and Emergency Response procedures have been adapted from Appendix F of the 5th edition of the CDC/NIH publication entitled "Biosafety in Microbiological and Biomedical Laboratories (BMBL)". These guidelines are intended for laboratories where select agents are used or stored. Appendix F of the BMBL is being revised to include biosecurity policies and procedures in meeting the regulatory mandate of 42 CFR 73 and will include information regarding personnel, risk assessments and inventory controls.

A. Laboratory Security Planning

1. Involve safety and security experts in the evaluation and development of recommendations for given facility or laboratory.
2. Review security practices regularly. Principal investigators should ensure that laboratory workers and visitors understand security requirements and are trained and equipped to follow written procedures.
3. Review security practices whenever an incident occurs or a new public health threat is identified.
4. Security plans should receive periodic performance testing to determine their effectiveness. Test procedures can vary from a simple check of keys, locks and alarms to a full scale facility exercise.
5. An annual inspection of laboratory security will be jointly conducted by the Responsible or Alternate Facility Official, Principal Investigator and other parties as appropriate. Inspection results and corrective actions taken will be documented.

B. Select Agent/Toxin Storage Security:

1. Select Agent/Toxin laboratories and storage areas should be separate from the public areas of the building in which they are located.
2. Laboratories and storage areas should be locked when they are not in direct view of laboratory staff.
3. Secure access and monitoring controls via key or electronic locking pass keys, combination key pad and use of lock-boxes to store materials in freezers or refrigerators.
4. The investigator must maintain a personnel list of those with access to locked freezers, refrigerators, cabinets where stocks of select agents/toxins are stored.

Modifications to this list require notification to the Office of Research Compliance and Assurance.

C. Personnel Security Procedures:

1. Background checks are required by the Attorney General's Office through the Department of Justice before new employees are assigned work in the area.
2. Record all entries into these areas, including entries made by visitors, maintenance and service workers into a permanent log book. Visitors will be required to wear "visitor badges" in bio-containment areas where select agents are used.
3. List of individuals working with select agents/toxins must be updated as needed to reflect the addition or removal of employees in this area and submitted to the Biosafety Office. This information is required by the Department of Health and Human Services.

D. Inventory and Accountability:

1. Laboratories must have a specific protocol for handling select agent/toxin sample inventories and must have designated areas for such activities.
2. Inventory of agents should be documented with each use.

E. Select Agent Transfer:

1. Select Agents/Toxins may only be transferred between laboratories that have been registered with the CDC
2. Select agents brought into or out of a laboratory or storage area to another facility must utilize the CDC Form 2 certification process
3. Investigators shipping select agents/toxins must receive training in "DOT Infectious & Diagnostic Materials Shipping".

F. Emergency Response Plan:

In the Event of an Emergency call 511 (University Police)

1. Laboratories must contain agent-specific and site-specific biosafety manuals.
2. Emergency contact numbers should be readily accessible to all personnel working with select agents/toxins.
3. Immediately notify laboratory directors, workers, and Office of Research Compliance and Assurance as biosafety issues occur.
4. All personnel should be knowledgeable of decontamination procedures, emergency medical treatment and first aid.
5. Special procedures should address the hazards of the specific agents.

G. Incident Reporting:

1. Department of Health and Human Services or USDA should be notified immediately if select agents/toxins are discovered missing, released outside the laboratory, involved in worker exposures or infections. Additionally, all incidents should be reported to local and state public health authorities.

Section VI

Biosafety References

BIOSAFETY REFERENCE MATERIALS

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21. USACOM Biological Hazards Safety Manual.

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23. Morbidity and Mortality Weekly Reports 3 7: No.S-4, 1-19. April 1, 1988,

24. Department of Transportation (49 CFR, Parts 171-180) Hazardous Materials Regulations.

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ATTACHMENT 1

Universal Precautions for Handling Human Blood, Body Fluids and Tissues in Research Laboratories

1. Assume **ALL** human blood, plasma, serum, body fluids (semen, saliva, tears, cerebrospinal and amniotic fluid, milk and cervical secretions), and tissues to be contaminated with Human Immunodeficiency Virus (HIV) and/or Hepatitis Viruses (e.g., HBV) or other Bloodborne Pathogens (See attached partial listing). Handle these human biohazards with appropriate care!

2. Gain knowledge--Be prepared:

   a. Personnel should understand their risk categorization before initiating work:

      Category I & II: Personnel occupationally, occasionally or frequently exposed to blood, body and tissues.

      Category III: Personnel never perform tasks with or around such materials.

   b. Be familiar with the CDC/ NIH Manual "Biosafety in Microbiological and Biomedical Laboratories," view biosafety videos and be familiar with the USACOM Biosafety Manuals. Ask your supervisor to explain any procedures or concepts not clear to you ***before*** beginning work.

   c. Category I and II personnel must be offered the Hepatitis B vaccination.

3. ***Remember*****:** The most susceptible route of laboratory infection for HIV and HBV is by accidental needle sticks, contamination of the mucous membranes, or through broken, abraded. or irritated skin. Use appropriate caution and protection to prevent such contact.

4. Avoid spilling, splashing or open aerosolization of human blood or body fluids. Wear latex gloves, protective lab garments and face/eye shields when handling human materials

5. Understand the principles of good microbiological practice ***before*** working with biohazardous materials. Examples include use of aseptic technique, proper decontamination procedures, emergency biohazard spill management, and proper use of biosafety equipment. Develop proficiency ***before*** beginning work.

6. Use Biosafety Level-2 work practices, containment and laboratories when handling human materials where droplet and aerosol production are likely Avoid aerosol generating activities in handling human materials. When such procedures are necessary, use biosafety cabinets or other containment and personal protective equipment.

7. When culturing or manipulating known HIV or HBV, use Biosafety Level-3 (BL-3) procedures. Any procedure which requires concentration of HIV, HBV or other human viruses from human materials should be handled under BL-3 containment and handling conditions. Use appropriate biosafety level conditions (BL-2 or BL-3) when handling non-human primates and other animals inoculated with human pathogenic materials.

8. Dispose of human and animal biohazardous waste or materials in accordance with CDC/ NIH biosafety and institutional guidelines.

9. Decontaminate laboratory protective garments, gloves and protective equipment to render them non-infectious.

10. Clean all work areas and equipment used in handling human biohazardous materials with proven disinfectant (e.g., 1: 10 dilution of Clorox) when concluding work to protect personnel from accidental infection.

11. Assume human serological and biological reagents (e.g., antibody, antigen or antisera) used in the laboratory are contaminated with HIV or other viruses and handle accordingly

12. Understand your facility's medical surveillance program and be familiar with the appropriate standard operating procedures for accidental exposure to human materials. Specific measures must be followed as per CDC/NIH Guidelines in the Universal Precautions. The specimens involved must be identified and tested for HIV and HBV and procedures followed.

13. Report ***every*** accident to your supervisor.

14. Responsibility for instituting, training and monitoring of biosafety practices in laboratories handling human materials, HIV or HBV rests with the Laboratory Director or the designated Principal Investigator (PI). These individuals must categorize positions, provide facilities, biosafety equipment, biosafety procedures, and training to employees accepting such work assignments to permit the safe conduct of the work. These responsible individuals must ascertain the proficiency of the employee in performing the assigned task ***before*** permitting the work to begin.

15. Laboratory personnel have a clear responsibility to fully understand and consistently adhere to the biosafety practices detailed in the Biosafety Manual as well as to the biosafety guidelines detailed here and by the CDC and NIH. Responsibility for conscious or thoughtless non-compliance with or violation of these guidelines falls on the laboratory worker.

ATTACHMENT 2

USA Hepatitis B Vaccination Program

To comply with the OSHA Bloodborne Pathogens Standard, USA will make the following available to employees in Category I or Category II who may be reasonably anticipated to come into contact with blood or other potentially infectious materials during the performance of their job:

1. Vaccine effective against the Hepatitis B virus is available from the Urgent Care Clinic, the medical care provider for the College of Medicine's Occupational Health Program.

