Interim Final Version -----Interim Final Version

MANUAL FOR INVESTIGATORS USING BIOLOGICAL AGENTS AND RECOMBINANT DNA IN RESEARCH

Occupational and Environmental Safety
Institutional Biological and Recombinant DNA Safety (IBRDS) Committee
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TABLE OF CONTENTS

EMERGENCY INFORMATION

Emergency Response

The primary objectives of emergency response are to reduce and eliminate harm to personnel; reduce and eliminate harm to property; and minimize business interruption. The top priority is the safety and health of individuals.

Injuries

- Determine extent, avoid further injury to victim,
- Provide 1st aid at scene, avoid contact with body fluids
- If more than 1st aid is required, call 911 for assistance, and ensure decontamination of victim
- Assist emergency personnel upon arrival
- Secure the scene for accident investigation by OES or Supervisor.
- NOTE: Select agent exposure requires immediate notification to CDC and/or APHIS. Notify RO of exposures, he/she will notify CDC.

Gas Leaks

- Control Ignition Sources
- Call Police or Facility Services
- Turn off gas if location of valve is known and safe to do so
- Follow guidance of Facility Services and OES
- If Significant, evacuate and keep people out

Fires and Fire Alarm

- Remain Calm, DO NOT ENTER Dangerous areas
- Pull fire alarm and evacuate building according to building plan
- Call Campus Police (911) provide description of emergency, where, what, DO NOT HANG UP until dispatcher has,
- Assure complete evacuation, perform headcount
- Do not re-enter building until ALL CLEAR is given by Campus Police

Radiation Emergency

- For spills, notify Campus Police (911) AND Radiation Safety (578-2747)
- Prevent spread of contamination:
  - –Contaminated personnel remain near vicinity of lab
  - –Secure the lab area

NOTE: Radioactive materials in LSU labs are such that taking care of the emergency will pose little or no exposure potential to people involved

Bomb Threats

- Remain Calm. Do not hang up
- Get details: “when, where, why, what”
- Note caller’s voice style, background noises, caller ID.,etc.
- Call campus police (578-3231) immediately
- Notify Supervisor and observe work areas for suspicious packages
- Follow instructions of Campus Police

Note: Remain calm, most threats are bogus

Chemical Spills

If the person involved can clean up the spill or stop the release safely, then it is appropriate to do so. If not, take the following steps:

•Notify Supervisor and determine Severity Level:

I. Minor-control by lab, no OES or Police response

II. Moderate-lab personnel unable to control or clean-up. OES will control activities with assistance from Campus Police

III. Large-Large, may require building evacuation

IV. Major-Major portion of campus affected or threatening neighbors

•Call Campus Police (911) and OES (578-5640) for level II or greater.
•Obtain MSDS and make available to emergency personnel
•Protect yourself and others from exposure by closing doors,
•Control ignition sources if flammables are involved
•Evacuate as necessary to protect personnel health and safety
•Follow directions from OES and Campus Police

Note: Chemical incidents which result in hospitalization, evacuation, release off site etc., require notification to State Police. OES will normally make this notification. It must be made within one hour of occurrence.

Bio-safety Incidents

If the person involved can clean up the spill or stop the release safely, then it is appropriate to do so. If not, take the following steps:

• Notify supervisor and determine Severity Level:

I. Minor-control by lab, no OES or Police response

II. Moderate-lab personnel unable to control or clean-up. OES will control activities with assistance from Campus Police

III. Large-Large, may require building evacuation

IV. Major-Major portion of campus affected or threatening neighbors

SECURE THE AREA

•Notify others in vicinity to avoid exposure
•Call Campus Police (911) if there is a threat outside the lab and begin evacuation
•Injured personnel should be decontaminated before transport
•Technical information regarding the agent should be provided to medical and emergency response personnel

NOTE: Select agent exposure and releases require immediate notification to CDC and/or APHIS. Immediately notify RO of Severity II or greater incidents and exposures, he/she will notify CDC. For offsite release or loss of agents/toxins, local and state enforcement and response agencies will be notified by RO.

Bio-safety Incidents Pre-Planning

Each lab is to establish a lab specific emergency incident pre-plan which addresses:

- Contamination scenarios

- Decontamination procedures and re-occupancy criteria for
    - Personnel
    - Equipment
    - Area

Laboratory Line of Authority

For use in case of emergency, each lab shall post internally and outside the laboratory entrance, a line of authority containing names and 24-hour emergency contact telephone numbers designating primary, secondary and third level authority for the lab. In addition, the outside of the laboratory shall be posted with a list of significant hazards contained within the laboratory to advise emergency personnel. A standard set of pictograph labels for many hazards will be available from the Institutional Biological and Recombinant DNA Safety (IBRDS) Committee.

Emergency Phone Numbers

As part of laboratory worker training, each person working in the laboratory shall be supplied with a list of emergency numbers and the line of authority for the laboratory. Such information shall also be posted adjacent to every telephone in the laboratory and should be maintained up to date (note 'date updated' on list) and in readable format.

FIRE/FIRST AID/POLICE From Off Campus	Call 911 **LSUPD** 225 578 3231 **LSUPD**
HOSPITAL/EMS From off campus	Call 911 **LSUPD** 225 578 3231 **LSUPD**
STUDENT HEALTH SERVICES	578-6271
POISON CONTROL	Call 911 – (provide name of material for reference purposes) 1-800-256-9822 (Poison Control Center)
EMERGENCY SERVICES	Call 911 **LSUPD**
CHEMICAL/BIOLOGICAL ACCIDENTS AND SPILLS OR RELEASES *****plus***** **If BIOLOGICAL/rDNA MATERIALS** involved- *****plus***** If **RADIOACTIVE MATERIALS** involved	Call 911 **LSUPD** **OES/RO** at 578-8507 workdays 761-1318 off-hours **Bio-safety Officer (Vet School)** 578-9918 workdays 767-0742 off hours **IBRDS Committee Chair** at 578-4194 workdays 769-3486 off hours **Radiation Safety Office** at 578-2747 workdays 296-0443 off hours

General Laboratory Procedures

The following general procedures have been approved by the IBRDS Committee. They reflect a sincere effort to help the PI conduct research of the highest quality, while complying with all current local, state and federal regulations and guidelines pertaining to the use of biological agents and/or recombinant DNA in research.

1. No food or drinks are allowed in the laboratory areas where experiments with biological agents and recombinant DNA are carried out.
2. No smoking or tobacco products are permitted anywhere within the research laboratories.
3. Only authorized personnel are permitted in the laboratories where infectious agents and/or recombinant DNA work is conducted. Authorized personnel are defined as institutional investigators and their assistants, institutional officials, laboratory employees and authorized custodial and maintenance personnel who are qualified through training or experience to conduct themselves in a safe manner. (See Section V for select agent research)
4. Report all emergency situations involving biological/ rDNA research to LSU Police, Occupational and Environmental Safety (OES), the Biosafety Officer and Responsible Official (RO), and the IBRDS Committee Chairperson. 911 may be used to contact LSU Police. All other emergency numbers should be posted in the laboratory and at the entrance door to the laboratory.
5. All experiments with biological agents and /or recombinant DNA work must be in pre-approved facilities (approved by university and appropriate state/federal agencies). and may only occur in the designated laboratory or approved field isolation facility.
6. Requests for exceptions to these requirements should be communicated to the IBRDS Committee Chairperson in writing prior to beginning any work, to provide documentation for future reference. Any incident involving biological agents or recombinant DNA that could cause a potential biohazard for employees, the general public, or the environment must be reported immediately to the IBRDS Committee, regardless whether it is an emergency situation or not.

Emergency Equipment

All personnel should be familiar with the location and use of all the emergency equipment in their laboratories. This includes fire extinguishers, eyewash stations, deluge showers, fire blankets, spill kit materials, respiratory protection devices, fire alarm pull stations and relevant decontamination procedures and supplies.

Evacuation Routes

All personnel should be familiar with the primary and secondary evacuation routes from their area to the nearest exit. The secondary route should be used when the first one is blocked. All personnel should be told what method is used to signal a building evacuation, either a building alarm or manually operated air horn. The responsible party shall lock the bio/rDNA laboratory after insuring the laboratory has been evacuated unless to do would endanger the live of the responsible party.

Spills and Emergencies

All laboratories shall stock appropriate decontamination materials to handle minor spill. Minor spills should be cleaned up immediately by trained laboratory personnel, providing the material is not immediately dangerous to life and health (IDLH,) and cleanup materials and equipment are available. Otherwise, evacuate the immediate area and call LSUPD at 225- 578-3231 or 911. ***On spills, releases or inventory losses involving select agents, call the LSU Police, Occupational and Environmental Safety (OES), the Biosafety Officer/ Responsible Official (RO), and the IBRDS Committee Chairperson These numbers shall accompany written emergency procedures for each laboratory..***

For spills of moderate size, call OES. Again assuming the material is not IDLH level, OES personnel will provide technical assistance and guidance to laboratory personnel in cleaning up.

For moderate-to-large spills of IDLH-level materials or for large spills of ordinarily dangerous materials, e.g. acid, etc.:

1. Evacuate the area of the spill, or in larger incidents, the entire building, either personally or with the assistance of the building authority .The persons leaving the building should gather at a point up-wind from the building. If the agreed meeting site is unsafe an alternate site should be identified and included in the training regime.

2. Call the emergency number and report the incident. Ask the dispatcher to notify the fire department, LSU Police Department, and OES.

Those involved in the incident are to remain available outside the building to assist the emergency groups. After the initial notification, the laboratory authority and the department head are to be notified. Do not move from the incident site, as it can cause contamination of large areas. If someone has been potentially exposed, inform campus police when the initial emergency call is made.

If there is a fire of any but the smallest size (where there is confidence that it can be put out without risk of spreading and endangering anyone), call 911 and report the fire. Again the building is to be evacuated.

If there is an emergency involving personal injury, call 911 and ask for EMS (ambulance). If an eye injury or skin exposure is involved, assist the injured person to an eyewash station, deluge shower, or combination unit. Provide first aid/CPR as needed.

Medical Treatment

All emergency medical treatment cases other than first aid should be handled by notifying LSU Police by calling 911. The Police will, in turn, call the EMS response personnel and guide them to the right location. Be sure to provide accurate and thorough information about the location and the seriousness of the injuries/illnesses. Do not hang up with the LSU Police until you are told to do so or they hang up. It is important that they get all the pertinent information before they dispatch a unit.

I. GENERAL

Purpose

LSU & A&M College, LSU Agricultural Center, Pennington Biomedical Research Center; and Hansen's Disease Center have established an Inter-Institutional Biological and Recombinant DNA Safety (IBRDS) Committee to ensure the safe conduct of research using biological agents and recombinant DNA technology.

Preface

A knowledge and understanding of the information presented in this handbook is mandatory for those investigators using biological agents and recombinant DNA in their research. The contents of this manual are derived from directions established by the IBRDS Committee, institutional policies, the CDC manual entitled ***"Biosafety in Microbiological and Biomedical Laboratories, 4th Edition***" and the ***NIH Guidelines***. Readers are encouraged to examine these documents to assure that the latest revisions are taken into account when making decisions regarding hazardous agents/toxins. Information in this manual is not inclusive of all the information available and necessary for making all decisions, but is intended to be a ready reference for information on the procedures, roles and responsibilities in place in the institution.

Scope

The IBRDS Committee is responsible for devising and implementing policies and procedures that provide adequate precautions and safeguards to prevent the dissemination of biological agents of any kind that can directly or indirectly spread in humans, animals and plants. Such agents include, but are not limited to, infectious organisms of bacterial, viral, rickettsial, chlamydial, prional, parasitic or fungal origin that can independently infect and spread in humans, animals or plants. Other agents include those that can potentially change the genetic make up of an animal or plant by becoming a permanent part of their genetic make up, and any other biological agent that can indirectly spread by physical means or through any other biological vector system. IBRDS is also responsible for all experimentation with recombinant DNA technology .The committee works closely with the Biosafety Officer and RO (both members of the IBRDS Committee) to review and approve all research facilities and procedures using infectious agents and recombinant DNA for appropriate containment of biological materials, including viruses, cell cultures and protists.

Responsibilities

The quality of research is enhanced through careful planning and forethought in a safe environment. The primary mission of the IBRDS Committee is to ensure that research involving biological agents of humans, animals and plants, and/or recombinant DNA technology is conducted within existing federal and state laws and guidelines that aim to protect the safety of workers, the general public, animals, plants and the environment The IBRDS Committee is obligated to require information from the principal investigator for a thorough review of proposed research. It seeks to satisfy all federal and state laws and guidelines without impeding the research of the participating

institutions and individual laboratories. The level of IBRDS Committee review will be proportional to the potential hazards presented in each research protocol, in accordance with all federal and state guidelines.

Authority

The procedures of the IBRDS are entirely consistent with the "Guidelines for Research Involving Recombinant DNA Molecules of the Federal Register", latest edition, the CDC Biosafety in Medical and Biomedical Laboratories", and with institutional policies that established the IBRDS Committee as an interinstitutional committee.

II. APPLYING FOR APPROVAL TO USE BIOLOGICAL AGENTS AND RECOMBINANT DNA

Requirements for a Principal Investigator (PI) or Director.

The PI or project director of a research protocol must be a member of the participating Institutions as a full or part-time employee or equivalent. Under special circumstances, a visiting scientist from another institution may be eligible to use biological agents and/or recombinant DNA at any of the participating Institutions; but the PI of the protocol must still be an employee of the institution in which the work will be performed. The PI has authority over all other personnel listed on the protocol submitted for IBRDS compliance, and is responsible for all aspects of the care and use of biological agents and recombinant DNA.

Risk Assessment

Risk assessment is ultimately a subjective process. The investigator must make an initial risk assessment based on the Risk Group (RG) of an agent (see NIH Guidelines - Appendix B, Classification of Human Etiologic Agents on the Basis of Hazard). Agents are classified into four Risk Groups (RGs) according to their relative pathogenicity for healthy adult humans by the following criteria: (1) Risk Group 1 (RG1) agents are not associated with disease in healthy adult humans. (2) Risk Group 2 (RG2) agents are associated with human disease which is rarely serious and for which preventive or therapeutic interventions are often available. (3) Risk Group 3 (RG3) agents are associated with serious or lethal human disease for which preventive or therapeutic interventions may be available. (4) Risk Group 4 (RG4) agents are likely to cause serious or lethal human disease for which preventive or therapeutic interventions are not usually available.