2. Employees will are offered the Hepatitis B vaccine, free of charge at the time of initial training. Employees who decline the vaccine must sign the hepatitis B immunization compliance form to record the fact they are declining. The PI is responsible for maintaining records of acceptance or declination of the vaccine.

3. Employees who accept the hepatitis B vaccine should forward the hepatitis B acceptance form to the Office of Research Compliance and Assurance, CSAB 118 scheduling the vaccine or call 460-6509.

4. Employees who have been previously immunized should provide medical records indicating the date and place of vaccination. A medical record of this proof of exemption must be kept on file by the PI.

5. In the event of accidental exposure to Hepatitis B virus, post-exposure medical evaluation and follow up including post -exposure prophylaxis, which may include Hepatitis B vaccination in the case of individuals not previously vaccinated.

ATTACHMENT 3

If Accidental Contact/Exposure Occurs

1. Cleanse the affected skin area immediately with surgical disinfectant soap, diluted Clorox (0.05%), or other approved disinfectant.

2. If exposure is to eyes via splash, rinse eyes for at least 15 minutes with water.

3. Flush exposed tissues or mucous membranes with clean water or physiological saline.

4. Identify and secure the offending sample to contain its biohazardous content and to allow for testing if necessary.

5. Report all exposures as soon as possible to the supervisor/department chair.

6. Appropriate post-exposure evaluation and follow up must be undertaken as per OSHA CFR 29 PART 1910.1030 and USA policy:

    a. Document the route(s) of exposure and circumstances under which the exposure incident occurred.

    b. Identify and document the source individual, test for HIV and HBV (if agreement is obtained) and make results available to employee.

    c. Obtain permission from employee to collect and test their blood for presence of HIV (If consent is given for collection of baseline but not for HIV testing, the sample shall be preserved for at least 90 days, in case the employee elects to have the sample tested).

    d. Provide post-exposure prophylaxis when medically indicated.

    e. Provide employee with counseling by a qualified medical professional and obtain written confirmation these services were offered.

ATTACHMENT 4

Job Categorization

Managers must assign all employees into one of three hazard categories prior to commencing work. The manager may assign employees to any of the hazard groups based on their risk assessment of the work undertaken by the employee. The following lists show those categories to which certain employees should be assigned.

Category I (Regular exposure possible)

Occupational health nurse
Occupational health physician
Phlebotomist
Scientist or lab assistant handling blood/body fluids/tissues or human excrement

Category II (Some exposure possible)

Animal worker handling non-human primate or other animals or their blood, body fluids or tissues injected with human materials.
Emergency Response Team
Site services staff such as: glassware operations, cleaning staff, maintenance workers servicing biohazard labs, specimen packers, etc.

Category III (No exposure required by job assignment)

Secretarial Staff
Administrative Staff
Library Staff
Computing Staff
Food Services
Regulatory Affairs Staff
Clinical Compliance Staff

ATTACHMENT 5

Hazardous Tasks and Operations Listing

Laboratories

Receiving and Processing Operations

1. Clinical Specimen Transport Operations:

    a. Packing, transporting and unpacking of clinical specimens of biohazardous materials.

    b. Handling culture isolates derived from human clinical specimens.

    c. Handling human tissues and cells for culture, pathological, histological or other microscopic examination, including biopsy of specimens, lymphocytes, tumors and necrotic materials.

    d. Handling animal body fluids and tissues from sources injected or exposed to human biohazardous materials.

    e. Handling human tissue or body fluid, reagents, sera, plasma, growth factor or other tissue or body fluid extracts.

2. Specific Tasks of Significant Risk:

    a. Opening packaged, OSHA listed, human biohazardous materials that may have leaked or broken in transit or have been packed by an individual using contaminated gloves.

    b. Packaging human biohazardous materials known to be positive for HIV, HBV or other bloodborne pathogens.

    c. Handling racks or containers previously contaminated with human biohazardous materials.

    d. Clean-up and proper disposal of contaminated packing materials and broken or leaking containers or specimen tubes or other shipping units.

    e. Clean-up of reusable containers used to handle biohazardous materials (shipping containers, transport boxes, etc.) or plastic containers for red biohazard bags that may have leaked when loaded with biohazardous materials.

    f. Laboratory or specimen forms shipped with biohazardous samples that could possibly be contaminated with specimens.

    g. Use and cleaning of pipetting aides, work areas, pour stations, automatic machinery, assembly line belts, robotic systems, tubes, or racks used to distribute or sample specimens.

    h. Handling, processing, cleaning, servicing or repairing of incubators, cold rooms, freezers or other storage/holding areas, or processing equipment (e.g., centrifuges, robotic systems, assembly lines, splash screens, biosafety cabinets, slide makers, microtomes, sample chambers, etc.) that is used to store, process, test or other-wise come into contact with human biohazardous materials.

    I. Handling or cleaning biohazard waste containers or specimen discard containers used to hold human biohazardous materials.

    j. Working in storage areas for biohazard waste (handling waste containers, cleaning floors, moving containers, etc.).

    k. Handling potentially contaminated laundry from areas where human biohazardous materials are used.

    l. Opening improperly labeled packages which may contain human biohazardous materials.

Work Operations Handling Human Biohazardous Materials

1. Testing Operations Involving Human Biohazardous Materials.

a. Placing biohazardous specimens into instruments (e.g., blood or gas analyzers, other instruments or machines such as: flow cytometers, pressurized sampling devices, automatic pipettors, gel analyzers, robotic systems, SMAK machines, microtomes, centrifuges, HPLCs, extraction devices or other type instruments).

b. Sampling and loading serological or separatory /extraction operations.

c. Microbiological culture operations, lymphocyte or other blood component separation operations involving preparation of human blood or body fluids for analysis or further testing.

d. Cleaning, servicing or repair of equipment, waste discharge systems or their components, vacuum lines, vacuum pumps (from lyophilizers, centrifuges, gel dryers, vacuum devices, etc.) used to handle or process human biohazardous materials.

e. Handling or processing of recyclable (washable or cleanable) non-disposable lab-ware items used to handle or contain human biohazardous materials.

f. Processing of biomedical waste (collection, handling, transport, sterilization-process, cleaning of waste containers) or other biohazardous materials.

g. Handling, labeling, processing, storage or retrieval of human biohazardous materials.

2. Specific Tasks Using Human Biohazardous Materials:

a. Pipetting, pouring or other type of distributive or sampling operation.

b. Centrifugation (includes sample preparation, loading of sample into centrifuge container, centrifugation step and opening of centrifuge and centrifuge container), column chromatography (includes sample preparation, loading of column, collection of sample eluent and handling of separated fractions and purified materials), chemical extraction (includes sample preparation, extraction process and handling of all end product materials). in all cases, assume the material is biohazardous unless the process used is proven to render the material non-infectious.

c. Clean-up and decontamination of work areas, instruments, equipment or other materials which may have come in contact or has been contaminated with human biohazardous materials.

d. Clean-up and decontamination of biohazardous spills, sharps clean-up, or biohazardous waste disposal procedures.

e. Determination and recording of results handling potentially contaminated test equipment, culture plates, instruments or other devices used in the biohazardous operation.

f. Any step in the phlebotomy or bleeding of human patients or of animals known to be intentionally exposed to human pathogens (includes venipuncture, finger sticks, cut-downs, ear sticks or other invasive procedure which might result in the worker becoming exposed to human blood or body fluid).

g. Needle/ syringe or other sharps handling and disposal procedure involved where these devices have been exposed to human biohazardous materials.

h. Microbiological operations involving human biohazardous materials.

I. Serological testing procedures involving human biohazardous materials.

j. Animal tissue/blood harvesting, processing, sampling and disposal activities involving human biohazardous materials.

k. Handling, sampling and disposal of animals that have been challenged or injected with human biohazardous materials.

l. Removal, decontamination, containment and disposal of personal protective equipment (e.g., gloves, lab coats, respirators, masks, goggles, disposable lab attire, shoe covers, or other lab wear).

Large Scale Units Processing Biohazardous Materials

All activities included above in "Laboratories" as well as the following:

1. All scale-up procedures for the culturing of cells, tissue culture and/or fermentations involving the use of human biohazardous materials.