Guidelines from CDC include the following considerations in Risk Assessment:

- The pathogenicity of the infectious or suspected infectious agent, including disease incidence and severity (i.e., mild morbidity versus high mortality, acute versus chronic disease).
- The route of transmission (e.g., parenteral, airborne, or by ingestion) of newly isolated agents may not be definitively established. Agents that can be transmitted

by the aerosol route have caused most laboratory infections. It is wise, when planning work with a relatively uncharacterized agent with an uncertain mode of transmission, to consider the potential for aerosol transmission.

- Agent stability is a consideration that involves not only aerosol infectivity (e.g., from spore-forming bacteria), but also the agent's ability to survive over time in the environment.
- The infectious dose of the agent is another factor to consider. Infectious dose can vary from one to hundreds of thousands of units. The complex nature of the interaction of microorganisms and the host presents a significant challenge even to the healthiest immunized laboratory worker, and may pose a serious risk to those with lesser resistance. The laboratory worker's immune status is directly related to his/her susceptibility to disease when working with an infectious agent.
- Approved researchers who become immuno-suppressed as a result of chemotherapy or other underlying disease, may wish to discuss their increased risk of susceptibility when working with pathogerns, with the Biological Safety Officer.
- The concentration (number of infectious organisms per unit volume) will be important in determining the risk
- The origin of the potentially infectious material is also critical in doing a risk assessment.
- The availability of data from animal studies, in the absence of human data, may provide useful information ~~in~~ for a risk assessment. Information about pathogenicity, infectivity, and route of transmission in animals may provide valuable clues. Caution must always be exercised, however, in translating infectivity data from one species of animal to another species.
- The established availability of an effective prophylaxis or therapeutic intervention is another essential factor to be considered. The most common form of prophylaxis is immunization with an effective vaccine.
- Medical surveillance ensures that the safeguards decided upon, in fact, produce the expected health outcomes, and
- Risk assessment must also include an evaluation of the experience and skill level of at-risk personnel such as lab workers and maintenance, housekeeping, and animal care personnel.

A final assessment of risk based on these considerations is then used to set the appropriate containment conditions for the experiment.

Training

All persons involved in the use of biological agents and recombinant DNA must have received appropriate training. The PI is to be familiar with the handling of biological agents or recombinant DNA samples, and the guidelines outlined in this handbook. The PI is responsible for the training of personnel listed in the protocol. The Biosafety Officer, RO and the chair of the IBRDS Committee are to be readily available for answering questions about safe and practical handling of biological agents and recombinant DNA samples.

Protocol Form

The PI must submit the appropriate institutional routing form for documentation of review and approval of research projects using biological agents and/or recombinant DNA. The form must include identification of any biological agents infectious to plants or animals, rDNA, and/or select agents/toxins. Assistance is available from the IBRDS Chairperson, OES Office, Biosafety Officer, RO, and/or any member of the IBRDS Committee. It is strongly recommended that investigators seek consultation during the planning stage of a project involving infectious agents or recombinant DNA. ***Prior consultation and approval by appropriate personnel is necessary for select agent/toxin research***.

Use of any radioactive materials must be reviewed and approved by the Radiation Safety Officer. Use of other hazardous materials, including chemicals and biological agents must satisfy additional requirements determined by the Occupational and Environmental Safety (OES) Office, the Biosafety Officer and RO. The involvement of human subjects must be indicated and approved by the Human Subjects Committee. The involvement of animal subjects must be indicated and approved by the Institutional Animal Care and Use Committee (IACUC).

In general, many grants can receive approval after submission but prior to receiving funds. Approvals for select agent/toxin research and associated rDNA research must be received prior to submittal of the grant request. Requests requiring approvals from the IACUC must be *submitted to the IACUC* prior to the grant request being sent in by the institution.

Submission of Protocol Applications

The typed Protocol Review and Approval Form is submitted to the IBRDS Chairman or IBRDS Secretary for review at the next meeting.

Final Paperwork

A copy of the protocol review and approval form will be signed and mailed by the Chairman of IBRDS Committee to the Principal Investigator for each approved protocol.

Protocol modifications

Rather than submitting a new protocol, a PI with an approved protocol may submit an addendum to make minor changes such as:

1. Addition or deletion of personnel
2. Extension of time.
3. Addition or deletion of strains of the same organism or their host.
4. Addition or deletion of a gene that does not significantly alter the original protocol in intent or the Biosafety level.

A request for modifications to an existing protocol is submitted on a separate form that requires restatement of the objective of the original (parent) protocol and justification for the changes. A request for modifying an existing research protocol cannot be used if:

1. The changes increase the required Biosafety Level necessary to work with the altered or new agent.

2. There is a change in species of the host not previously approved.

3. There is a change in the overall objective of the research.

The IBRDS Committee makes the final decision as to whether an addendum rather than a new full protocol application is sufficient for applying for permission for a specific procedure or change in protocol.

Pilot Studies (For biological agents and/or rDNA, excluding Select Agents/Toxins)

No research can be performed with biological agents and/or recombinant DNA without prior approval of the IBRDS Committee. However, sometimes an investigator needs to perform pilot experiments to determine the feasibility of a study or obtain information about the success rate or the reproducibility so that a good protocol can be submitted. In these cases the investigator should still submit a protocol stating what is to be done and why. Because the investigator does not have sufficient information to justify the use of the infectious agents and/or recombinant DNA, etc., the investigator can state that this is a pilot study, request approval for a short period of time (e.g. 1-2 months) using a small quantity of the infectious agent, host, vector, or gene. If the pilot studies are successful, it may be possible to expand approval to the full time and extend the project by applying for approval of a modified protocol as described above.

III. PROCEDURES AND CLASSIFICATION FOR EXPERIMENTS WITH BIOLOGICAL AGENTS AND/OR RECOMBINANT DNA

(See Section V for additional information on experiments involving select agents/toxins)

A. Assessing the Risk

Experiment classifications must be consistent with the latest edition of the NIH guidelines at http://www4.od.nih.gov/oba/rac/guidelines/guidelines.html, and the CDC BMBL manual at http://www.cdc.gov/od/ohs/biosfty/bmbl4/bmbl4toc.htm.

In deciding on the appropriate containment for an experiment, the initial risk assessment from Appendix B, Classification of Human Etiologic Agents on the Basis of Hazard (NIH Guidelines), should be followed by a thorough consideration of the agent itself and how it is to be manipulated. Factors to be considered in determining the level of containment include agent factors such as: virulence, pathogenicity, infectious dose, environmental stability, route of spread, communicability, operations, quantity, availability of vaccine or treatment, and gene product effects such as toxicity, physiological activity, and allergenicity. Any strain that is known to be more hazardous than the parent (wild-type) strain should be considered for handling at a higher containment level. Certain

attenuated strains or strains that have been demonstrated to have irreversibly lost known virulence factors may qualify for a reduction of the containment level compared to the Risk Group assigned to the parent strain.

B. Experiments with Biological Agents.

All projects that are declared by the Principal Investigator to deal with biological agents that require BL1 or BL2(small scale) biological agents or the corresponding safety levels PI, P2 for experimentation with plants require only submission of the IBRDS Documentation of Review and Approval Form and a full copy of the project's abstract as submitted to the funding agency.

All projects that propose work with biological agents that require BL2 (large scale) or BL3 level containment are required to submit the appropriate protocol review and approval form and two full copies of the complete grant application or other material describing in detail the proposed work and all containment procedures.

C. Experiments with Recombinant DNA.

All projects that propose the use of recombinant DNA experimentation that falls under any of the NIH/IBRDS exemption categories only require submission of the appropriate protocol review and approval form and a full copy of the abstract describing the proposed work. Sufficient detail shall be included to allow a trained person to make an informed decision regarding potential risk of the proposed work.

All projects that propose work with recombinant DNA that do not fall under any of the current exemption categories of the NIH/IBRDS guidelines are required to submit the appropriate institutional protocol review and approval form and two full copies of the grant application or other material describing in detail the proposed work and all containment procedures.

Exempt categories of experiments using recombinant DNA: (refer also to the NIH Guidelines).

1. Those that are not in organisms or viruses.

2. Those that consist 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.

3. Those that consists 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 species) or when transferred to another host by well established physiological means; also, those that consist entirely of DNA from a 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).

4. 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 segments may be a synthetic equivalent.

5. Other classes of recombinant DNA molecules as determined by the NIH Director and specified in the NIH Guidelines.

Exempt status can be anticipated by reviewing the guidelines above, the NIH Guidelines, or by discussion with the Chairperson of the IBRDS Committee.

When the institution conducts recombinant DNA research that requires IBRDS Committee approval in accordance with Appendix P of the NIH Guidelines (Physical and Biological Containment for Recombinant DNA Research Involving Plants), the institution shall appoint at least one individual with expertise in plant, plant pathogen, or plant pest containment principles (who is a member of the Institutional Biosafety Committee) to act as the Plant, Plant Pathogen, or Plant Pest Containment Expert.

When the institution conducts recombinant DNA research that requires IBRDS Committee approval in accordance with NIH Guidelines - Appendix Q (Physical and Biological Containment for Recombinant DNA Research Involving Animals), the institution shall appoint at least one individual with expertise in animal containment principles (who is a member of the Institutional Biosafety Committee).

D. Experiments with Biological Agents and/or Recombinant DNA and whole Plants (See Section V of this manual for select agents)

All projects that are declared by the Principal Investigator to deal with biological agents that require BL1-P or BL2-P(small scale} biological agents for experimentation with plants require only submission of the appropriate institutional protocol review and approval form and a full copy of the project's abstract as submitted to the funding agency.

All projects that propose work with biological agents that require BL2-P+(large scale) or BL3-P level containment are required to submit the appropriate institutional protocol review and approval form and two full copies of the complete grant application or other material describing in detail the proposed work and all containment procedures.

All projects that propose the use of recombinant DNA experimentation that falls under any of the NIH/IBRDS exemption categories require only submission of the appropriate institutional protocol review and approval form and a full copy of the abstract describing the proposed work.

All projects that propose work with recombinant DNA that do not fall under any of the current exemption categories of the NIH/IBRDS guidelines (see also section B above) are required to submit the institutional protocol review and approval form and two full copies of the grant application or other material describing in detail the proposed work and all containment procedures.

*The following steps are required for conducting transgenic field experiments with plants***.**

1. Complete permit for release APHIS 2000
2. Obtain approval of IBRDS Committee
3. Submit APHIS 2000 to APHIS
4. Notify LDAF and regional USDA Officer (Texas)
5. Obtain written approval with permit number from APHIS.

D. Experiments with Biological Agents and/or Recombinant DNA Using Animals

If experimental animals are used, institutional management must provide facilities, staff, and established practices that reasonably ensure appropriate levels of environmental quality, safety, and care. Laboratory animal facilities are simply a special type of laboratory. As a general principle, the biosafety level (facilities, practices, and operational requirements) recommended for working with infectious agents in vivo and in vitro are comparable. Work with vertebrates requires separate approval from the animal use committee.

However, it is well to remember that the animal room can present some unique problems. In the microbiological laboratory, hazardous conditions are caused by personnel or by the equipment being used. In the animal room, the activities of the animals themselves can present new hazards. Animals may generate aerosols, they may bite and scratch, and they may be infected with a zoonotic disease.

Researchers who wish to perform research at any Animal Biosafety Level (ABSL) are required to submit the institutional protocol review and approval form and two full copies of the grant application or other material describing in detail the proposed work and all containment procedures.

NOTE: ***In addition to IBRDS requirements, federal and state agency rules and procedures apply if select agents are in use.***

IV . IBRDS PROCEDURES

Appointments

The LSU Vice Chancellor for Research and Graduate Studies appoints the IBRDS Committee Chairman, Vice-Chairman and Committee Members after consultation with the Director of the LSU Agricultural Experiment Station, the Director of the Pennington Biomedical Research Center, and the Director of the Hansens Disease Center. At least five (5) people are appointed including two individuals who are not associated with the participating institutions, and one member from the laboratory technical staff. A minimum of one member is appointed from each participating Institution. Members can be reappointed for sequential one year terms. The IBRDS chairman may appoint additional members as needed after consultation, with other Committee Members. The Director, Occupational and Environmental Safety and the Biosafety Officer are invited to attend and participate in committee meetings and proceedings.

In order to ensure the competence necessary to review and approve recombinant DNA activities, the IBRDS Committee should:

- Include persons with expertise in recombinant DNA technology, biological safety, and physical containment, and
- Include, or have available as consultants, persons knowledgeable in institutional commitments and policies, applicable law, standards of professional conduct and practice, community attitudes, and the environment

Responsibilities

The primary mission of the IBRDS Committee is to ensure that research involving biological agents of humans, animals and plants, and/or recombinant DNA technology is conducted within existing Federal and State laws and guidelines that aim to protect the safety of workers, the general public, animals, plants and the environment. The IBRDS Committee is obligated to require information from the Principal Investigator for a thorough review of proposed research. The IBRDS Committee seeks to satisfy all federal and state laws and guidelines without impeding the research thrust of the participating institutions and individual laboratories. The quality of research is enhanced through careful planning and forethought in a safe environment The level of IBRDS review will be proportional to the potential hazards presented by each research protocol, in accordance with all federal and state guidelines.

Specifically, the IBRDS Committee is required to:

1. Review technical and safety-related aspects of the use of all biological materials, infectious agents/toxins and recombinant DNA.

2. Develop a safety and operations manual for use of biological agents.

3. Promulgate a Biosafety Program in conjunction with the Offices of Occupational Environmental Safety in the participating institutions that satisfies federal, state and local

laws and regulations.

4. Maintain records of all committee meetings, inspections, protocols, and personnel training.

5. Review protocols and facilities upon request and periodically as adopted by the committee. Classify and certify facilities with respect to appropriate biosafety levels .

6. Identify members of the IBRDS to the NIH Office for Recombinant DNA Activities (ORA) in accordance with NIH guidelines.

IBRDS Committee Protocol Review

At periodic meetings the committee discusses each protocol brought for review, and votes whether to approve or disapprove proposed protocols. A simple majority rules. Committee members listed on the protocol may be present for the discussion, but must leave the room for the vote. It is not unusual for a protocol to be approved pending specific modifications. Protocols that have been exempted from full committee review should be recorded and maintained in the committee records.

Administrative Approval

The Chairperson of the Committee has the authority to grant interim approval of protocol modifications (but not new protocols) outside of the Committee, but these interim approvals must be confirmed by the membership at the next scheduled Committee meeting. If it is not confirmed, the PI must stop the procedure as soon as he or she is notified of the Committee's ruling. (On select agents, RO approval must be obtained in addition to IBRDS Committee approval. See LSU Policy Statement “Select Agent Research”)

Administrative Actions

Upon learning of any possibility that biological agents or recombinant DNA are used in an unapproved or unsafe way, the IBRDS Committee has the authority and responsibility (depending on the severity of the problem) to:

1. Warn the PI, and ask for immediate correction of the problem:

I. Suspend approval of the relevant portion of a protocol, and/or

3. Suspend authorization for the use of biological agents and/or recombinant DNA by the PI.

The IBRDS Committee may, at its option, act by making a recommendation to the PI. Failure to abide by the recommendation of the Committee may result in disciplinary action. Upon acting to correct a discovered discrepancy at LSU, the IBRDS Committee shall prepare a report to the Vice-Chancellor for Research and Graduate Studies, after which the Vice Chancellor has the option to recommend disciplinary action to the Chancellor, if appropriate, consistent with PS-36. For other participating institutions, the IBRDS Chairperson will report this to the appropriate administrative officer.

The IBRDS Committee will also notify the agency providing funds for the infectious agents and recombinant DNA studies, and, if deemed necessary, work with the department director and other administrative staff in each participating institution to resolve the issue. (See Section V for select agent procedures) The Committee has the option to continue the suspension of approval for the use of biological agents or recombinant DNA by the PI until the problem is rectified.

Periodic Meetings

The IBRDS Committee will normally meet quarterly. The Chairperson may call for a special meeting if so required. The meeting will be conducted by the Chairperson, or in his or her absence, the Vice Chairperson. A quorum is defined as greater than 50% of voting membership. Business can be conducted in the absence of a quorum but no action will be official until the absent members are polled for their votes on the specific issues.

Minutes will be recorded by the Secretary, distributed to the membership at least two (2) days before the next meeting, and a vote for their approval will be held as the first order of business of each meeting. A tape recorder can be used by the Secretary, but the tape of each meeting is to be erased after the minutes for that meeting are approved.

The Chairperson, Biosafety Officer and RO will give reports on their activities since the last meeting. If any administrative actions are reported, the committee will then vote on whether or not to confirm the actions.

This will be followed by Old and New Business matters.

The last order of business will be the review of protocols and addenda. Review of each proposal will be assigned to a primary and a secondary reviewer that are members of the IBRDS Committee. These reviewers will discuss their findings and submit a brief typewritten review for each proposal. Each reviewer may include comments from outside consultants, but the consultants have no authority to withhold, approve, or vote on protocols.

Annual Report to NIH on Recombinant DNA activities

For each institution, the IBRDS Committee Chairperson shall file an annual report with NIH/OBA which includes: (I) a roster of all Institutional Biosafety Committee members clearly indicating the Chair, contact person, Biological Safety Officer (if applicable), plant expert (if applicable), animal expert (if applicable), human gene therapy expertise or ad hoc consultant(if applicable); and (ii) biographical sketches of all Institutional Biosafety Committee members (including community members)

Changing Policy

Changes to this policy of the IBRDS Committee may be made by a majority vote of the committee members during regular meetings. A 50% quorum of the committee members is needed for any

change in policy.

V. REQUIREMENTS FOR RESEARCH INVOLVING SELECT AGENTS/TOXINS

Background on Laws and Regulations on "Select Agents"

The threat of illegitimate (terrorist) use of infectious agents/toxins has attracted interest from the perspective of public health and national security. There is increasing concern that certain "select" agents could be used in a way that would have serious adverse consequences for human health and safety and plant and animal life. In this section, regulated HHS/USDA select agents/toxins are sometimes referred to as simply "select agents" or "listed agents".

"The Antiterrorism and Effective Death Penalty Act of 1996"* and the *"Uniting and Strengthening America by Providing Appropriate Tools Required to Intercept and Obstruct Terrorism Act (USA PATRIOT Act) of 2001"

These laws established provisions that prohibit access to select agents/toxins by individuals who are specifically restricted under federal law. The USA PATRIOT Act also regulates the possession, usage, disposal or transfer of select agents. This law required the Department of Health and Human Services to issue rules to implement these provisions. The Center for Disease Control implemented new regulations to meet the requirements of this statute. Specifically, the law was designed to

a) Establish a system of safeguards to be followed when specific agents are transported;
b) Collect and provide information concerning the location where certain potentially-hazardous agents are transferred;
c) Track the acquisition and transfer of these specific agents;
d) 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.);
e) Follow safeguards where agents are stored to prevent an unauthorized user from gaining access to the facility areas where select agents are stored or used; comply with registration requirements which indicate the point of origin for the user and importer, including storage requirements of five years;
f) Provide specific training to ensure anyone working with biohazards understands the law and knows how to support safe handling and security related to select agents.
g) Prevent access to restricted individuals as follows: (Quoted from the Law)

".....PUBLIC LAW 107-56-OCT. 26, 2001
SEC. 175b. POSSESSION BY RESTRICTED PERSONS.
(a) No restricted person ... shall ship or transport in interstate or foreign commerce, or possess in or affecting commerce, any biological agent or toxin, or receive any biological agent or toxin that has been shipped or transported in interstate or foreign commerce, if the biological agent

or toxin is listed as a select agent... and is not exempted under subsection (h) of such section 72.6, or appendix A of part 72 of the Code of Regulations.
(b) In this section:

(1) The term 'select agent' does not include any such biological agent or toxin that is in its naturally-occurring environment, if the biological agent or toxin has not been cultivated, collected, or otherwise extracted from its natural source.

(2) The term 'restricted person' means an individual who:

(A) is under indictment for a crime punishable by imprisonment for a term exceeding 1 year;
(B) has been convicted in any court of a crime punishable by imprisonment for a term exceeding 1 year;
© is a fugitive from justice;
(D) is an unlawful user of any controlled substance (as defined in section 102 of the Controlled Substances Act (21 U.S.C.802));
(E) is an alien illegally or unlawfully in the United States;
(F) has been adjudicated as a mental defective or has been committed to any mental institution;
(G) is an alien (other than an alien lawfully admitted for permanent residence) who is a national of a country as to which the Secretary of State, pursuant to ...., has made a determination (that remains in effect) that such country has repeatedly provided support for acts of international terrorism (Currently Cuba, Iran, Iraq, Libya, North Korea, Sudan and Syria); or

(H) has been discharged from the Armed Services of the United States under dishonorable conditions.

(3) The term 'alien' has the same meaning as in section 1010(a)(3) of the Immigration and Nationality Act (8 U.S.C. 1101(a)(3)).

(4) The term 'lawfully admitted for permanent residence' has the same meaning as in section 101(a)(20) of the Immigration and Nationality Act (8 U.S.C. 1101(a)(20)).....

Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (The Tauzin Act)

In 2002, the passage of Public Law 107-188, Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (TAUZIN ACT) further defined our country's response to bioterrorism and expanded the coverage. It includes the following titles:

Title I – National Preparedness for Bioterrorism and other Public Health Emergencies
Title II – Enhancing Controls on Dangerous Biological Agents & Toxins
Title III – Protecting Safety and Security of Food and Drug Supply
Title IV – Drinking Water Security and Safety
Title V – Other Provisions

Title II, which impacts research, includes the following Chapters:

Subtitle A - Department of Health & Human Services (HHS)
Subtitle B - Department of Agriculture "Agricultural Bioterrorism Protection Act of 2002"
Subtitle C - Interagency Coordination Regarding Overlap Agents and Toxins
Subtitle D - Criminal Penalties Regarding Certain Biological Agents and Toxins

This Title further expands the restrictions on access to select agents, expands the number of select agents to include plant pathogens, provides for notification of possession of select agents to federal agencies, and revises the approach to safeguarding access. Under Title II, HHS and USDA were directed to develop:

Standards/procedures governing transfer, possession, and use to ensure proper training & appropriate skills to handle select agents, proper lab facilities to contain them and procedures to dispose of them;
Security measures to prevent access to select agents/toxins that may be used in domestic or international terrorism or for any other criminal purpose;
Procedures to protect the public safety in the event of transfer or potential transfer of listed agents or toxins in violation of provisions in the law and regulations established by HHS and USDA.

Under provisions of the law, the person seeking to possess or use select agents must:
Have legitimate need to handle or use select agents or toxins;
Submit the names and other identification for such individuals to the Secretary and Attorney General promptly after determining the individual's need to access (to be done periodically thereafter – no less than every 5 yrs.)
Deny access to listed agents & toxins by individuals whom the Attorney General has identified as restricted persons

HHS and USDA completed the "notification of possession" requirements and issued regulations in 2002 as required in the law. This section outlines the requirements for compliance with the regulations issued on December 13, 2002. The HHS regulations are located in 42 CFR Part 73 and 42 CFR Part 1003, and the USDA/APHIS regulations are in 7 CFR Part 331 and 9 CFR Part 121.

The timeline for compliance with the regulations are shown in the table which follows:

Time Line for Compliance HHS/USDA Select Agent/Toxin Regulations	
Deadlines (2003)	Parts of Regulations Required to be in Effect
Feb. 7	All sections of regulations relating to purpose and scope, prohibitions, listed agents/toxins/pathogens and exemptions, RO, safety & emergency response (incl. training), records, inspections, notification of theft/loss/release, penalties, appeals

Mar. 12	Application due, certifying compliance with effective sections and that the applications for DOJ review for entity and RO are submitted, Transfer Provisions in effect
April 12	Application for DOJ review for individuals submitted, Entity and RO review completed by DOJ
June 12	Individual DOJ review complete, Security Plan development complete
Sept. 12	Security Plan implemented, Training for security provisions completed.
Nov. 12	Full compliance required, Registration section effective

Definition of "Select Agents/Toxins"

"Select Agents" is a term that is used to describe a range of microorganisms such as viruses, bacteria, fungi, rickettsiae, genetically modified microorganisms, and toxins. Select agents are sometimes referred to as "listed agents" and "select agents/toxins" In the USDA regulations, a select agent is called a "biological agent", and is defined as: "Any microorganism (including, but not limited to, bacteria, viruses, fungi, rickettsiae, or protozoa), or infectious substance, or any naturally occurring, bioengineered, or synthesized component of any such microorganism or infectious substance, capable of causing:
(1) Death, disease, or other biological malfunction in a human, an animal, a plant, or another living organism;
(2) Deterioration of food, water, equipment, supplies, or material of any kind; or
(3) Deleterious alteration of the environment." Similar definitions are found in the HHS regulations.

Likewise, "toxin" is defined in USDA regulations as "The toxic material or product of plants, animals, microorganisms (including, but not limited to, bacteria, viruses, fungi, rickettsiae, or protozoa), or infectious substances, or a recombinant or synthesized molecule, whatever their origin and method of production, and includes:
(1) Any poisonous substance or biological product that may be engineered as a result of biotechnology
produced by a living organism; or
(2) Any poisonous isomer or biological product, homolog, or derivative of such a substance.

Another definition is "overlap agent or toxin", which is any microorganism (including, but not limited to, bacteria, viruses, fungi, rickettsiae, or protozoa) or toxin that poses a risk to both human and animal health and that is listed as a select agent. This term is used to help allocate the select agents to the appropriate regulatory agency in the government. High Consequence Plant Pathogens is a term used by APHIS to describe plant pathogens that are select agents. HHS calls their

Similar definitions are found in the HHS regulations.

SELECT AGENTS AND TOXINS

Except for exclusions listed below, the viruses, bacteria, fungi, toxins, genetic elements, recombinant nucleic acids, and recombinant organisms specified in this list are Department of Health and Human Services (HHS) select agents and toxins, United States Department of Agriculture (USDA) high consequence livestock pathogens, or HHS/USDA overlap agents. Animal and Plant Heath Inspection Service (APHIS) plant pathogens regulated as select agents are also listed below.

Transfers are regulated. If you intend to import, purchase or otherwise obtain, ship or transfer possession of any agent from or to any individual or entity, both inside or outside of Louisiana State University, contact OES in advance.

IF YOU POSSESS ANY OF THESE AGENTS AND HAVE NOT PREVIOUSLY DECLARED THEM TO THE RESPONSIBLE OFFICIAL (RO), IMMEDIATELY CONTACT OES AT 225-578-8507

Viruses:

- African horse sickness virus [α]
- African swine fever virus [α]
- Akabane virus [α]
- Avian influenza virus (highly pathogenic) [α]
- Bluetongue virus (exotic) [α]
- Camel pox virus [α]
- Cercopithecine herpesvirus 1 (Herpes B virus) [β]
- Classical swine fever virus [α]
- Crimean-Congo haemorrhagic fever virus [β]
- Eastern Equine Encephalitis virus [χ]
- Ebola viruses [β]
- Foot-and-mouth disease virus [α]
- Goat pox virus [α]
- Hendra virus [χ] I

· Japanese encephalitis virus [α]
· Lassa fever virus [β]
· Lumpy skin disease virus [α]
· Malignant catarrhal fever virus (exotic) [α]
· Marburg virus [β]
· Menangle virus [α]
· Monkeypox virus [β]
· Newcastle disease virus (exotic) [α]
· Nipah virus [χ] I
· Peste des petits ruminants virus [α]
· Rift Valley fever virus [χ]
· Rinderpest virus [α]
· Sheep pox virus [α]
· South American Haemorrhagic Fever viruses (Junin, Machupo, Sabia, Flexal, Guanarito)[β]
· Swine vesicular disease virus [α]
· Tick-borne encephalitis complex (flavi) viruses [Central European Tick-borne encephalitis,
· Far Eastern Tick-borne encephalitis (Russian Spring and Summer encephalitis, Kyasanur Forest disease, Omsk Hemorrhagic Fever)] [β]
· Variola major virus (Smallpox virus) and Variola minor virus (Alastrim) [β]
· Venezuelan Equine Encephalitis virus [χ]
· Vesicular stomatitis virus (exotic) [α]
· Yellow fever virus *

Fungi:
· Coccidioides immitis [χ]
· Coccidioides posadasii [β]

PRION
· Bovine spongiform encephalopathy agent [α]

Bacteria:
· Bacillus anthracis [χ]
· Brucella abortus [χ]
· Brucella melitensis [χ]
· Brucella suis [χ]
· Burkholderia mallei (formerly Pseudomonas mallei) [χ]
· Burkholderia pseudomallei (formerly Pseudomonas pseudomallei) [χ]
· Clostridium botulinum (and botulinum neurotoxin producing species of Clostridium) [χ]
· Cowdria ruminantium (Heartwater) [α]
· Coxiella burnetii [χ]
· Francisella tularensis [χ]
· Mycoplasma capricolum/ M. F38/M. mycoides capri (contagious caprine pleuropneumonia) [α]

- Mycoplasma mycoides mycoides (contagious bovine pleuropneumonia) [α]
- Rickettsia prowazekii [β]
- Rickettsia rickettsii [β]
- Yersinia pestis [β]

Toxins:

- Abrin [β]
- Aflatoxin*
- Botulinum neurotoxin [χ]
- Clostridium perfringens epsilon toxin [χ]
- Conotoxins [β]
- Diacetoxyscirpenol [β]
- Ricin [β]
- Saxitoxin [β]
- Shigatoxin [χ]
- Shiga-like ribosome inactivating proteins [β]
- Staphylococcal enterotoxins [χ]
- Tetrodotoxin [β]
- T-2 toxin [χ]

[α] USDA high consequence livestock pathogens
[β] HHS select agents and toxins
[χ] HHS/USDA overlap agents and toxins
* To be removed from this list in February 2003
I Nipah and Hendra Complex Viruses were previously listed as Equine Morbillivirus Virus

Genetic Elements, Recombinant Nucleic Acids, and Recombinant Organisms:

1. Listed viruses, bacteria, fungi, and toxins that have been genetically modified.
2. Select agent viral nucleic acids (synthetic or naturally derived, contiguous or fragmented, in host chromosomes or in expression vectors) that can encode infectious and/or replication competent forms of any of the select agent viruses.
3. Nucleic acids (synthetic or naturally derived) that encode for the functional form(s) of any of the toxins listed if the nucleic acids:
   (I) are in a vector or host chromosome;
   (ii) can be expressed in vivo or in vitro; or
   (iii) are in a vector or host chromosome and can be expressed in vivo or in vitro.