2. All handling of equipment (fermentors, centrifuges, transfer lines, closed system chromatography, etc.) which may be potentially contaminated with human biohazardous materials.

3. All waste lines leading to holding tanks and sterilization units used to sterilize or otherwise treat (e.g., autoclave, chemical sterilization or other approved method of sterilization).

4. All liquid and solid biohazardous wastes generated until the waste has been rendered non-infectious by a proven method.

Vivarial (Animal Work) Procedures

Activities involving the use and handling of animals which have been injected or otherwise contaminated with human biohazardous materials as follows:

1. Handling and care of animals used in the challenge, testing or which have otherwise been injected with human biohazardous materials.

2. Handling or processing of blood, tissue or body fluids of animals which have been contaminated with human biohazardous materials (e.g., autopsy, necropsy, non-fixed tissue mount, cell culture, etc.).

3. Handling, processing and/ or treatment of all wastes generated from animals contaminated with human biohazardous materials (e.g., excreta, urine, bedding, tissue, etc.).

4. Handling of all equipment, instruments (surgical sharps), syringes and needles which may have become contaminated by human biohazardous materials.

5. Routine cleaning of all facilities (cages, pens, rooms, etc.) where animals which have been contaminated with human biohazardous materials.

6. Clean-up of any spill of biohazardous materials associated with the work performed in the animal area.

Emergency Response/Medical Staff

1. Employees who, as part of their job, are required to respond to emergencies where there is the possibility of exposure to human blood or other body fluids are categorized as Category I personnel and must follow the "Universal Precautions" and comply with the USACOM Exposure Control Plan related to human bloodborne pathogens and the OSHA Standard.

2. Medical personnel who are exposed to human blood or other body fluids are categorized as Category I and II personnel and must adhere to the USACOM Exposure Control Plan and must follow "Universal Precautions".

3. All Category I and II employees are to be offered the Hepatitis B vaccine within 10 working days of handling potentially infectious materials, must be given training in safely working with these materials, as outlined in the USACOM Biosafety Manual and the OSHA Standard; and, supervisors must document this training and the offer and acceptance or decline of the Hepatitis vaccine.

ATTACHMENT 6

Extract from Department of Health and Human Services
Guidelines for Research Involving Recombinant DNA Molecules

The newest version of the "Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines) is dated September 2009. In time, these Guidelines will be updated and the newest published version will dictate our College's Guidelines for rDNA research applications for approval where an IBC decision or input is mandated. The PI leading the research is responsible for reading the most recent Guidelines and implementing the required activities. When the Guidelines indicate that an rDNA protocol must be registered and/or approved by the IBC, the PI must recognize this requirement, cite the section and page numbers of the latest Guidelines wich require such registration on the IBC rDNA application, and file the rDNA registration application presented on page 36. Note that Appendix B now terms Etiologic Agents by RISK GROUPS [RGs 1-4]. New emerging pathogens may be added in the future and these can be identified by going to http://oba.od.nih.gov/rdna/nih_guidelines_oba.html

The following excerpts from Appendices A and C are provided for quick reference to "exempt hosts".

APPENDIX A. EXEMPTIONS UNDER SECTION III-F-5--SUBLISTS OF NATURAL EXCHANGERS

Certain specified recombinant DNA molecules that consist entirely of DNA segments from different species that exchange DNA by known physiological processes, though one or more of the segments may be a synthetic equivalent are exempt from these *NIH Guidelines* (see Section III-F-5, *Exempt Experiments*). Institutional Biosafety Committee registration is not required for these exempt experiments. A list of such exchangers will be prepared and periodically revised by the NIH Director with advice from the RAC after appropriate notice and opportunity for public comment (see Section IV-C-1-b-(1)-(c), *NIH Director--Specific Responsibilities*). For a list of natural exchangers that are exempt from the *NIH Guidelines*, see Appendices A-I through A-VI, *Exemptions Under Section III-F-5 Sublists of Natural Exchangers*. Section III-F-5, *Exempt Experiments*, describes recombinant DNA molecules that are: (1) composed entirely of DNA segments from one or more of the organisms within a sublist, and (2) to be propagated in any of the organisms within a sublist (see *Classification of Bergey's Manual of Determinative Bacteriology*; 8th edition, R. E. Buchanan and N. E. Gibbons, editors, W illiams and Wilkins Company; Baltimore, Maryland 1984). Although these experiments are exempt, it is recommended that they be performed at the appropriate biosafety level for the host or recombinant organism (see *Biosafety in Microbiological and Biomedical Laboratories*, 3rd edition, May 1993, U.S. DHHS, Public Health Service, Centers for Disease Control and Prevention, Atlanta, Georgia, and NIH Office of Biosafety, Bethesda, Maryland).

Appendix A-I. Sublist A

Genus Escherichia
Genus *Shigella*
Genus *Salmonella* - including *Arizona*
Genus *Enterobacter*
Genus *Citrobacter* - including *Levinea*
Genus *Klebsiella* - including *oxytoca*
Genus *Erwinia*
Pseudomonas aeruginosa, Pseudomonas putida, Pseudomonas fluorescens, and Pseudomonas mendocina
Serratia marcescens
Yersinia enterocolitica

Appendix A-II. Sublist B

Bacillus subtilis
Bacillus licheniformis
Bacillus pumilus
Bacillus globigii
Bacillus niger
Bacillus nato
Bacillus amyloliquefaciens
Bacillus aterrimus

Appendix A-III. Sublist C
Streptomyces aureofaciens
Streptomyces rimosus
Streptomyces coelicolor

Appendix A-IV. Sublist D

Streptomyces griseus
Streptomyces cyaneus
Streptomyces venezuelae

Appendix A-V. Sublist E
One way transfer of *Streptococcus mutans* or *Streptococcus lactis* DNA into *Streptococcus sanguis*

Appendix A-VI. Sublist F
Streptococcus sanguis
Streptococcus pneumoniae
Streptococcus faecalis
Streptococcus pyogenes
Streptococcus mutans

APPENDIX C. EXEMPTIONS UNDER SECTION III-F-8

Section III-F-8 states that exempt from these *NIH Guidelines* are "those that do not present a significant risk to health or the environment (see Section IV-C-1-b-(1)-(c), *NIH Director--Specific Responsibilities*), as determined by the NIH Director, with the advice of the RAC, and following appropriate notice and opportunity for public comment. See Appendix C, *Exemptions under Sections III-F-8*, for other classes of experiments which are exempt from the *NIH Guidelines*." The following classes of experiments are exempt under Section III-F-8:

Appendix C-I. Recombinant or Synthetic Nucleic Acid Molecules in Tissue Culture

Recombinant or synthetic nucleic acid molecules containing less than one-half of any eukaryotic viral genome (all viruses from a single family being considered identical -- see Appendix C-IX-E, *Footnotes and References of Appendix C*), that are propagated and maintained in cells in tissue culture are exempt from these *NIH Guidelines* with the exceptions listed in Appendix C-I-A.

Appendix C-I-A. Exceptions

The following categories are not exempt from the *NIH Guidelines*: (i) experiments described in Section III-B which require NIH/OBA and Institutional Biosafety Committee approval before initiation, (ii) experiments involving DNA from Risk Groups 3, 4, or restricted organisms (see Appendix B, *Classification of Human Etiologic Agents on the Basis of Hazard*, and Sections V-G and V-L, *Footnotes and References of Sections I through IV*) or cells known to be infected with these agents, (iii) experiments involving the deliberate introduction of genes coding for the biosynthesis of molecules that are toxic for vertebrates (see Appendix F, *Containment Conditions for Cloning of Genes Coding for the Biosynthesis of Molecules Toxic for Vertebrates*), and (iv) whole plants regenerated from plant cells and tissue cultures are covered by the exemption provided they remain axenic cultures even though they differentiate into embryonic tissue and regenerate into plantlets.