Other Restrictions

We cannot perform the following experiments without approval from HHS/APHIS:

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

Experiments involving deliberate formation of recombinant DNA containing genes for the biosynthesis of listed toxin lethal for vertebrates at an LD50 <100 ng/kg body weight

Exclusions to the select agent/toxin regulations:

1. Any select agent or toxin that is in its naturally occurring environment provided it has not been intentionally introduced, cultivated, collected, or otherwise extracted from its natural source.
2. Non-viable select agent organisms or nonfunctional toxins.
3. Fixed tissues that bear or contain select agents or toxins.
4. Genetic elements or sub-units of agents or toxins, if the genetic elements or sub-units are not capable of causing disease.
5. The vaccine strain of Junin virus (Candid #1).
6. The vaccine strain of Rift Valley fever virus (MP-12).
7. Venezuelan Equine encephalitis virus vaccine strain TC-83.
8. The medical use of toxins for patient treatment.
9. The following toxins (in the purified form or in combinations of pure and impure forms) if the aggregate amount under the control of a principal investigator does not, at any time, exceed the amount specified:
   - 100 mg of Abrin
   - 0.5 mg of Botulinum neurotoxins
   - 100 mg of Clostridium perfringens epsilon toxin
   - 100 mg of Conotoxins
   - 1,000 mg of Diacetoxyscirpenol
   - 100 mg of Ricin
   - 100 mg of Saxitoxin
   - 100 mg of Shigatoxin
   - 100 mg of Shiga-like ribosome inactivating proteins
   - 5 mg of Staphylococcal enterotoxins
   - 100 mg of Tetrodotoxin
   - 1,000 mg of T-2 toxin

Note: IF YOU EXCEED OR PLAN TO EXCEED THESE TOXIN LIMITS PLEASE CONTACT OES IMMEDIATELY AT 225-578-8507

The HHS/USDA administrator may exclude from this list attenuated strains of select agents or toxins upon a determination that they do not pose a severe threat to the public health and safety. Application must be submitted by the entity for exclusion

ANIMAL AND PLANT HEALTH INSPECTION SERVICE (APHIS) PLANT PATHOGENS REGULATED AS SELECT AGENTS

Viruses:

- Plum pox potyvirus

Fungi:

- Peronosclerospora philippinensis
- Phakopsora pachyrhizi
- Sclerophthora rayssiae var. zeae
- Synchytrium endobioticum

Bacteria:

- Liberobacter africanus
- Liberobacter asiaticus
- Ralstonia solanacearum, race 3, biovar 2
- Xanthomonas oryzae pv. oryzicola
- Xylella fastidiosa (citrus variegated chlorosis strain)

EXEMPTIONS FROM HHS/USDA REQUIREMENTS ON SELECT AGENT/TOXIN REGULATIONS:

(Consult with the RO for additional information)

(a) An entity is exempt from the provisions of the regulations, other than rules on transfers, provided that all of the following apply:

(1) The only activities conducted by the entity that are subject to this part concern select agents or toxins that are contained in specimens or in isolates from specimens presented for diagnosis, verification, or proficiency testing;

(2) Upon identification of a select agent or toxin as the result of diagnosis or verification, the entity immediately reports to the appropriate Secretary by telephone, facsimile, or e-mail any of the following: Variola major virus (Smallpox virus) and Variola minor (Alastrim), Bacillus anthracis, Yersinia pestis, Botulinum neurotoxins, Francisella tularensis, Ebola viruses, Marburg virus, Lassa fever virus, South American Haemorrhagic Fever viruses (Junin, Machupo, Sabia, Flexal, Guanarito); and any high consequence animal or plant pathogen.

(3) The entity reports as required under Federal, State, or local law, to appropriate authorities;

NOTE: (APHIS by phone - 301-734-5519, by email to juan.a.roman@aphis.usda.gov ; HHS notifications must go to Select Agents Program, Centers for Disease Control and Prevention, 1600 Clifton Road, NE, Mail Stop E 79, Atlanta, Georgia 30333 or by email at lrsat@cdc.gov)

(4) After the diagnosis, verification, or proficiency testing, the entity either transfers the specimens or isolates containing a select agent or toxin from the specimens to a facility eligible for receiving them under this part, or destroys them on-site by autoclaving, incineration, or by a sterilization or neutralization process sufficient to cause inactivation;

(5) The entity transfers or destroys those select agents or toxins used for diagnosis or testing within seven days after identification, unless directed otherwise by the Federal Bureau of Investigation or other law enforcement entity after consultation with the Secretary; and

(6) The entity transfers or destroys those select agents or toxins used for proficiency testing within 90 days after receipt; and

(7) The entity prepares a record of the identification and transfer or destruction, submits the completed form to the appropriate Secretary within seven days after identification, and maintains
a copy of the record for a period of three years.

(b) Unless USDA or HHS issues an order making specific provisions of these rules applicable in order to protect the public health and safety, products that are, bear, or contain listed select agents or toxins that are cleared, approved, licensed, or registered under any of the following laws, are exempt from the provisions of these regulations insofar as their use is only for the approved purpose and meets the requirements of such laws:

(1) The Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301 et seq);
(2) Section 351 of the Public Health Service Act pertaining to biological products (42 U.S.C. 262);
(3) The Act commonly known as the Virus-Serum-Toxin Act (21 U.S.C. 151-159); or
(4) The Federal Insecticide, Fungicide, and Rodenticide Act (7 U.S.C. 136 et seq).

(c) The Secretary may exempt from the requirements of this part on a case-by-case basis an investigational product that is, bears, or contains a select agent or toxin, when such product is being used in an investigation authorized under a Federal Act referred to in paragraph (b) of this section and additional regulation under this part is not necessary to protect public health and safety. To apply for an exemption an applicant must submit to the Secretary a completed form certifying that the product is being used in an investigation authorized under a Federal Act referred to in paragraph (b) of this section, and that additional regulation under this part is not necessary to protect public health and safety. The Secretary shall make a determination regarding the application within 14 calendar days after receipt, provided the application meets all of the requirements of this section and the application establishes that the investigation has been authorized under the cited Act. The Secretary will provide a written decision granting the request, in whole or in part, or denying the request. The applicant must notify the Secretary when an authorization for an investigation no longer exists. This exemption automatically ceases when such authorization is no longer in effect.

(d) The Secretary may temporarily exempt an entity from the requirements of this part, in whole or in part, based on a determination that the exemption is necessary to provide for the timely participation of the entity in response to a domestic or foreign public health emergency. With respect to the emergency involved, the exemption may not exceed 30 days, except that the Secretary may grant one extension of an additional 30 days. To apply for an exemption or an extension of an exemption, an applicant must submit to the Secretary a completed form establishing the need to provide for the timely participation of the entity in a response to a domestic or foreign public health emergency. The Secretary will provide a written decision granting the request, in whole or in part, or denying the request.

(e) Upon request of the USDA Secretary, after the USDA Secretary has granted an exemption based on a finding that there is an agricultural emergency, the HHS Secretary may

temporarily exempt an entity from the applicability of the requirements of this part, in whole or in part, to provide for the timely participation of the entity in response to the agricultural emergency. With respect to the emergency, the exemption under this part may not exceed 30 days, except that upon the request of the USDA Secretary, the HHS Secretary may grant one extension of an additional 30 days.

(f) An individual or entity receiving diagnostic reagents and vaccines that are, bear, or contain listed agents or toxins, also known as high consequence livestock pathogens or toxins, that are produced at USDA diagnostic facilities will be exempt from the requirements of these regulations.

Possession, Use, and Transfer of Biological Agents And Toxins

LSU and AgCenter labs or other facilities that wish to work with Select Agents and Toxins must register the research project through OES with the Institutional Biological Safety and Recombinant DNA (IBRDS) Committee and the RO and follow all requirements under the laws and regulations as described in this section.

DEFINITIONS.

The following definitions are found in the USDA regulations on select agents/toxins. These definitions can equally be applied in most cases to HHS regulations by simply inserting "HHS Secretary" instead of "Administrator" or "APHIS Administrator":

Administrator. The Administrator, Animal and Plant Health Inspection Service, or any person authorized to act for the Administrator. In the HHS regulations, the corresponding term is "Secretary".

Animal and Plant Health Inspection Service (APHIS). The Animal and Plant Health Inspection Service of the United States Department of Agriculture. APHIS is the agency to which the authority to enforce the regulations from USDA is delegated. Likewise, CDC is generally administering the HHS regulations.

Attorney General. The Attorney General of the United States or any person authorized to act for the Attorney General.

Centers for Disease Control and Prevention (CDC). The Centers for Disease Control and Prevention of the United States Department of Health and Human Services.

Clinical laboratory. A laboratory facility that receives patients and collects specimens for processing or

shipping to another laboratory.

Diagnostic laboratory. A laboratory facility that receives specimens for the purpose of determining the identities of pests, pathogens, contaminants, or causes of disease.

Entity. Any government agency (Federal, State, or local), academic institution, corporation, company,

partnership, society, association, firm, sole proprietorship, or other legal entity. LSU and the AgCenter are one combined entity under the regulations at this time.

Import. To move into, or the act of movement into, the territorial limits of the United States.

Interstate. From one State into or through any other State, or within the District of Columbia, Guam, the Virgin Islands of the United States, or any other territory or possession of the United States.

Permit. A written authorization by the Administrator to import or move interstate biological agents or toxins, under conditions prescribed by the Administrator.

Proficiency testing. A sponsored, time-limited analytical trial whereby one or more analytes, previously confirmed by the sponsor, are submitted to the testing laboratory for analysis and where final results are graded, scores are recorded and provided to participants, and scores for participants are evaluated for acceptance.

Responsible official. The individual designated by an entity to act on its behalf. This individual must have the authority and control to ensure compliance with the regulations in this part.

Specimen. A sample of material collected for use in testing, such as tissues, gastrointestinal contents, feces, bodily fluids (blood, serum, etc.), soil, water, feed or feed ingredients, swabs, cultures, and suspensions.

State. Any of the several States of the United States, the Commonwealth of the Northern Mariana Islands, the Commonwealth of Puerto Rico, the District of Columbia, Guam, the Virgin Islands of the United States, or any other territory or possession of the United States.

Other definitions from the HHS regulations of importance to our activities are:

Principal investigator means the one individual who is designated by the entity to direct a project or program and who is responsible to the entity for the scientific and technical direction of that project or program.

Verification means the processes required to assure the accuracy, precision, and the analytical sensitivity and specificity of any procedure used for diagnosis.

PURPOSE AND SCOPE OF REGULATIONS

The federal regulations set forth requirements regarding the possession or use in the United States, receipt from outside the United States, or transfer within the United States, of select agents and toxins. The requirements are designed to implement provisions of the Public Health Security and Bioterrorism

Preparedness and Response Act of 2002 (Public Law 107–188). The Act was designed to provide protection against the effects of misuse of select agents and toxins whether inadvertent or the result

of terrorist acts against the United States homeland or other criminal acts. The agents and toxins subject to requirements under this part are those that have the potential to pose a severe threat to public health and safety.

REGISTRATION

The university and/or agcenter may not possess or use in the United States, receive from outside the United States, or transfer within the United States, any select agent or toxin unless we have been

granted a certificate of registration by the HHS Secretary or the APHIS Administrator.

Prior to registration, a Responsible Official must be designated, along with alternate responsible officials as desired. The responsible official has the authority to assure that the compliance requirements are carried out, and to bind LSU and the AgCenter to commitments made in the registration process. Without the certificate of registration from APHIS or CDC we are prohibited from possessing, using, or transferring any agent or toxin listed as a select agent/toxin.

Registration depends upon approval of the biosafety, containment, and security plans. Our biosafety, containment, and security procedures must be commensurate with the risk of the agent or toxin, given its intended use. The requirements for these are discussed in detail in this manual under Biosafety and Security Plans. A certificate of registration will be valid for only the specific agents or toxins listed in the certificate and specific activities and locations.

The registration request will be disapproved if any of the following is found:

- The Attorney General identifies the RO as within any of the categories described as "restricted persons", or
- The Attorney General identifies the RO as reasonably suspected by any Federal law enforcement or intelligence agency of committing a crime set forth in U.S.C.2332b(g)(5) or knowing involvement with an organization that engages in domestic or international terrorism or with any other organization that engages in international crimes of violence or being an agent of a foreign power as defined in 50U.S.C.1808, or
- The RO does not have a lawful purpose to possess, use or transfer select agents or toxins, or
- The RO is an individual who handles or uses select agents or toxins and he/she does not have the necessary training or skills to handle such agents or toxins, or
- LSU/AgCenter does not meet the biosafety, containment and security requirements prescribed, or
- There are egregious or repeated violations of the biosafety, containment or security requirements, or
- HHS/USDA determines that such action is necessary to protect human, animal or plant health or animal or plant products.

(a) To apply for a certificate of registration we must:

(1) Obtain a registration application number from the HHS Secretary (CDC Form 0.1319) or APHIS (APHIS Form 2044). Apply for approval for the Responsible Official and submit the information requested to the HHS Secretary or the USDA Secretary.