Appendix C-II. Escherichia coli K-12 ***Host-Vector Systems***

Experiments which use *Escherichia coli* K-12 host-vector systems, with the exception of those experiments listed in Appendix C-II-A, are exempt from the *NIH Guidelines* provided that: (i) the *Escherichia coli* host does not contain conjugation proficient plasmids or generalized transducing phages; or (ii) lambda or lambdoid or Ff bacteriophages or non-conjugative plasmids (see Appendix C-VIII-B, *Footnotes and References of Appendix C*) shall be used as vectors. However, experiments involving the insertion into *Escherichia coli* K-12 of DNA from prokaryotes that exchange genetic information (see Appendix C-VIII-C, *Footnotes and References of Appendix C*) with *Escherichia coli* may be performed with any *Escherichia coli* K-12 vector (e.g., conjugative plasmid). When a non-conjugative vector is used, the *Escherichia coli* K-12 host may contain conjugation-proficient plasmids either autonomous or integrated, or generalized transducing phages. For these exempt laboratory experiments, Biosafety Level (BL) 1 physical containment conditions are recommended. For large-scale fermentation experiments, the appropriate physical containment conditions need be no greater than those for the host organism unmodified by recombinant or synthetic nucleic acid molecule techniques; the Institutional Biosafety Committee can specify higher containment if deemed necessary.

Appendix C-II-A. Exceptions

The following categories are not exempt from the *NIH Guidelines*: (i) experiments described in Section III-B which require NIH/OBA and Institutional Biosafety Committee approval before initiation, (ii) experiments involving DNA from Risk Groups 3, 4, or restricted organisms (see Appendix B, *Classification of Human*

Etiologic Agents on the Basis of Hazard, and Sections V-G and V-L, *Footnotes and References of Sections I through IV*) or cells known to be infected with these agents may be conducted under containment conditions specified in Section III-D-2 with prior Institutional Biosafety Committee review and approval, (iii) large-scale experiments (e.g., more than 10 liters of culture), and (iv) experiments involving the cloning of toxin molecule genes coding for the biosynthesis of molecules toxic for vertebrates (see Appendix F, *Containment Conditions for Cloning of Genes Coding for the Biosynthesis of Molecules Toxic for Vertebrates*).

Appendix C-III. Saccharomyces ***Host-Vector Systems***

Experiments involving *Saccharomyces cerevisiae* and *Saccharomyces uvarum* host-vector systems, with the exception of experiments listed in Appendix C-III-A, are exempt from the *NIH Guidelines*. For these exempt experiments, BL1 physical containment is recommended. For large-scale fermentation experiments, the appropriate physical containment conditions need be no greater than those for the unmodified host organism; the Institutional Biosafety Committee can specify higher containment if deemed necessary.

Appendix C-III-A. Exceptions

The following categories are not exempt from the *NIH Guidelines*: (i) experiments described in Section III-B which require NIH/OBA and Institutional Biosafety Committee approval before initiation, (ii) experiments involving DNA from Risk Groups 3, 4, or restricted organisms (see Appendix B, *Classification of Human Etiologic Agents on the Basis of Hazard*, and Sections V-G and V-L, *Footnotes and References of Sections I through IV*) or cells known to be infected with these agents may be conducted under containment conditions specified in Section III-D-2 with prior Institutional Biosafety Committee review and approval, (iii) large-scale experiments (e.g., more than 10 liters of culture), and (iv) experiments involving the deliberate cloning of genes coding for the biosynthesis of molecules toxic for vertebrates (see Appendix F, *Containment Conditions for Cloning of Genes Coding for the Biosynthesis of Molecules Toxic for Vertebrates*).

Appendix C-IV. Kluyveromyces ***Host-Vector Systems***

Experiments involving *Kluyveromyces lactis* host-vector systems, with the exception of experiments listed in Appendix C-IV-A, are exempt from the *NIH Guidelines* provided laboratory-adapted strains are used (i.e. strains that have been adapted to growth under optimal or defined laboratory conditions). For these exempt experiments, BL1 physical containment is recommended. For large-scale fermentation experiments, the appropriate physical containment conditions need be no greater than those for the unmodified host organism; the Institutional Biosafety Committee may specify higher containment if deemed necessary.

Appendix C-IV-A Exceptions

The following categories are not exempt from the *NIH Guidelines*: (i) experiments described in Section III-B, which require NIH/OBA and Institutional Biosafety Committee approval before initiation; (ii) experiments involving DNA from Risk Groups 3, 4, or restricted organisms (see Appendix B, *Classification of Human Etiologic Agents on the Basis of Hazard*, and Sections V-G and V-L, *Footnotes and References of Sections I through IV*) or cells known to be infected with these agents may be conducted under containment conditions specified in Section III-D-2 with prior Institutional Biosafety Committee review and approval; (iii) large-scale experiments (e.g., more than 10 liters of culture), and (v) experiments involving the deliberate cloning of genes coding for the biosynthesis of molecules toxic for vertebrates (see Appendix F, *Containment Conditions for Cloning of Genes Coding for the Biosynthesis of Molecules Toxic for Vertebrates*).

Appendix C-V. Bacillus subtilis ***or*** Bacillus licheniformis ***Host-Vector Systems***

Any asporogenic *Bacillus subtilis* or asporogenic *Bacillus licheniformis* strain which does not revert to a spore-former with a frequency greater than 10^{-7} may be used for cloning DNA with the exception of those experiments listed in Appendix C-V-A, *Exceptions*. For these exempt laboratory experiments, BL1 physical containment conditions are recommended. For large-scale fermentation experiments, the appropriate physical containment conditions need be no greater than those for the unmodified host organism; the Institutional Biosafety Committee can specify higher containment if it deems necessary.

Appendix C-V-A. Exceptions

The following categories are not exempt from the *NIH Guidelines*: (i) experiments described in Section III-B which require NIH/OBA and Institutional Biosafety Committee approval before initiation, (ii) experiments involving DNA from Risk Groups 3, 4, or restricted organisms (see Appendix B, *Classification of Human Etiologic Agents on the Basis of Hazard*, and Sections V-G and V-L, *Footnotes and References of Sections I through IV*) or cells known to be infected with these agents may be conducted under containment conditions specified in Section III-D-2 with prior Institutional Biosafety Committee review and approval, (iii) large-scale experiments (e.g., more than 10 liters of culture), and (iv) experiments involving the deliberate cloning of genes coding for the biosynthesis of molecules toxic for vertebrates (see Appendix F, *Containment Conditions for Cloning of Genes Coding for the Biosynthesis of Molecules Toxic for Vertebrates*).

Appendix C-VI. Extrachromosomal Elements of Gram Positive Organisms

Recombinant or synthetic nucleic acid molecules derived entirely from extrachromosomal elements of the organisms listed below (including shuttle vectors constructed from vectors described in Appendix C), propagated and maintained in organisms listed below are exempt from these *NIH Guidelines*.

Bacillus amyloliquefaciens
Bacillus amylosacchariticus
Bacillus anthracis
Bacillus aterrimus
Bacillus brevis
Bacillus cereus
Bacillus globigii
Bacillus licheniformis
Bacillus megaterium
Bacillus natto
Bacillus niger
Bacillus pumilus
Bacillus sphaericus
Bacillus stearothermophilus
Bacillus subtilis Bacillus
thuringiensis Clostridium
acetobutylicum
Lactobacillus casei

Listeria grayi
Listeria monocytogenes
Listeria murrayi
Pediococcus acidilactici
Pediococcus damnosus
Pediococcus pentosaceus
Staphylococcus aureus
Staphylococcus carnosus
Staphylococcus epidermidis
Streptococcus agalactiae
Streptococcus anginosus
Streptococcus avium
Streptococcus cremoris
Streptococcus dorans
Streptococcus equisimilis
Streptococcus faecalis
Streptococcus ferus
Streptococcus lactis
Streptococcus ferns
Streptococcus mitior
Streptococcus mutans
Streptococcus pneumoniae
Streptococcus pyogenes

Streptococcus salivarius
Streptococcus sanguis
Streptococcus sobrinus
Streptococcus thermophilus

Appendix C-VI-A. Exceptions

The following categories are not exempt from the *NIH Guidelines*: (i) experiments described in Section III-B which require NIH/OBA and Institutional Biosafety Committee approval before initiation, (ii) experiments involving DNA from Risk Groups 3, 4, or restricted organisms (see Appendix B, *Classification of Human Etiologic Agents on the Basis of Hazard*, and Sections V-G and V-L, *Footnotes and References of Sections I through IV*) or cells known to be infected with these agents may be conducted under containment conditions specified in Section III-D-2 with prior Institutional Biosafety Committee review and approval, (iii) large-scale experiments (e.g., more than 10 liters of culture), and (iv) experiments involving the deliberate cloning of genes coding for the biosynthesis of molecules toxic for vertebrates (see Appendix F, *Containment Conditions for Cloning of Genes Coding for the Biosynthesis of Molecules Toxic for Vertebrates*).