(b) Minimum information required includes:

(i) Identification information (e.g., name, address, contact numbers, identification number assigned by the Attorney General);

(ii) The name, source, and characterization information on select agents and toxins included in the

registration, and quantities held at the time of the application;

(iii) The location, including building and room and floor plans for each building and room, where each select agent or toxin will be stored or used;

(iv) Information addressing safety, security, emergency response plans, and training, including descriptions of any equivalent measures adopted pursuant to requirements in the regulations;

(v) The name, position, and identification information regarding the Responsible Official, including the

identification number assigned by the Attorney General;

(vi) A list of individuals who will need access to select agents and toxins;

(vii) A certification statement signed by the Responsible Official attesting to the accuracy of the information submitted; and

(viii) Any other information necessary for the determination.

(c) An application that covers any HHS select agents or toxins (regardless of whether it also covers overlap select agents or toxins) must be submitted to the HHS Secretary. An application that covers only overlap select agents or toxins may be submitted to either the HHS Secretary or

the USDA Secretary.

(d) A certificate of registration will be valid only for the specific select agents and toxins, and the specified activities and locations that are consistent with the information provided by the entity upon which the certificate of registration or amendment was granted. The Responsible Official must promptly notify the HHS Secretary or APHIS Administrator in writing, if a change occurs in any information submitted to the HHS Secretary in the application for the certificate of registration or

amendments. This includes modifications to the list of individuals approved under § 73.8, changes in area of work, or changes in protocols or objectives of studies. To apply for an amendment to a certificate of registration to add select agents or toxins or to change specified activities or locations, an entity must obtain the relevant portion of the registration application package and submit the information requested in the package to the agency that issued the certificate of registration. The package must be submitted to the appropriate address specified in the package.

(e) In response to an application to the HHS Secretary for a certificate of registration or amendment for select agents and toxins, the HHS Secretary will issue a certificate of registration or amendment if it is determined that the stated activities would have a lawful purpose (based on information submitted by the applicant or otherwise obtained by the HHS Secretary) and meet the requirements of the regulations. Otherwise, the application for a certificate of registration or amendment will be denied. HHS and APHIS will share approval responsibilities on overlap agents/toxin. The determination of whether a certificate of

registration or amendment will be granted may be contingent upon inspection or submission of additional information.

(f) A certificate of registration will cover activities at only one general physical location (a building or a complex of buildings at a single mailing address).

(g) Unless terminated sooner in accordance with this paragraph, a certificate of registration will be valid for up to three years. To obtain a new certificate of registration an entity must submit a new application. (Note: To help ensure timely processing of an application for a certificate of registration or amendment, the applicant should submit the application at least eight weeks prior to the expiration date.)

(1) The HHS Secretary will terminate a certificate of registration based on a determination that the recipient no longer conducts activities covered by the certificate.

(2) Also, the HHS Secretary may terminate a certificate of registration based on a security risk assessment under § 73.8 or failure to comply with the provisions of this part, and may take such action immediately if necessary to protect the public health or safety. Upon such termination, any select agent or toxin in the possession of the entity must be destroyed or transferred as directed by the HHS Secretary.

(h) An entity must provide notice in writing to the HHS/USDA Secretary at least five business days before destroying a select agent or toxin, if the destruction would be for the purpose of discontinuing activities with a select agent or toxin covered by a certificate of registration.

This will allow the HHS/USDA Secretary to observe the destruction or take other action as appropriate.

RESPONSIBILITIES OF THE RESPONSIBLE OFFICIAL

(a) The responsible official is responsible for ensuring compliance with the regulations, including:

(1) Developing and implementing a Biosafety and Security Plan;

(2) Allowing only approved individuals within the entity to have access to any select agents or toxins (see below); For each individual identified by the responsible official as having a legitimate need to handle or use agents or toxins, the responsible official must submit that individual's name and identifying information to APHIS and the Attorney General.

(3) Providing appropriate training in biosafety, containment, and security procedures for all personnel;

(4) Transferring agents or toxins only to registered individuals or entities;

(5) Ensuring that all visitors are informed of and follow the entity’s security requirements and procedures;

(6) Notifying APHIS or CDC, as applicable, of changes in circumstances affecting registration;

(7) Providing timely notice of any theft, loss, or release of a biological agent or toxin;

(8) Maintaining detailed records of information necessary to give a complete accounting of all of the activities related to select agents or toxins.

(b) In addition to the requirements in paragraph (a) above, the responsible official for a diagnostic laboratory or other entities possessing, using, or transferring select agents or toxins that are contained in specimens presented for diagnosis must immediately report the identification of such agents or toxins to USDA/HHS and to other appropriate authorities when required by Federal, State, or local law. (During emergencies or outbreaks, or in endemic areas, the enforcement agencies may require less frequent reporting.)

(c) In addition to the requirements in paragraph (a) of this section, the responsible official must ensure that the following experiments are not conducted unless approved by HHS/USDA, after consultation with experts:

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

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

RESTRICTING ACCESS TO BIOLOGICAL AGENTS AND TOXINS

(a) An individual may not have access to select agents or toxins unless approved by APHIS or CDC. APHIS will grant, limit, or deny access of individuals to listed agents or toxins. APHIS or CDC will grant, limit, or deny access of individuals to overlap agents or toxins. HHS will grant, limit, or deny access to HHS select agents or toxins.

(b) The responsible official is responsible for ensuring that only approved individuals within the entity have access to any select agents or toxins. The responsible official must request such access for only those individuals who have a legitimate need to handle or use agents or toxins, and who have the appropriate training and skills to handle such agents or toxins.

(c) The responsible official must provide appropriate training in biosafety, containment, and security procedures to all individuals with access to select agents and toxins.

(d) For each individual identified by the responsible official as having a legitimate need to handle or use agents or toxins, the responsible official must submit that individual's name and identifying information to the CDC/USDA, as applicable, for the agent/toxin(s) involved.

(e) In addition, the responsible official must submit information about the individual's training and skills (e.g., curriculum vitae for principal investigators and researchers, and a description of training completed by support personnel).

(f) APHIS/CDC may expedite the access approval process for individuals upon request by the responsible official and a showing of good cause (e.g., public health or agricultural emergencies, national security, impending expiration of a research grant, a short-term visit by a prominent researcher).

(g) APHIS/CDC will notify the responsible official if an individual is granted full or limited access, or denied access to listed agents or toxins, and will also notify the individual if he/she is denied access or granted only limited access. An individual may appeal the decision to deny or limit access. LSU/AgCenter may not appeal the denial or limitation of an

individual's access to listed agents or toxins. Access approval is valid for 5 years; thereafter, the responsible official shall request renewal of access approval every 5 years for as long as the individual needs access to select agents or toxins.

(h) The responsible official must immediately notify APHIS/CDC when an individual's access to select agents or toxins is terminated, providing the reasons for terminating access.

BIOSAFETY AND SECURITY PLAN

(In the HHS regulations, these two plans, biosafety and security, are treated separately and require separate programs for registration. In the USDA/APHIS regulations for plant pathogens there is no requirement for a "Safety Plan" in the registration process, as the safety of workers is not an issue of concern.)

(a) As a condition of registration, the responsible official must develop and implement a Biosafety and Security Plan. The Biosafety and Security Plan must contain sufficient information and documentation to describe the biosafety and containment procedures, and the security systems and procedures. The plan must be commensurate with the risk of the agent or toxin, given its intended use. In developing a safety plan, LSU and the LSU AgCenter has adopted the biosafety standards and requirements for BSL 2, 3, or 4 operations, as they pertain to the respective select agents, that are contained in the CDC/NIH publication, ''Biosafety in Microbiological and Biomedical Laboratories,'' including all appendices except Appendix F. This publication is available on the CDC Web site at http://www.cdc.gov. For toxins, we have adopted the specific requirements for handling toxins found in 29 CFR 1910.1450, ''Occupational Exposure to Hazardous Chemicals in Laboratories'' and 29 CFR 1910.1200, ''Hazard Communication".

(1) The biosafety and containment procedures must be sufficient to contain the agent or toxin (e.g., physical structure and features of the entity, and operational and procedural safeguards). At a minimum, the plan must address containment, personnel safety and health, and inventory control.

(2) The security systems and procedures must be designed according to a site-specific risk assessment and must provide graded protection in accordance with the threat posed by the agent or toxin:

(i) The site-specific risk assessment should involve a threat assessment and risk analysis in which threats are defined, vulnerabilities examined, and risks associated with those vulnerabilities are identified.

(ii) The security systems, including appropriate and effective security equipment, and procedures must be tailored to address site-specific characteristics and requirements, ongoing programs, and operational needs and must mitigate the risks identified.

(iii) The plan must describe inventory control procedures, personnel suitability for those individuals with access to select agents or toxins, physical security, and cybersecurity. The plan must also contain provisions for routine cleaning, maintenance, and repairs; provisions for securing the area (e.g., card access, key pads, locks) and protocols for changing access numbers or locks following staff changes; procedures for loss or compromise of keys, passwords, combinations, etc.; procedures for reporting suspicious persons or activities, loss or theft of listed agents or toxins, release of listed agents or toxins,

or alteration of inventory records; provisions for the control of access to containers where listed agents and toxins are stored; and procedures for reporting and removing unauthorized persons.

(iv) With respect to areas containing listed agents or toxins, an entity or individual must adhere to the following security requirements or implement measures to achieve an equivalent or greater level of security as the provisions below:

(A) Allow unescorted access only to approved individuals who are performing a specifically authorized function during hours required to perform that job, and provide procedures for removal of anyone in violation of this requirement;

(B) Allow individuals not approved for unescorted access to conduct routine cleaning, maintenance, repairs, and other non-laboratory functions only when escorted and continually monitored by approved individuals;

(C) Provide for the control of access to containers where listed agents and toxins are stored by requiring that such containers be locked when not in the direct view of an approved individual and by using other monitoring measures, as needed;

(D) Require the inspection of all packages upon entry and exit;

(E) Establish a protocol for intra-entity transfers, including provisions for ensuring that the packaging and movement, is conducted under the supervision of an approved individual;

(F) Require that approved individuals do not share with any other person their unique means of accessing the area or listed agents or toxins; and

(G) Require that approved individuals immediately report any of the following to the responsible official:

Any loss or compromise of keys, passwords, combinations, etc.;

Any suspicious persons or activities;

Any loss or theft of listed agents or toxins;

Any release of a listed agent or toxin; and

Any sign that inventory and use records for listed agents and toxins have been altered or otherwise compromised.

(3) The Biosafety and Security Plan must also include incident response plans for containment breach, security breach, inventory violations, non-biological incidents such as workplace violence, and cybersecurity breach. The emergency response plan must address the following:

The hazards associated with the use of the select agents and toxins;

Any hazards associated with response actions that could lead to a spread of a select agent or toxin;

Planning and coordination with outside parties;

Personnel roles, lines of authority, training, and communication;

Emergency recognition and prevention;

Safe distances and places of refuge;

Site security and control;

Evacuation routes and procedures;

Decontamination;

Emergency medical treatment and first aid;

Emergency alerting and response procedures;

Critique of response and follow up;
Personal protective and emergency equipment; and
Special procedures needed to protect individual with access to areas where select agents or toxins are handled or stored.

The incident response plans must address personnel safety and health, containment, inventory control, and notification of managers and responders. The incident response plans must also tie in with entity-wide plans and address such events as bomb threats, severe weather (floods, hurricanes, tornadoes), earthquakes, power outages, and other natural disasters or emergencies. The emergency response plan must comply with the OSHA Hazardous Waste Operations and Emergency Response Standard at 29 CFR 1910.120.

(4) The Biosafety and Security Plan must be reviewed, performance tested, and updated annually under the direction of the responsible official. The plan must also be reviewed and revised, as necessary, after any incident.

(4) The Responsible Official or his or her designee must conduct regular inspections (at least annually) of the laboratory(s) where select agents and toxins are stored or used to ensure compliance with all of the procedures and protocols of the safety plan. The results of these inspections must be documented, and any deficiencies identified during inspections must be corrected.

(5) The Biosafety and Security Plan must have provisions for enforcement of safety, health, environmental and security rules and procedures.

TRAINING

(a) We must provide information and training on safety and security for working with select agents and toxins to each individual approved for access and each unapproved individual working in, or visiting, areas where select agents and toxins are handled or stored. The information and training must meet the requirements of this section and must ensure that all individuals who work in, or visit, the areas understand the hazards of select agents and toxins present in the area.

(b) The entity must provide information and training at the time of an individual's initial assignment to a work area where select agents or toxins are present and prior to assignments involving new exposure situations. The entity must provide refresher raining annually.

(c) The Responsible Official must provide appropriate training in safety, containment, and security to all individuals with access to areas where select agents and toxins are handled or stored.

(d) In lieu of initial training for those individuals already involved in handling select agents or toxins, the Responsible Official may certify in writing that the individual has the required knowledge, skills, and abilities to safely carry out the duties and responsibilities.

(e) The entity must ensure that each individual with access to areas where select agents or toxins are handled or stored received and understood the training required by this section unless certified under paragraph (d) above. We must record the identity of the individual trained, the date of training, and the means used to verify that the employee understood the training.

TRANSFER OF BIOLOGICAL AGENTS AND TOXINS

Select agents and toxins may only be transferred to individuals or entities registered to possess, use, or transfer that particular agent or toxin. However, the sender of an select agent or toxin may be an individual or entity that has a certificate of registration for the agent or toxin, an individual or entity that is exempt from the requirements of this part, or an individual or entity located outside of the United States. Select agents or toxins may only be transferred under the conditions of this section and must be authorized by APHIS/CDC prior to the transfer. Coordinate all shipments through the RO, who will verify that all requirements are met.

(a) In addition to the permit required, select agents or toxins may be imported or moved interstate only with the prior authorization of APHIS or CDC, as appropriate, for the agent/toxin. To obtain such authorization, the sender and the responsible official for the recipient must complete and submit APHIS Form 2041 or CDC Form EA-101 to APHIS or CDC, as appropriate, in accordance with paragraph (c) of this section.

(b) Intrastate movement. Biological agents or toxins listed in § 121.3 may be moved intrastate only with the prior authorization of APHIS or, for overlap agents or toxins, APHIS or CDC. To obtain such authorization, the sender and the responsible official for the recipient must complete and submit APHIS Form 2041 or CDC Form EA-101 to APHIS or CDC, respectively and as appropriate, in accordance with paragraph (c) below:

(c) APHIS Form 2041 and CDC form EA-101, process and procedures.

(1) Prior to each transfer, the responsible official for the recipient and sender must complete APHIS Form 2041, and the sender must submit the form to APHIS or, for overlap agents or toxins, to APHIS or CDC. HHS select agents/toxin transfer paperwork must be submitted on EA-101 to CDC.

(2) APHIS or CDC will authorize the transfer based on a finding that the recipient has a certificate of registration covering the transfer of the listed agent or toxin.

(3) The responsible official for the recipient must notify the agency authorizing the transfer (either APHIS or CDC) and the sender upon receipt of the agent or toxin by mailing or faxing a completed Form 2041or EA-101 to APHIS or CDC within 2 business days.

(4) The responsible official for the recipient must notify APHIS or CDC immediately if the agent or toxin has not been received within 48 hours after the expected delivery or if the package containing the agent or toxin is leaking or has been damaged.

(d) The sender must comply with all applicable laws governing packaging and shipping in 7CFR330 and 9CFR122 and other existing laws and regulations regarding packaging and shipping.

INVENTORY CONTROLS

(a) An important aspect of security in working with select agents is the control of inventory. As such, inventory practices must be able to detect loss of select agents. Good inventory practices involving select agents should have the following characteristics:

Be dynamic: At any point in time, a loss of product can be detected by simply reviewing the inventory.

Be Secure: The amount of select agents on hand should not be made public, and the inventory records must be protected from unauthorized access and catastrophic loss.

Be Accurate: Keeping up with select agent use must take into consideration the usage methods, the characteristics of the agents(s) being used, and practical methods of measuring quantities.

An inspection by the Department of Health and Human Services revealed a process in use by one of our research lab which was considered to be effective . The following is a description of this process:

"The inventory log identified the number of vials, as well as strains of the materials, that were located in each distinctively identifiable container. The PI then recorded usage of the vials separately on index cards. The index cards therefore contained a running total of the inventory. The PI and research assistants actually used these index cards, rather than the inventory log to see how much stock of a particular strain they had remaining. These index cards were then used to update the inventory log once or twice a year. The PI was able to record usage this way because only complete vials of working stock were used. If a complete vial was not used, the remaining amount in the vial was destroyed via autoclaving. In addition, this PI recorded all transfers in the logbook. The information includes date shipped or received, transferor or transferee, and number of vials and strains."

While the above approach may not fit all research protocols, the concepts are shown to be effective and are provided as guidance only. Each PI will need to determine the approach that is effective for their labs.

(b) In maintaining an accurate, current inventory of each select agent and toxin held, the following information for each select agent and toxin must be recorded:

(1) The name, characteristics, and source data;

(2) The quantity held on the date of the first inventory (toxins only);

(3) The quantity acquired, the source, and date of acquisition;

(4) The quantity, volume, or mass destroyed or otherwise disposed of and the date of each such action;

(5) The quantity used and date(s) of the use (toxins only);

(6) The quantity transferred, the date of transfer, and individual to whom it was transferred (this includes transfers within an entity when the sender and the recipient are covered by the same certificate of registration);

(7) The current quantity held (toxins only);

(8) Any select agent or toxin lost, stolen, or otherwise unaccounted for; and

(9) A written explanation of any discrepancies.

INFORMATION AND CYBERSECURITY

Information that should be considered sensitive and protected include the following:

1. Diagrams, descriptions, etc. providing exact location and identity of select agent materials.
2. Inventory information
3. Security information, including information relating to security incidents and investigations, recommendations on security improvements, and key control information. Obviously, codes, passwords, and other similar information should be guarded. Information regarding identification of employees who have access to select agents should not be shared with the public.
4. Transactions from automated access control systems, testing and maintenance of security systems, visitor logs.
5. Information on research, especially information on findings, conclusions, and procedures relating to the research involved. This is an evolving area, and will be more defined in the future.
6. Registration information, including data and information accumulated for the registration process, and transfer documents,

Security of sensitive research and inventory data is very important in safeguarding information that may be useful to anyone wishing to misuse the agents/toxins in the laboratory. For this reason, computer security and file management must be carefully analyzed for vulnerability.

Password protection is very important for computer access. Use a combination of not less than 6 combination alpha numeric characters, and not a common, easily remembered one like a birthday or name. Passwords shall be changed every 90 days, and settings shall reflect “lockout after three unsuccessful tries at log on”. "Reset Count After" shall be several hours, and lockout duration setting should be "forever".

On computers used for connection to Internet or intranet systems, there is always a risk of hacking and intrusion by outsiders. For this reason, sensitive data should be on computers that are NOT linked to the outside world. Dedicated computers should be designated as such, and care must be taken to prevent inadvertent connections to outside systems.

Firewalls are important to provide additional security and should be used for all major installations. If it is necessary to communicate sensitive information electronically, consult

with the information and data systems department to obtain the most secure connections and processes.

Upon terminating research projects or when changing and disposing of media, cleansing of files and disks is necessary to prevent inadvertent loss of important and sensitive information. Each lab must establish written procedures for cleansing hard drives, disks and other data containing media prior to removal from the lab.

Information on computers must be backed up with copies kept in a secure location off the premises.

E-mail messages are generally thought to be in the "public domain" and thus not secure.

RECORDS

(a) The responsible official must maintain complete, up-to-date records of information necessary to give an accounting of all of the activities related to select agents or toxins.
Such records must include the following:

(1) The Biosafety and Security Plan;
(2) A current list of all individuals with access to select agents or toxins;
(3) Training records for individuals with access to such agents or toxins;
(4) Accurate and current inventory records (including source and characterization data);
(5) Permits and transfer documents issued by APHIS and CDC;
(6) Security records (e.g., transactions from automated access control systems, testing and maintenance of security systems, visitor logs);
(7) Biosafety, containment, and security incident reports.

(b) The responsible official must maintain such records for 3 years.

(c) All records must be produced upon request to APHIS or CDC inspectors, and appropriate Federal, State, or local law enforcement authorities.

INSPECTIONS BY GOVERNMENT OFFICIALS

(a) To ensure compliance with the regulations, any APHIS or CDC inspector must be allowed, without previous notification, to enter and inspect the entire premises, all materials and equipment, and all records required to be maintained by this part.

(b) Prior to issuing a certificate of registration to an entity or individual, APHIS or CDC may inspect and evaluate the premises and records to ensure compliance with the regulations and the biosafety, containment, and security requirements.

NOTIFICATION IN THE EVENT OF THEFT, LOSS, OR RELEASE OF A BIOLOGICAL AGENT OR TOXIN.

(a) The responsible official must orally notify APHIS/CDC and appropriate Federal, State, or local law enforcement agencies immediately upon discovery of the theft or loss of agents or toxins listed in § 121.3. The oral notification must be followed by a written report (APHIS Form 2043) within 7 days. Notification must be made regardless of whether the materials are subsequently found or not and whether the person responsible has been identified.

The notification will include the following:

(1) The name of the select agent or toxin and any identifying information (e.g., strain or other characterization information);

(2) An estimate of the quantity lost or stolen;

(3) An estimate of the time during which the theft or loss occurred; and

(4) The location (building, room) from which the theft or loss occurred.

(b) The responsible official must orally notify APHIS/CDC immediately upon discovery that a release of an agent or toxin has occurred outside of the biocontainment area. When reporting a release the following must be provided:

(1) The name of the select agent or toxin and any identifying information (e.g., strain or other characterization information);

(2) An estimate of the quantity released;

(3) The time and duration of the release;

(4) The environment into which the release occurred (e.g., in building or outside of building, waste system);

(5) The location (building, room) from which the release occurred;

(6) The number of individuals potentially exposed at the facility.

(7) Actions taken to respond to the release; and

(8) Hazards posed by the release.

The oral notification shall be followed by a written report (APHIS Form 2043) within 7 days. Upon notification and a finding that the release poses a threat to animal or plant health, or animal or plant products, APHIS will notify relevant Federal, State, and local authorities, and the public, if necessary. If the release involves an overlap agent or toxin, APHIS will also notify the Secretary of Health and Human Services.

(c) The responsible official must orally notify APHIS of a theft, loss, or release of an agent or toxin by calling (866) 994–5698. A copy of APHIS Form 2043 may be obtained by writing to National Center for Import and Export, VS, APHIS, 4700 River Road Unit 40, Riverdale, MD 20737–1231; or by calling (301) 734–3277. The form is also available on the Internet at http://www.aphis.usda.gov/vs/ncie.bta.html. APHIS Form 2043 may be mailed to the same address or faxed to (301) 734–3652. For HHS agents, CDC notifications must be submitted to the Select Agent Program, Center for Disease Control and Prevention, 1600 Clifton Road, NE., Mail Stop E 79, Atlanta, Georgia 30333, or by e-mail at lrsat@cdc.gov.

ENFORCEMENT

Criminal Penalties.

The Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (Public Law 107– 188) provides specific criminal penalties for violation of provisions of this part. This is in addition to any other criminal penalties that would apply for violation of provisions of this part.

Section 231 of the Act sets out the criminal penalties for violations of the regulations, and states that who ever transfers a biological agent or toxin to a person who the transferor knows or has reasonable cause to believe is not registered shall be fined or imprisoned for no more than 5 years, or both. It further states that whoever knowingly possesses a biological agent or toxin without registering under the regulations shall be fined or imprisoned no more than 5 years, or both.

False, or fraudulent statements on the Government forms, required in the part for registration of facilities, is subject to a fine and/or imprisonment for an individual, and a fine for an organization.

Civil Money Penalties.

For violations of section 351A(b) or (c) of the Public Health Service Act and 42 CFR part 73, the OIG may impose a penalty of not more than $250,000 in the case of an individual, and not more than $500,000 in the case of any other person.

APPEALS OF DECISIONS

In some cases, APHIS or CDC may reject a registration request or other request. If such occurs, and an appeal is to be made, coordinate all appeal activity through the responsible official.

Sources of additional information

Please contact the Office of Occupational and Environmental Safety (OES) at 225-578-5640.

Additional resources can also be found at:

www.oes.lsu.edu/
www.research.lsu.edu/biosafety/ibsrd.html
www.cdc.gov/od/ohs/lrsat.htm
www.cdc.gov/od/ohs/biosfty/imprtper.htm

VI. LABORATORY SECURITY AND EMERGENCY RESPONSE FOR MICROBIOLOGICAL AND BIOMEDICAL LABORATORIES

Laboratory biosafety guidelines have traditionally emphasized the use of good work practices, appropriate containment equipment, well designed facilities, and administrative controls to minimize risks of accidental infection or injury for laboratory workers, and to prevent contamination of the environment outside the laboratory. The purpose of these guidelines is to address laboratory security issues in an effort to prevent the use or possession of select agents by unauthorized individuals who have intent to cause harm or impact our environment adversely. These instructions are intended to prevent attempts of terrorism intended by the use or possession of dangerous biological agents.

In response to these concerns, the following guidelines address laboratory security issues (e.g., preventing unauthorized entry to laboratory areas and preventing loss of select agent inventories. The following paragraphs are offered as guidelines for laboratories using biological agents or toxins capable of causing serious or fatal illness to humans or animals. Most of these laboratories would be working under BSL-3 or -4 conditions, with a few listed under BSL-2. However, research, clinical, and production laboratories working with newly identified human pathogens, high-level animal pathogens, and/or toxins not covered by BSL-3 or –4 recommendations, should also follow these guidelines to minimize opportunities for accidental or intentional removal of these agents from the laboratory.

Recognize that laboratory security is related to, but different than, laboratory safety.

- Involve both safety and security experts in the evaluation and the development of recommendations for a given facility or laboratory. Consult with the IBRDS Committee about the levels of security desired for agents specific to the laboratory. Contact the Office of Occupational and Environmental Safety for additional safety and security support.

- Review safety policies and procedures periodically (at least annually). Management should review policies to ensure that they are adequate for current conditions and consistent with other facility-wide policies and procedures. Laboratory supervisors should ensure that all laboratory workers and visitors understand security requirements and are trained and equipped to follow established procedures.

- Review safety policies and procedures whenever an incident occurs or a new threat is identified. Provide training to all individuals who will be responsible for working with select agents or in the areas where select agents may be stored.

Control access to areas where biological agents or toxins are used and stored.

- Laboratories and animal care areas should be separate from the public area of the buildings in which they are located.

- Laboratory animal care areas should be locked at all times.

- Card-keys or similar devices should be used to permit entry to laboratory and animal care areas.

- All entries should be recorded, either by card-key electronically or by security admittance. This record should include visitors, maintenance workers, repairmen and others who need one –time or occasional entry to the areas.

- Guests should be registered with building security and issued identification badges which should have their name and a length of time which the badge may be used. Badges should be returned at the time they expire. Badges must be coded to prevent unauthorized copies being made.

Know who is in the laboratory area.

All workers should be evaluated to ensure their background meets the requirements for the security criteria according to the PATRIOT Act and other federal laws and rules. Specific individuals are restricted from using, possessing, or transporting any select agents. It is the responsibility of facility administrators and laboratory directors, including principal investigators, to understand these laws and implement them. Depending on the biological agents involved and the type of wok being done, a background check and or security clearance may be appropriate before new employees are assigned to the laboratory area.

A method of tracking guests or visitors should be implemented. Badges should be worn by employees working in areas where select agents are used or stored. Visitors or guest should wear badges or be escorted by authorized employees during their visit. A temporary badge should be prepared which includes a badge expiration date for visitors staying for an extended period of time. Badges worn in BL3 labs cannot be taken out, so temporary badging or other means may be necessary to assure proper security.

Know what materials are being brought into the laboratory area.

All packages should be screened (visual and/or x-ray) before being brought into the laboratory area. Deliveries of select agents must have all necessary approvals/forms and be coordinated through the RO. Identification of the sender should be visible and the address label should be inspected. An individual's name should be noted as a recipient. Any packages that lack clearly marked identification should be evaluated further by security. Procedures for suspicious packages should be followed for any package that looks out of place, and suspicious packages/mail items should be evaluated by security. Any leaks in the container require that emergency spill containment and response be followed.

Packages containing specimens, bacterial or virus isolates, or toxins should be opened in a biosafety cabinet or other appropriate containment device.

Know what materials are being removed from the laboratory area.

Biological materials/toxins for shipment to other laboratories must be packaged and labeled in conformance with all applicable local, federal, and international shipping regulations.

Select agent transfers must be approved and made by the RO. Required permits (e.g., PHS, DOT, DOC, USDA) should be in hand before materials are prepared for shipment. Instructions for permits are available through the CDC website or by calling the CDC at 404-636-3235.

The recipient (preferably) or receiving facility should be known to the sender, and the sender must ensure that materials are shipped to an approved facility equipped to handle those materials safely. Shipping or receiving select agents without proper approvals is a crime punishable by fines and prison time under federal law.