Appendix C-VII. The Purchase or Transfer of Transgenic Rodents

The purchase or transfer of transgenic rodents for experiments that require BL1 containment (See Appendix G-III-M, *Footnotes and References of Appendix G*) are exempt from the *NIH Guidelines*.

Appendix C-VIII. Generation of BL1 Transgenic Rodents via Breeding

The breeding of two different transgenic rodents or the breeding of a transgenic rodent and a non-transgenic rodent with the intent of creating a new strain of transgenic rodent that can be housed at BL1 containment will be exempt from the *NIH Guidelines* if:
(1) Both parental rodents can be housed under BL1 containment; and
(2) neither parental transgenic rodent contains the following genetic modifications: (i) incorporation of more than one-half of the genome of an exogenous eukaryotic virus from a single family of viruses; or (ii) incorporation of a transgene that is under the control of a gammaretroviral long terminal repeat (LTR); and
(3) the transgenic rodent that results from this breeding is not expected to contain more than one-half of an exogenous viral genome from a single family of viruses.

Appendix C-IX. Footnotes and References of Appendix C

Appendix C-IX-A. The NIH Director, with advice of the RAC, may revise the classification for the purposes of these *NIH Guidelines* (see Section IV-C-1-b-(2)-(b), *Minor Actions*). The revised list of organisms in each Risk Group is located in Appendix B.

Appendix C-IX-B. A subset of non-conjugative plasmid vectors are poorly mobilizable (e.g., pBR322, pBR313). Where practical, these vectors should be employed.

Appendix C-IX-C. Defined as observable under optimal laboratory conditions by transformation, transduction, phage infection, and/or conjugation with transfer of phage, plasmid, and/or chromosomal genetic information. Note that this definition of exchange may be less stringent than that applied to exempt organisms under Section III-F-6, *Exempt Experiments*.

Appendix C-IX-D. As classified in the *Third Report of the International Committee on Taxonomy of Viruses: Classification and Nomenclature of Viruses*, R. E. F. Matthews (ed.), Intervirology 12 (129-296), 1979.

Appendix C-IX-E. i.e., the total of all genomes within a Family shall not exceed one-half of the genome.

ATTACHMENT 7

University of South Alabama: Institutional Biosafety

BIOMEDICAL WASTE POLICY
COLLEGE OF MEDICINE

This policy is intended to provide guidance and insure compliance with the NIH/CDC, federal and state guidelines and restrictions of the University of South Alabama College of Medicine. This information describes the proper method for handling and disposing of biomedical waste produced from RESEARCH ACTIVITIES.

What is Considered Medical or Biomedical Waste?

Federal, State and local environmental laws consider medical waste to be certain laboratory and medical treatment apparatus:

1. *All sharps (contaminated and uncontaminated):*
   - ❖ Syringes with/without needles
   - ❖ Broken glass
   - ❖ Scalpels, razors and lancets
   - ❖ Glass pipettes
   - ❖ Specimen tubes, slides
2. *Human or animal blood, blood-products, body fluids and tissues*
3. *Cultures, infectious agents and associated biologicals:*
   - ❖ Used Petri plates containing culture agars
   - ❖ Specimens from bottles, medical, pathology and research laboratories
   - ❖ Discarded live and attenuated vaccines
   - ❖ Wastes from the production of biologicals
   - ❖ Culture flasks
4. *Other laboratory wastes including but not limited to:*
   - ❖ Surgical drapes and absorbents
   - ❖ Protective gloves, disposable lab coats, or masks
   - ❖ Specimen containers
   - ❖ All microorganisms constructed using rDNA
5. *All wastes that have been autoclaved.*
6. *Any medical equipment or disposables that have the appearance of medical wastes*

Further, all items in red biohazard bags are considered medical waste, even if the items are sterilized. Only red bags and collection containers meeting regulations shall be used for collection and disposal of biomedical waste. The College of Medicine has adopted a policy that all medical wastes will be disposed of properly by burning on site or by engaging the services of a licensed medical waste transporter. Chemicals and radioactive waste cannot be disposed of as biomedical waste.

Everyone who produces, handles, treats and/or disposes of biohazardous waste is responsible for the proper management of this waste stream. By assuming these responsibilities, regulatory compliance can be assured, and risks for exposure to employees and the community is greatly reduced.

Sharps Waste: Syringes, scalpels and razor blades, broken glass/plastic, pipettes, tips, etc. are required to be placed in red sharps containers and must be segregated at the point of use. Sharps containers *must*:

- Be disposed of and/or swapped when they are full.
- Have proper biohazardous labels outside of the containers.
- Be kept closed when not in use.

Segregation and Packaging of Waste:

Solid Non-Sharps Biohazardous Waste:

Infectious/potentially infectious/rDNA :
- human pathogens - animal pathogens - plant pathogens
- recombinant DNA - human/primate blood, blood products, body fluids - human/primate tissue
- any biological contaminated material (including unbroken plastic lab ware, gloves, etc.)

These wastes must be stored in supplied biohazardous waste tubs lined with a red biohazard bag.

Handling and Disposing of Biohazardous Wastes:

Biomedical waste must be separated at the point of origin by the generator. **All research-generated infectious waste containing large volumes of human or animal pathogens must be sterilized on site by autoclaving prior to disposal using autoclavable bags with approved biohazard symbol and built-in indicator strip confirming proper autoclaving temperature has been reached. Alternatively, heat-sensitive autoclave tape or indicator strips can be placed across the biohazard symbol prior to autoclaving. Autoclaved bags are then placed in a red biohazard bag after autoclaving. (Double bags are recommended if leakage and/or outside contamination may occur).** Red bags should be capable of passing the ASTM 125 pound drop test for filled bags. All bagged medical waste must be closed by twisting and hand tying in a single knot. All needle boxes and bucket-style containers used for glass and plastic sharps must be placed inside red bags and closed in the same manner. Biohazard bags must be placed into an approved biomedical waste container for transport from generation site to the biohazardous waste holding site. All red bags must be labeled with the following information before disposal: 1) name and room number of investigator's laboratory; 2) department; 3) phone number; and 4) date of disposal. Lids should be kept on the red containers at all times. Red Stericycle-issued waste containers are available at each facilities designated collection site.

For additional reference please refer to the Biological Waste and Sharps Disposal Flowchart.

For questions regarding the disposal of biomedical waste please call the Office of Research Compliance and Assurance at 460-6509

University of South Alabama *Rev.3/2011*
COLLEGE OF MEDICINE

Biological Waste and Sharps Disposal hart

Storage of medical waste by the generator must not exceed seven calendar days from the date initial storage Alabama Department of Environmental Management Land Division- Solid Waste Program Regulations. Chapter 335·13·7, Medical Waste

Biomedical WastJ!

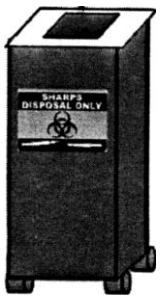
For any special cases please contact the Biosafety Officer at460-6339

Sharps

Razor Blades
Syringes with \without needles
Scapels
Lancets

Supplied RED SHARPS container

NO GLOVES!



Medicalllaboratory Glass & Plasitic Sharps

BROKEN

pasteur pipettes, pipette tips,culture dishes,petridishes, culture flasks, slide covers,specimen tubes,broken glass, innoculating loops, stirring devices

Solid Waste

GLOVES, disposable *dl .* gowns, & masks

Solid waste cultures/stocks from production of biologicals:
• waste serums,vaccine,antigen, antitoxins,humanJprimate cell lines
• discarded live/attenuated vaccines, biological toxins
·systems used to grow/ maintain infectious agents such as agars, gels and broths,unbrokenplastic labware

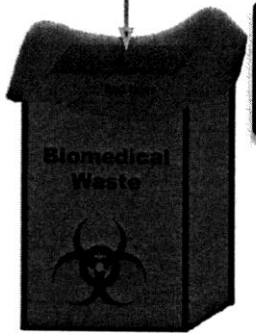
Small Volume solids

Large volume solids and ALL BSL-3 agents

Approved autoclavable bio-hazard bag

Approved Red\Orange Biohazard Bag

Autoclave w/heat indicator strip



Red biomedical waste container with supplied red liner by medical waste hauler

Note:Red biohazard bags OR red liners supplied by medical waster hauler should have information label alfaxed to bag before disposal

Liquid Waste

Human blood, anir ly fluids, liquid gr

Human blood, animal blood, body fluids,liquid growth media

Autoclaved and disposed down the sanitary sewer

Bleach (1:10-Dilution)

Liquids should sit for a minimum of 8 hours

Pour down sanitary sewer flushing w/cold water for a minimum of 10 minutes (pH 6-U)

Refer to guidelines on liquid waste disposal

TIE *BAGS WITH "HAND OVER" KNOTS LIKE* A *BALLOON before disposal.*

ATTACHMENT 9

Recommended guidelines for pouring biomedical liquid waste down the sanitary sewer

(1) Normally, if possible, all liquid biohazardous waste [spent liquid growth culture media containing microbial or human/nonhuman primate or other animal cells, diluted blood and tissue fluids, plasma, etc] in less than 4 gallon lots [the capacity of our liquid disposal containers] should be autoclaved in a certified autoclave and put down the sanitary sewer system; or

(2) Red-bagged and placed into the red biohazard waste hauler transport container with lid closed and taken to the holding area for incineration by the waste hauler

(3) Lots of liquid biohazardous waste [spent liquid growth culture media containing microbial or human/nonhuman primate or other animal cells, diluted blood and tissue fluids, plasma, etc] exceeding four gallons per day for a given laboratory may be disposed of by: (a) either autoclaving as in (1) above and discarded in the sanitary sewer system or (b) subjecting to inactivation by commercial 5.23% bleach mixed so as to effect a 1:10 dilution in the liquid to be inactivated [final active solution = 0.523 % bleach is the lowest acceptable bleach concentration for such inactivations] and left for a minimum of 8 hours covered and then disposed down the sanitary sewer, and flushing with cold water for a minimum of 10 minutes. *Other chemical deactivations can be justified in the lab specific exposure control plan.*

Note: In order to assure adequate inactivation time for exposure to the bleach, it is the PI's or lab supervisor's responsibility, to permanently maintain an official log book listing each lot of biohazardous liquid waste so treated by date and notation of biohazard content [i.e., E. coli culture media, human cell cultures, etc.] and exposure time [e.g., 8:00 AM to 8:00 PM] and then poured into the sanitary sewer. Hence, bleach treated liquids being held for inactivation in the labs must have a memo note sticker showing time and date of bleach exposure on the covering lid [to avoid mistakes regarding time of bleach addition]. Considering the high protein levels often present in our culture waste the liquids should be treated for at least 8 hours to allow the bleach to kill the cultured microbes or other microbial contaminants. The presence of a tag noting date and time of exposure will avoid mishaps and the recording of the inactivation period will ensure adequate killing time. Spore forming microbes and pathogens readily transmitted to animals by the aerosol route should be autoclaved when present in liquid wastes. BSL-3 rated organisms must be decontaminated (via autoclave or chemical deactivation).

The lab PI or supervisor must use good judgment in using chlorine inactivation. If one is, for example, inactivating concentrated microbial cell pastes these should be autoclaved rather than sanitized by bleach exposure in semi -liquid fluids as it might require days of exposure to industrial (12-15%) bleach concentrate to achieve disinfection. Also, labs using microbes that can be readily transmitted to humans by aerosols such as *Legionella* should not be inactivated by bleach exposure and poured down the drain unless they are tightly covered to strictly limit aerosolization during transport. If in doubt, err on the side of safety in disposal of all biohazardous waste. If you need help deciding, call the Office of Research Compliance and Assurance for assistance 460-6509.

Thus, any biohazardous waste undergoing bleach inactivation and found lacking such a treatment time tag laced on a tub cover or lacking an up to date official logbook will be considered in violation of the approved inactivation process. Waste log records must be kept for a minimum of three (3) years.

File: c:/bisafety/liquidwaste.disposal.doc
Approved 8/2002

ATTACHMENT 10

IBC Annual Inspections

LABORATORY INSPECTIONS:
All registered laboratories will be inspected on an annual basis by members of the IBC. This inspection will be done to determine adequate compliance with the standards for biosafety level containment as outlined in the *CDC/NIH Biosafety in Microbiological and Biomedical Laboratories* (BMBL) manual and the USA Biosafety Manual.

Audit assignments indicating team members and respective areas for auditing are prepared each year. Each team's group leader is responsible for coordinating the inspections with other members of the team. Checklists for every PI are distributed to the auditing team based on the biosafety level under which they have registrations. Each laboratory with a biohazardous or rDNA registration is inspected for a variety of compliance measures including safety, waste disposal, and best practices.

In addition, initial laboratory inspections for new investigators are required to assist in the establishment of research operations pertaining to USA's guidelines in biological safety. The purpose of these inspections is to assist in educating and informing investigators of biological safety practices and policies at the University of South Alabama. The laboratories of new investigators should be inspected approximately two weeks after receiving IBC approval.

ATTACHMENT 11

USA Biosafety Audits
Biosafety Level 1 Checklist for Labs

Protocol #s: _____
PI: _____ ***Office Location:*** _____
Department: _____ ***Lab Location:*** _____
Telephone: _____
Biohazard(s): _____
_____
Completed By (print): _____ ***Signature:*** _____
_____ _____
_____ _____
Date of Inspection: _____

Answer Yes, No or NA (not applicable), by placing an X in the appropriate box.

Biosafety Level 1	**YES**	**NO**	**N/A**	**Comments**
A. Standard Microbiological Practices				
1. Access limited to the lab when work is in progress.				
2. Persons wash hands after biohazardous work, after removing gloves and before exiting the lab?				
3. Are soap and towels available at the handwashing sink?				
4. Are eating/drinking/ applying cosmetics prohibited in the lab?				
5. Is food stored outside the work area, in cabinets or refrigerators designated for food only?				
6. Mouth pipetting prohibited; pipettors used				
7. Splashes and aerosols are minimized				
8. Glassware is minimized and use of durable plasticware is used whenever is possible.				
9. Are regulated sharps (e.g, needles, syringes, razor blades, lancets) discarded into puncture-resistant, red needle box?				
Biological Waste				
10. Sharps restricted to use when no alternative exists				
11. Are sharps containers no more than ¾ full? Have full containers been removed?				
12. Are all solid wastes, which are contaminated with biohazardous materials, discarded into red sharps containers, lined red tubs, or lined receptacles for later disposal in red tubs?				
13. Are all liquid wastes, which are contaminated with biohazardous materials, autoclaved or decontaminated with an effective disinfectant before they are poured down the sanitary sewer?				
14. All liquids poured down the sewer are maintained in a log book to assure adequate inactivation time for exposure to bleach. (e.g., info to include date treated/exposure time/notation of biohazard content)				
B. Special Practices				
1. Persons advised of hazards and have required immunizations.				
2. Is a BIOHAZARD sign posted at the lab entrance?				
3. Does the BIOHAZARD sign include information on the agent(s) used, biosafety level, PI's name/telephone?				
4. Is the biohazard symbol used to identify equipment, containers, refrigerators, etc. t**hat are used directly to handle, process, culture, incubate, and store biohazardous materials?**				
5. Supervisor ensures personnel receive appropriate biosafety training.				
6. Laboratory surfaces decontaminated on a weekly basis or after any spill of biological material.				
7. Clearly labeled spill kit containing absorbent material, gloves, disposable plastic scoops, tongs, biohazard bags and appropriate disinfectants are available in the laboratory.				
8. Spills and accidents reported to Supervisor and Biosafety Office. Medical				