Hand-carrying of microbiological materials and toxins to other facilities is rarely appropriate. If biological materials or toxins are to be hand carried on common carriers, all applicable regulations must be followed.

Contaminated or possible contaminated materials should be decontaminated before they leave the laboratory area. Chemicals and radioactive materials should be disposed of in accordance with local, state, and federal regulations.

Have an emergency plan.

Restricted access to laboratory areas can make an emergency response more difficult. This must be considered when emergency plans are developed.

An evaluation of the laboratory area by appropriate facility personnel, with outside experts if necessary, to identify both safety and security concerns should be conducted before an emergency plan is developed.

Facility administrators, laboratory directors, principal investigators, laboratory workers, the facility safety office, and facility security officials should be involved in emergency planning.

Police, fire, and other emergency responders should be informed as to the types of biological materials in use in the laboratory areas and assisted in planning their responses to emergencies in the laboratory areas.

Plans should include provision for immediate notification of (and response by) laboratory directors, laboratory workers, safety office personnel, or other knowledgeable individuals when an emergency occurs, so they can deal with biosafety issues if they occur.

Laboratory emergency planning should be coordinated with facility-wide plans. Such factors as bomb threats, severe weather (hurricanes, floods), earthquakes, power outages, and other natural (or unnatural) disasters should be considered when developing laboratory emergency plans. Planning includes training individuals how to respond during emergency events.

Have a protocol for reporting incidents.

Laboratory directors, in co-operation with facility safety and security officials, should have policies and procedures in place for reporting and investigation of incidents or possible incidents (e.g., undocumented visitors, missing chemicals, unusual or threatening phone calls).

Train all personnel to report incidents and provide an emergency contact list with procedures which should be followed during an emergency. Remember that violations of rules relating to select agents/toxins may be violations of federal regulations and the circumstances may dictate that the scene be preserved as a crime scene.

VII. PACKAGING AND SHIPMENT OF BIOLOGICAL MATERIALS

Introduction

The Office of Occupational and Environmental Safety (OES) has developed this guideline to assist in the shipment of biological materials and dry ice. This document includes information about how to properly classify, package, mark and label your shipment. This section also describes the training requirements necessary to ship biological materials and dry ice.

Shipped biological specimens, infectious agents and other biological materials are regulated by governmental and non-governmental, consensus development organizations. Penalties for non-compliance with the rules could result in significant fines.

Several agencies/associations regulate the shipment of biological materials including:

- International Air Transport Association (IATA).
- US Department of Transportation (DOT).
- US Public Health Service (PHS).
- Occupational Health and Safety Administration (OSHA).

Infectious substances and other dangerous goods must always be transported according to the appropriate regulations. Carrying dangerous goods by hand, for example, in a vial in your pocket or in luggage, is strictly prohibited. IATA/DOT regulations cover your checked luggage, materials you carry on, or materials you carry in your pockets when you board an airplane. Persons who violate IATA regulations are subject to fines and criminal prosecution.

IATA regulations are commonly encountered since they regulate materials transported by air and are generally the most restrictive. For these reasons, this guide pays special attention to IATA protocols.

Training Requirements

Federal rules require that anyone wishing to ship biological materials or dry ice must first have shipping training. If you are going to package biological materials or dry ice for shipment, or fill out a Declaration for Dangerous Goods form, you must follow the training certification requirements outlined below.

1. ***Read this guideline.*** This guideline will provide familiarity with the general provisions relating to the regulations and detailed training in the requirements applicable to shipping infectious materials and dry ice.

2. ***Have a current bloodborne pathogen training certification from OES.*** This training ensures that you are familiar with the hazards presented by infectious materials, proper handling, and emergency response procedures.

3. ***Submit to OES an*** Intent to Ship Hazardous Materials ***form*** (Appendix B)**.** OES will review this form with you, and upon successful completion, will certify you to ship only those materials that are listed on your Intent form.

Shipping regulations change frequently so it is necessary to repeat training certification every two years. Training sessions reviewing the material in this guideline are available from OES. Call OES at 578 8507 to schedule training or to ask questions regarding the shipment of biological materials and dry ice.

Shipping Overview

Follow these steps when shipping biological materials and dry ice.

Classify your materials for shipment. See Shipment Types.

1. Package, mark and label your material(s) appropriately. See Packaging

2. Fill out the Declaration for Dangerous Goods form. Available from Carrier

3. If you are shipping Select Agents, special regulations apply.

4. If you plan on importing or exporting biological materials, special regulations apply.

Shipment Types

For shipment purposes, biological materials are categorized into four classes:

A. Diagnostic specimens

B. Biological products

C. Genetically modified organisms and micro-organisms

D. Infectious agents

Read each material section carefully to determine how to classify a material. If you are shipping a biological material that *cannot cause disease*, infectious substance regulations do not apply. **Note:** All specimens or packaging containing dry ice or liquid nitrogen must be shipped properly (see Other Packaging Requirements). All samples preserved with flammable or toxic materials, such as ethanol or formalin, must be shipped appropriately.

The regulations allow for a certain amount of professional judgment when classifying biological materials for shipment. IATA does not apply the "Universal Precautions" definition in regard to infectious materials (where all human blood is treated as potentially infectious). For example, blood collected for routine screening by an insurance agency would not necessarily need to be treated as an infectious material. However, blood collected to verify the diagnosis of HIV would be treated as an infectious material. Keep this in mind when reading the definitions in the following sections. If you are still not sure how to classify a material for shipment after reviewing the following sections, contact OES at 578-8507.

A. Diagnostic Specimens

Diagnostic specimens are human or animal materials that have a relatively low probability of containing pathogens. When shipped for the purpose of screening, study or diagnosis, the materials are considered Diagnostic Specimens. These materials include human or animal tissue samples, blood, excreta, etc. Diagnostic specimens are not considered to be a hazardous material by IATA, though the following packaging and shipping requirements apply.

Note: Diagnostic specimens must be shipped as an Infectious Substance when "the source patient or animal has or may have a serious human or animal disease which can be readily transmitted from one individual to another, directly or indirectly, and for which effective treatment and preventative measures are not usually available."

1. Packaging

The basic triple packaging concept applies to diagnostic specimens. Purchase packaging for use with diagnostic specimens. Such packaging must comply with IATA Packing Instruction 650. See Appendix A for packaging suppliers. Be sure to specify if the shipment is a refrigerated sample (ice packs or dry ice).

For diagnostic specimens, the maximum quantity for primary receptacle is 500 mL or 500 g and outer packaging must not contain more than 4 L or 4 kg.

2. Labeling

The sender and recipient's addresses must be printed and clearly displayed. If packaged with dry ice, a Class 9 diamond label (Figure 1) must be placed on one side of the outer package. If the package is shipped by air, the following text should appear on the outer container:

"DIAGNOSTIC SPECIMEN PACKED IN COMPLIANCE
WITH IATA PACKING INSTRUCTION 650."

B. Biological Products

Biological products are defined as biological materials used in the prevention, diagnosis, treatment or cure of diseases in humans or animals and certified by the USDA or FDA. Examples of biological products include certain viruses, therapeutic serums, toxins, antitoxins, vaccines, blood and blood products. Biological products that meet the definition of an infectious material must be shipped as an infectious substance. Biological products that have no or very low probability to produce disease and those packaged for final distribution for use for personal or animal health care by medical professionals are not subject to special shipping regulations but should be shipped safely.

C. Genetically Modified Organisms and Microorganisms

Genetically modified organisms or microorganisms that are dangerous, infectious, or carried by an animal host are regulated for transportation. For the following guidelines, make sure to distinguish those that apply to *organisms vs. microorganisms*.

A genetically-modified *microorganism* which meets the definition of an infectious substance must be classified as an infectious substance for transportation. For these materials, follow instructions for shipping an infectious substance.

Genetically-modified *microorganisms* which are not infectious substances but which are capable of altering animals, plants or microbiological substances in a way that is not normally the result of natural reproduction can be transported when classified as a Miscellaneous Hazard (Class 9). These materials are packed for shipment in the same way as infectious substances, except there are no specific testing requirements for the packaging; this packaging variation is IATA Packing Instruction 913. You may not be able to purchase packages designed for Packing Instruction 913. In this case, use packages designed for infectious substances (Packing Instruction 605) and use a Class 9 label (Figure 1). These materials are shipped with the proper shipping name, "Genetically modified micro-organisms" and UN 3245. The maximum allowable quantity per primary receptacle is 100 mL or 100 g. There is no maximum net quantity per package.

Genetically modified *organisms* that are known or suspected to be dangerous to humans, animals or the environment cannot be transported by air. Animals which contain, or are contaminated with, genetically-modified *microorganisms* or *organisms* that meet the definition of an infectious substance cannot be shipped by air.

D. Infectious Substances

Infectious substances are materials known to be, or are reasonably suspected to contain, an animal or human pathogen. A pathogen is a virus, microorganism (including its viruses, plasmids, or other genetic elements), proteinaceous infectious particle (prion) or recombinant microorganism (hybrid or mutant) that is known or reasonably expected to cause infectious disease in humans or animals. Microorganisms that are unlikely to cause human or animal disease, i.e. no or very low, individual or community risk, do not have to be shipped as infectious substances.

1. Packaging

The triple packaging concept, explained below applies to infectious substances. Purchase packaging approved for use with infectious substances. These packages must comply with IATA Packing Instruction 602. See Appendix A for a list of packaging suppliers. Make sure to specify if you are shipping a refrigerated sample (ice packs or dry ice). The maximum quantity of infectious substance that can be shipped by air cargo in one package is 4 L or 4 kg. The maximum quantity that may be shipped via passenger aircraft is 50 ml or 50 g.

2. Labeling

The sender and recipient's addresses must be printed and clearly displayed. The container should be labeled with the name and telephone number of a person responsible for the shipment. If packaged with dry ice, a Class 9 diamond label (Figure 1) must be placed on one side of the outer package. The container should be labeled with an infectious substance label (Figure 2). When shipping over 50 mL or 50 g of infectious substance, you must also put a Cargo Aircraft Label on the outer container (Figure 3).

When shipping infectious substances by air, you must make advance arrangements with the consignee and the operator to ensure that the shipment can be transported and delivered without delay. In the "Additional Handling Instructions" section of the Shipper's Declaration for Dangerous Goods, include the following statement:

"Prior arrangements as required by the IATA Dangerous Goods Regulations 1.3.3.1 have been made."

There are two proper shipping names for infectious substances:

A. Infectious substance, affecting humans (UN 2814); and

B. Infectious substance, affecting animals (UN 2900).

If you have any reason to believe the infectious material could affect humans you should ship your material as UN 2814. Infectious materials that can affect humans and animals should be shipped as UN 2814. Infectious materials that can only affect animals should be shipped as UN 2900.

Figure 1.

Figure 2.

Figure 3.

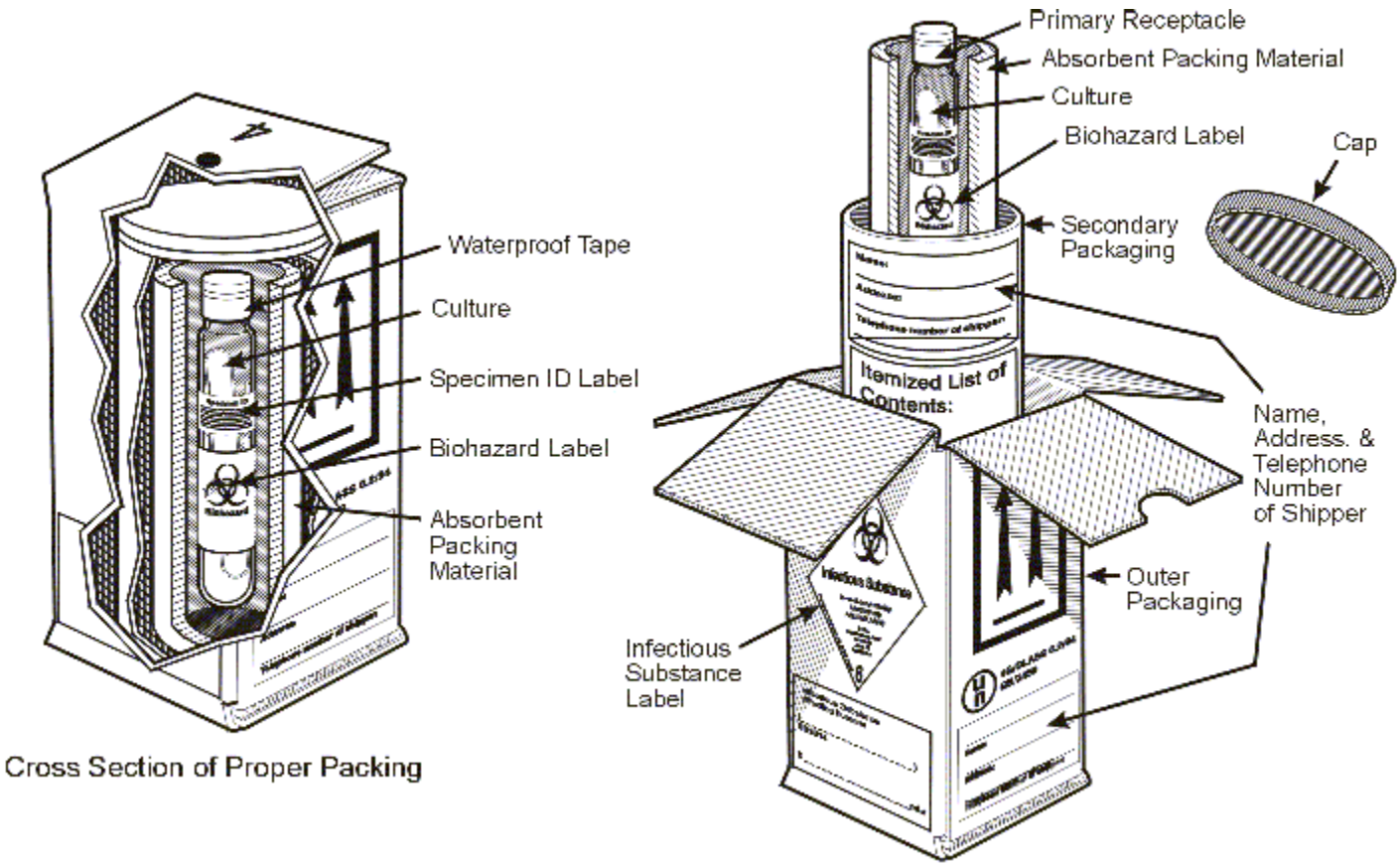
Packaging Biological Materials

Potentially hazardous biological materials must be packaged to withstand leakage of contents, shocks, temperature, pressure changes and other conditions that can occur during ordinary handling in transportation. Packaging your material(s) appropriately is accomplished by purchasing certified packaging. Refer to Appendix A for vendors that can supply certified packaging for biological materials. When ordering, specify what category of material(s) you will be shipping: *infectious substances, diagnostic specimens, dry ice, ice packs*, etc. Different categories have slightly different packaging needs, but all follow the basic triple packaging requirements described below.