follow-up as appropriate.				
9. Copy of USA College of Medicine Biosafety Manual/Exposure Control Plan is available in laboratory.				
Biosafety Level 1	**YES**	**NO**	**N/A**	**Comments**
C. Safety Equipment (Primary Barriers)				
1. Biosafety cabinet and other containment devices or personnel protective equipment used when:				
a.) potential for splashes/aerosols				
b.) high concentrations or large volumes of agents used				
2. When biohazardous materials must be manipulated outside a Class II biological safety cabinet, do lab personnel use face protection (e.g., goggles, mask, face shield) for unexpected splashes to the face?				
3. Lab coats worn and removed prior to leaving the lab.				
4. Hangers are provided for laboratory coat storage.				
5. Gloves worn when working with agents. Alternatives to powdered latex available.				
D. Laboratory Facilities (Secondary Barriers)				
1. Does lab contain a wrist-operated handwashing sink?				
2. Are bench tops impervious to water and resistant to acids, solvents and disinfectants?				
4. Easily cleaned. No carpet or rugs. Chairs covered with vinyl or suitable material for ease of decontamination.				
5. Eyewash readily available. Checked weekly by staff.				
E. Personnel Training				
1. Documented bloodborne pathogen/biosafety training?				
2. Documented emergency response (accidental exposure plan)				
3. Documented hazard communication (MSDS, chemical hygiene plan)				

Do any staff personnel have concerns about health/safety at work?

Additional comments/observations:

USA Biosafety Audits
Biosafety Level 2 Checklist for Labs

Protocol #s: _____
PI: _____ ***Office Location:***
Department: _____ ***Lab Location:***
Telephone: _____
Biohazard(s): _____
_____
Completed By (print): _____ ***Signature:*** _____
_____ _____
_____ _____
Date of Inspection: _____

Answer Yes, No or NA (not applicable), by placing an X in the appropriate box.

Biosafety Level 2	**YES**	**NO**	**N/A**	**Comments**
A. Standard Microbiological Practices				
1. Access limited to the lab when work is in progress.				
2. Persons wash hands after biohazardous work, after removing gloves and before exiting the lab?				
3. Are soap and towels available at the handwashing sink?				
4. Are eating/drinking/ applying cosmetics prohibited in the lab?				
5. Is food stored outside the work area, in cabinets or refrigerators designated for food only?				
6. Mouth pipetting prohibited; pipettors used				
7. Splashes and aerosols are minimized				
8. Glassware is minimized and use of durable plasticware is used whenever is possible.				
9. Are regulated sharps (e.g, needles, syringes, razor blades, lancets) discarded into puncture-resistant, red needle box?				
Biological Waste				
10. Sharps restricted to use when no alternative exists				
11. Are sharps containers no more than ¾ full? Have full containers been removed?				
12. Are all solid wastes, which are contaminated with biohazardous materials, discarded into red sharps containers, lined red tubs, or lined receptacles for later disposal in red tubs?				
13. Are all liquid wastes, which are contaminated with biohazardous materials, autoclaved or decontaminated with an effective disinfectant before they are poured down the sanitary sewer?				
14. All liquids poured down the sewer are maintained in a log book to assure adequate inactivation time for exposure to bleach. (e.g., info to include date treated/exposure time/notation of biohazard content)				
B. Special Practices				
1. Lab access restricted when working with infectious agents. No minors allowed.				
2. Persons advised of hazards and have required immunizations.				
3. Is a BIOHAZARD sign posted at the lab entrance?				
4. Does the BIOHAZARD sign include information on the agent(s) used, biosafety level, PI's name/telephone?				
5. Is the biohazard symbol used to identify equipment, containers, refrigerators, etc. t**hat are used directly to handle, process, culture, incubate, and store biohazardous materials?**				
6. Are lab personnel offered appropriate immunizations?				

7. Are lab personnel provided with information regarding immune competence and conditions that may predispose them to infection?				
8. Supervisor ensures personnel receive appropriate biosafety training.				
8. Do lab personnel exercise a high degree of precaution with all contaminated sharp items, including needles/syringes, slides, pipettes, capillary tubes and scalpels?				
9. Laboratory surfaces decontaminated on a daily basis or after any spill of biological material.				
10. Clearly labeled spill kit containing absorbent material, gloves, disposable plastic scoops, tongs, biohazard bags and appropriate disinfectants are available in the laboratory.				
Biosafety Level 2				
11. Spills and accidents reported to Supervisor and Biosafety Office. Medical follow-up as appropriate.	**YES**	**NO**	**N/A**	**Comments**
12. Copy of USA College of Medicine Biosafety Manual/Exposure Control Plan is available in laboratory.				
C. Safety Equipment (Primary Barriers)				
1. Biosafety cabinet and other containment devices or personnel protective equipment used when:				
a.) potential for splashes/aerosols				
b.) high concentrations or large volumes of agents used				
2.Are eye and face protection disposed of with other contaminated laboratory waste or decontaminated before use?				
3. When biohazardous materials must be manipulated outside a Class II biological safety cabinet, do lab personnel use face protection (e.g., goggles, mask, face shield) for unexpected splashes to the face?				
4. Is the Biosafety cabinet functional and current on inspection?				
5. Lab coats worn and removed prior to leaving the lab.				
6. Hangers are provided for laboratory coat storage.				
7. Gloves worn when working with agents. Alternatives to powdered latex available.				
D. Laboratory Facilities (Secondary Barriers)				
1. Does lab contain a wrist-operated handwashing sink?				
2. Are bench tops impervious to water and resistant to acids, solvents and disinfectants?				
3. Provide lockable doors for restricted agents (42 CFR 72.6)				
4. Easily cleaned. No carpet or rugs. Chairs covered with vinyl or suitable material for ease of decontamination.				
5. Eyewash readily available. Checked weekly by staff.				
E. Training of Personnel				
1. Documented bloodborne pathogen/biosafety training?				
2. Documented emergency response (accidental exposure plan)				
3. Documented hazard communication (MSDS, chemical hygiene plan)				

Do any staff personnel have concerns about health/safety at work?

Additional comments/observations:

USA Biosafety Audits
Biosafety Level 3 Checklist for Labs

Protocol #s:
PI: ***Office Location:***
Department: ***Lab Location:***
Telephone:
Biohazard(s):

Completed By (print): ***Signature:***

Date of Inspection:

Answer Yes, No or NA (not applicable), by placing an X in the appropriate box.

Biosafety Level 3	**YES**	**NO**	**N/A**	**Comments**
A. Standard Microbiological Practices				
1. Access strictly limited to the lab.				
2. Persons wash hands after biohazardous work, after removing gloves and before exiting the lab?				
3. Are soap and towels available at the handwashing sink?				
4. Are eating/drinking/ applying cosmetics prohibited in the lab?				
5. Is food stored outside the work area, in cabinets or refrigerators designated for food only?				
6. Mouth pipetting prohibited; pipettors used				
7. Splashes and aerosols are minimized				
8. Glassware is minimized and use of durable plasticware is used whenever is possible.				
9. Are regulated sharps (e.g, needles, syringes, razor blades, lancets) discarded into puncture-resistant, red needle box?				
Biological Waste				
10. Sharps restricted to use when no alternative exists				
11. Are sharps containers no more than ¾ full? Have full containers been removed?				
12. Are all solid wastes, which are contaminated with biohazardous materials, discarded into red sharps containers, lined red tubs, or lined receptacles for later disposal in red tubs?				
13. Are all liquid wastes, which are contaminated with biohazardous materials, autoclaved or decontaminated with an effective disinfectant before they are poured down the sanitary sewer?				
14. Insect and rodent control program in place. Exterior walls sealed/holes covered to prevent access.				
15. Work surfaces disinfected 1x per day and after spills				
16. Lab contains an unobscured glass panel so occupants working in the BL-3 units can be seen from the outside. When the room is unoccupied the door must be locked.				
B. Special Practices				
1. Access restricted to required personnel. No minors allowed.				
2. Persons advised of hazards and have required immunizations.				
3. Is a BIOHAZARD sign posted at the lab entrance?				

4. Does the BIOHAZARD sign include information on the agent(s) used, biosafety level, PI's name/telephone? *(Note: Select Agents are not posted)*				
5. Is the biohazard symbol used to identify equipment, containers, refrigerators, etc. t**hat are used directly to handle, process, culture, incubate, and store biohazardous materials?**				
6. Are lab personnel provided with information regarding immune competence and conditions that may predispose them to infection?				
7. Are lab personnel offered appropriate immunizations?				
8. Supervisor ensures personnel receive appropriate biosafety training.				
9. Do lab personnel exercise a high degree of precaution with all contaminated sharp items, including needles/syringes, slides, pipettes, capillary tubes and scalpels?				
10. Laboratory surfaces decontaminated on a routine basis and after any spill of biological material.				
Biosafety Level 3	**YES**	**NO**	**N/A**	**Comments**
11. Clearly labeled spill kit containing absorbent material, gloves, disposable plastic scoops, tongs, biohazard bags and appropriate disinfectants are available in the laboratory.				
12. Spills and accidents reported to Supervisor and Biosafety Office. Medical follow-up as appropriate.				
13. Has the PI developed lab-specific biosafety procedures (e.g., Exposure Control Plan) and incorporated them into Standard Operating Procedures? Are lab personnel required to read the procedures?				
14. Gloves are changes frequently accompanied by handwashing.				
15. Copy of USA College of Medicine Biosafety Manual/Exposure Control Plan is available in laboratory.				
16. Supervisor ensures personnel demonstrate proficiency in standard and specific microbiological procedures.				
C. Safety Equipment (Primary Barriers)				
1. Are eye and face protection disposed of with other contaminated laboratory waste or decontaminated before use?				
2. Biosafety cabinet and other containment devices or personnel protective equipment used when:				
a.) potential for splashes/aerosols				
b.) high concentrations or large volumes of agents used				
3. When biohazardous materials must be manipulated outside a Class II biological safety cabinet, do lab personnel use face protection (e.g., goggles, mask, face shield) for unexpected splashes to the face?				
4. Is the Biosafety cabinet functional and current on inspection?				
5. When biohazardous materials must be manipulated outside a Class II biological safety cabinet, do lab personnel use face protection (e.g., goggles, mask, face shield) for unexpected splashes to the face?				
6. Side or back fastening gowns worn and removed prior to exiting lab.				
7. Hangers are provided for laboratory coat storage.				
8. Gloves worn when working with agents. Alternatives to powdered latex available.				
D. Laboratory Facilities (Secondary Barriers)				
1. Does lab contain a wrist-operated handwashing sink?				
2. Are bench tops impervious to water and resistant to acids, solvents and disinfectants?				
3. Provide lockable doors for restricted agents (42 CFR 72.6)				
4. Easily cleaned. No carpet or rugs. Chairs covered with materials such as vinyl for ease of decontamination.				
5. Eyewash readily available and checked weekly.				
6. Lab separated from building traffic. Two self-closing doors for entry. Clothes change room may be included.				
7. Wastes decontaminated, preferably within laboratory. Boxes not brought into laboratories, supplies emptied prior to entry.				

8. A continuous air flow into the lab must be maintained during the work of pathogens. All exhaust air must be HEPA filtered and released to the outside atmosphere via independent ducting. Lab has negative pressure air control to provide time for proper and safe disinfection.				
9. Isolated vacuum lines protected with HEPA filters and liquid disinfectant traps.				
E. Training of Personnel				
1. Documented bloodborne pathogen/biosafety training?				
2. Documented emergency response? (accidental exposure plan)				
3. Documented hazard communication? (MSDS, chemical hygiene plan)				

Do any staff personnel have concerns about health/safety at work?

Additional comments/observations:

Attachment 11:

Requirements for Possession of Exempt Quantities of CDC Select Agent Toxins

A) Scope of Document:

This document outlines institutional requirements on possession of exempt quantities of Center for Disease Control (CDC) Select Agent (SA) Toxins. These requirements have been established to ensure:

- safe laboratory handling, use, and storage procedures,
- effective tracking and security of the regulated toxins, and
- compliance with federal regulations

B) Exempt Quantities of CDC Select Agent Toxins:

The regulations permit each Principal Investigator (PI) possession of a specified amount of toxin without seeking CDC registration. SA Toxins and the allowable maximum exempt quantities (per PI) includes:

Maximum Quantities Allowable Per PI for Exemption:

HHS Toxins [§73.3(d)(3)]	*Amount*
Abrin	1000mg
Botulinum neurotoxins	1 mg
Clostridium perfringens epsilon toxin	100 mg
Short, paralytic alpha conotoxins	100 mg
Diacetoxyscirpenol (DAS)	10,000 mg
Ricin	1000 mg
Saxitoxin	100 mg
Shiga-like ribosome inactivating proteins	100 mg
Shigatoxin	500 mg
Staphylococcal enterotoxins (subtypes A-E)	100 mg
T-2 toxin	10,000 mg
Tetrodotoxin	500 mg

The above list of permissible toxin amounts is available at CDC's website at: https://www.selectagents.gov/PermissibleToxinAmounts.html

Furthermore, the following toxins are exempt:

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

Due to penalties affiliated with noncompliance with the SA regulations, it is essential that each lab using/storing toxins maintains current inventory information. The total quantity of toxin per Plin a laboratory should be maintained below the above thresholds at all times.

C) Requirements for Possession of Exempt Quantities of CDC Select Agent Toxins

1) Registration and approval with the Institutional Biosafety Committee

2) Standard Operating Procedures (SOPs): All laboratories using biologically-derived toxins must have written SOPs for their use to include:
   - potential exposure hazards during sample preparation and experimental manipulations (e.g. aerosol generation when transferring, mixing, or centrifuging)
   - use of sharps; (excretion by animals; etc.)
   - safety procedures that will be employed to minimize risk (e.g. protective clothing, use of biological safety cabinet, sharps disposal procedures, waste disposal procedures, etc.)
   - proper material disposal techniques
   - accidental spill/exposure procedures.

3) Personnel Training: Provide initial lab-specific safety training to staff on toxin-involved processes, with updates as necessary. Ensure documented training is maintained for at least three years. Training should include:

   • toxin-associated hazards
   • engineering controls used to minimize exposure (i.e., fume hood use)
   • personal protective equipment to be used when handling toxin (PPE)
   • safe handling and storage
   • proper decontamination and disposal
   • administrative requirements (recordkeeping, inventory, security).

4) Proper PPE: Appropriate personal protection is to be provided (i.e., gloves, safety goggles, lab coat or disposable lab coat). NOTE: If respirators are necessary, contact Safety and Environmental Compliance (SEC) at 460-7070.

5) Engineering Controls: Proper use of fume hood, biosafety cabinet or glove box with toxin-associated procedures.

6) Inactivation and Disposal: **Refer to the USA Biosafety Manual and Exposure Control Plan, Section V, Select Agents and Toxins.** Contact Safety and Environmental Compliance at 460 7070 prior to disposal of remaining stock and/or empty containers.

7) Storage/Security: Items must be:
   • Stored with compatible materials; AND
   • Provided one layer of physical security (i.e., toxin secured within a locked freezer, or secured within a permanently fixed lockbox)

8) Inventory Maintenance: The lab must keep track of who uses the stock (and who has access to the freezer), but it is not necessary to record each use.

9) Documented Security Inspection:
   All laboratories possessing exempt quantities of select agents will be audited annually to review quantities and SOPs.

For any questions regarding CDC Select Agent possession contact the Office of Research Compliance and Assurance, 460-6625 or dlayton@southalabama.edu