A. Triple Packaging

Biological materials, excluding items discussed in B, pg 3, must be packaged according to the triple packaging principle depicted in Figure 4. The three elements of triple packaging include: *primary receptacle, leak-proof secondary container, and durable outer container*. Infectious substances, diagnostic specimens and genetically modified micro-organisms must be packaged in this way, with slight variations.

Figure 4 - Packaging and labeling of biological materials.



The ***primary container*** holds the biological material; it must be leak-proof. It must be labeled with the name of the contents. A leak-proof seal, such as a heat seal, skirted stopper or metal crimp, is required. If the container has a threaded lid, it must be secured with waterproof tape. Petri plates cannot be used as primary receptacles. Lyophilized substances can only be shipped in flame sealed glass ampoules or rubber stopped glass vials with metal seals. Packaging purchased for shipping infectious substances or diagnostic specimens usually does not include the primary container.

The ***secondary container*** holds one or more primary containers, and must also be leak-proof. This container must meet specific United Nations (UN) performance standards. Containers purchased from commercial vendors are designed to meet the necessary standards. If you are shipping any liquid, there must be enough absorbent material in the secondary container to absorb *all* of the liquid in the primary receptacle(s). If multiple primary containers are used, they must be wrapped to prevent contact between them so they do not break during transport.

The ***outer container*** must be at least 100 mm (4 inches) in the smallest overall external dimension, in order for required markings and labels to fit. The outer package must be of adequate strength for its capacity, mass, and intended use. It must also be certified with a UN specification mark. An **itemized list** of package contents must be included between the outer and secondary container. The outer package should be marked to identify hazardous contents, including the proper shipping name, UN number and net quantity for each substance.

B. Other Packaging Requirements

Overpacks. An overpack can be used to combine several triple packages into one large package. This may be done to save freight charges when shipping multiple samples. Each triple package inside the overpack must be properly marked and labeled. The outside of the overpack must bear the same markings and labels as the triple packages within. If packed with dry ice, the total net quantity of dry ice must be listed on the outer container. The overpack must also be marked with the statement:

"Inner Packages Comply with Prescribed Specifications."

Ice and Dry Ice. If a shipment includes ice or dry ice, special packaging must be purchased. If shipping with ice, the packaging must be leak-proof. If dry ice is used, the outer packaging must allow for the release of carbon dioxide gas when the solid sublimates. Ice or dry ice must be placed outside the secondary packaging. Interior supports must be provided to secure the secondary container as the refrigerant melts/sublimates. Dry ice is considered a miscellaneous hazard (Class 9) by IATA. Packages containing dry ice must bear a Class 9 label and be marked with the proper shipping name, UN number and net quantity, e.g., Dry Ice, UN1845, 3 KG. Certified packages for dry ice most likely will be pre-labeled and marked. A Declaration for Dangerous Goods is not required for shipments in which dry ice is the only hazardous material. Dry ice is included on the Declarations for shipments which include other hazardous materials such as infectious substances.

Liquid Nitrogen. Biological materials can be shipped in liquid nitrogen or dry shippers, which are insulated packages containing refrigerated liquid nitrogen fully absorbed in a porous material. Special packing regulations apply to shipments containing nitrogen. Contact OES if you need to ship materials with liquid nitrogen.

Shipper's Declaration for Dangerous Goods

A Declaration for Dangerous Goods form must be completed when shipping infectious substances or genetically modified micro-organisms. A Declaration is not required for shipments in which dry ice is the only hazardous material. Dry ice should be listed on Declarations for shipments containing infectious substances or genetically modified micro-organisms. A Declaration is not required if you are shipping diagnostic specimens (unless it must be classified as an infectious substance, see note). The Declaration is included with purchased shipping materials, or provided by the carrier. For Federal Express, these forms must be typed or computer generated. Improperly completed declarations are the most common cause of package refusal.

Refer to the Shipper's Declaration for Dangerous Goods for an explanation of each section:

a. **Shipper**: Enter your full name, address and telephone number.

b. **Consignee**: Enter full name and address of recipient. When shipping infectious substances, some shippers may require you to include the text, "Person responsible for the shipment," followed by your name and phone number.

c. **Transport Details**: Indicate here if your shipment is restricted to cargo aircraft only (if it is more than 50 ml or 50 g of an infectious substance). Airport of departure and airport of destination will be filled out by the carrier, leave blank.

d. **Shipment Type**: Cross out "radioactive" to indicate you are shipping a non-radioactive substance.

e. **Proper Shipping Name**: Enter the proper shipping name exactly as it appears in Table 1.

f. **Class or Division**: Enter appropriate hazard class as found in Table 1.

g. **UN or ID Number**: Enter appropriate UN number as found in Table 1.

h. **Packing Group**: For dry ice, enter "III" in this column. Biological materials are not assigned packing groups.

i. **Subsidiary Risk**: Leave this column blank.

j. **Quantity and Type of Packaging**: Enter the net quantity for each material here. Use only metric units. At the bottom of this column, indicate the number and type of packages used (usually, "all packed in one fibreboard box."). Do not spell like "fiberboard." If using an overpack, indicate here with "Overpack Used."

k. **Packing Instructions**: Enter appropriate packing instruction number. Refer to Table 1.

l. **Authorization**: Leave this column blank.

m. **Additional Handling Instructions**: Three things are required in this section:

1) The statement "Emergency Contact: (Enter 24 hour contact number for shipper)

2) The statement "Prior arrangements as required by the IATA Dangerous Goods Regulations 1.3.3.1 have been made."

3) The statement "Prepared according to ICAO/IATA."

n. **Signature and date**.

Declaration forms must be filled out in triplicate. Keep one copy and supply two to the carrier. Regulations require that you must retain your copy for *375 days*. Feel free to contact OES with any questions on how to fill out the declaration.

Table 1. Summary of Shipping Information

Shipment Type	Proper Shipping Name	UN Number	Hazard Class	Packing Group (PG)	Packing Instruction (PI)	Max. Net qty./pkg. for Passenger Aircraft	qt A
Infectious stance, ecting nans and sibly mals	Infectious substance, affecting humans (*technical name*)	UN 2814	6.2	-	602	50 ml or 50 g	c
Infectious stance, ecting only mals (not nans)	Infectious substance, affecting animals (*technical name*)	UN 2900	6.2	-	602	50 ml or 50 g	c
Diagnostic clinical cimen	Diagnostic specimens	UN 3373	-	-	650	4 L or 4 kg	c
Dry Ice	Dry Ice or Carbon Dioxide, solid	UN 1845	9	III	904	200 kg	
Non-ectious, nsducing etically dified *micro-nisms*	Genetically modified micro-organisms	UN 3245	9	-	913	No limit	

CDC Select Agents

The U.S. Department of Health and Human Services and USDA have developed a list of biological agents/toxins (see Section V) that have the potential to pose a severe threat to public health. Special regulations apply to the use and transfer of these materials, including registration with the LSU Interinstitutional Biological and Recombinant DNA Safety Committee (IBRDS) and the Centers for Disease Control and Prevention and/or USDA/APHIS. If you are planning to, or currently work with, any of the select agents listed below and have not registered, contact OES. Specific shipping restrictions apply to these agents/toxins.

Importing and Exporting Biological and Infectious Agents

Receiving and sending animals and animal-derived materials, infectious or biohazardous agents, biological toxins, and genetically modified organisms require the approval of federal agencies such as the Centers for Disease Control and Prevention (CDC), the United States Department of Agriculture (USDA), or the US Fish and Wildlife Service (USFWS). Regulations that govern the transfer of biological materials help to minimize or eliminate the possible threats to public health and agriculture.

A. Importation of Infectious Agents

For agents infectious to humans, CDC permit applications are found online at: http://www.cdc.gov/od/ohs. These agents include any infectious agent known or suspected to cause disease in humans, unsterilized specimens of human or animal tissues (including blood and other fluids), or vectors including infectious animals, bats, insects, arthropods and snails (see Appendix D for *HHS Select Infectious Agents*).

B. Importation of Plant/Animal Pests

A USDA/APHIS permit is required to import or domestically transfer a plant pest, plant or animal biological agent, or any material that might contain them. Some items that are included are bees, biological control organisms, butterflies and moths, genetically engineered plants and microorganisms, certain fruits and vegetables, noxious weeds, snails and slugs, soil, and wood products (see Appendix D for *APHIS Plant Pathogens* or *USDA High Consequence Livestock Pathogens or Toxins*). Consult the following web page for more information and permit applications: http://ups.com/using/services/export/prohibited.html

C. Importation of Fish and Wildlife

For transporting fish, wildlife, or endangered species, use the USFWS form 3-177 and 3-177A found at: http://forms.fws.gov/display.cfm?number1=100.

D. Export Guidelines for Infectious Agents of Humans, Animals, Plants, and Related Materials

The export of infectious agents and related materials is governed by the following federal regulation: 15 CFR Parts 730 to 799. An export license is required from the Department of Commerce, when exporting infectious agents of human, plant, and animal diseases, including genetic material, and products which might be used for culture of large

amounts of agents. Consult the following web page for specific items and procedures: http://www.bxa.doc.gov.

Storage

In general, infectious materials should only be stored under refrigeration in a refrigerator or freezer to prevent the rapid growth of the infectious agent. Infectious wastes, on the other hand, should only be stored for a minimum amount of time to prevent the rapid growth of bacteria and objectionable odors. When the infectious waste boxes are full and ready for pick-up, the waste disposal service shall be contacted and the boxes picked up.

The designated storage area for your infectious materials should:

- Be segregated for the storage of the infectious materials only. Post biohazard signs on doors, waste containers, refrigerators, and freezers.
- Be located in an area that has limited traffic flow and is not subject to being crushed or knocked over.
- Be in an area that will not exceed room temperature
- Be cleaned on a regular basis with a suitable hospital approved detergent-germicide. In case of a spill, consult the OES website under emergency procedures.

While on-site storage of infectious waste for more than 48 hours is not recommended, there may be times when a longer storage time may be necessary.

All animal carcasses, organs, and other large pieces of tissue must be refrigerated immediately to control objectionable odors.

If bacterial growth or objectionable odors are a concern, the infectious waste should be stored in a freezer or refrigerator until disposal.

Appendix A – Manufacturers of Certified Shipping Containers for Infectious Substances, Diagnostic Specimens & Dry Ice

Air Sea Atlanta
1234 Logan Circle
Atlanta GA 30318
Phone: 404-351-8600
http://www.airseaatlanta.com

All-Pak, Inc.
Corporate One West
1195 Washington Pike
Bridgeville, PA 15017
Phone: 800-245-2283
http://www.all-pak.com

Casing Corporation
P.O. Box 820369
Dallas, Texas 75382
Phone: 800-358-6866
http://www.casingcorp.com

CARGOpak Corporation
3215-A Wellington Court
Raleigh, NC 27615
Phone: 800-266-0652
http://www.cargopak.com

DG Supplies, Inc.
5 Boxal Drive
Cranbury, NJ 08512
Phone: 800-347-7879
http://www.dgsupplies.com

EXAKT Technologies, Inc.
7416 N Broadway Ext., Suite E
Oklahoma City, OK 73116
Phone: 800-923-9123
http://www.exaktpak.com

HAZMATPAC, Inc
5301 Polk St., Bldg 18
Houston, TX 77023
Phone: 800-347-7879
http://www.hazmatpac.com

Inmark, Inc.
220 Fisk Drive S.W.
Atlanta, GA 30336-0309
Phone: 800-646-6275
http://www.inmarkinc.com

Polyfoam Packers Corporation
2320 S. Foster Avenue
Wheeling, IL 60090
Phone: 888-765-9362
http://www.polyfoam.com

SAF-T-PAK, Inc.
10807 - 182 Street Edmonton, Alberta, Canada, T5S 1J5
Phone: 800-814-7484
http://www.saftpak.com

Source Packaging of New England, Inc.
405 Kilvert St.
Warwick, RI 02886
Phone: 800-200-0366
http://www.sourcepak.com

Com-Pac International, Inc.
800 Industrial Park Road
P. O. Box 2707
Carbondale, Illinois 62901
sales@com-pac.com

Appendix B – Intent to Ship Hazardous Materials

After reading the *LSU Shipment of Biological Materials and Dry Ice Guideline*, fill out this form to qualify to ship dangerous materials at LSU. OES will review this completed form and upon successful completion and demonstration of knowledge of applicable regulations you will be certified to ship those materials designated on this form.

1. What regulated material(s) might you ship via mail or courier service? List all hazardous materials that you intend to ship. Also, list the mailing service you intend to use.

2. What packaging will you use to ship your material(s)? Include company name and product number for chosen packaging for each material you intend to ship.

3. Check those that should appear on your package:

☐ Class 6.2 label

☐ Class 9 label

☐ Cargo Aircraft label

☐ Dry ice, UN 1845, net weight _____ kg

☐ Infectious substance, affecting humans (*technical name*), UN 2814, net quantity _____

☐ Infectious substance, affecting animals (*technical name*), UN 2900, net quantity _____

☐ Name, Address and Phone Number of Shipper

☐ Name and Address of Consignee

☐ Name and Phone Number of Person Responsible for Shipment

☐ "Inner Packages Comply with Prescribed Specifications."

☐ Genetically modified micro-organisms, UN 3245, net quantity _____

☐ "Diagnostic Specimen Packed in Compliance with IATA Packing Instruction 650"

4. Fill out attached Declaration for Dangerous Goods form (if your shipments require one). I understand the hazards associated with the materials noted above. Also, I understand the shipping requirements for those materials, as outlined in this guideline.

Print name:	
Signature:	
Date:	
Please return - in campus mail – to OES , 126 Public Safety Building.	

Appendix C Declaration of Dangerous Goods

Declaration of dangerous goods forms can be found on the carrier's website. An example is FedEx at: http://www.fedex.com/us/services/options/dangerousgoods/declarationforms.html

VIII. LABORATORY FACILITIES – DESIGN, EQUIPMENT AND PRACTICES

A safe laboratory is first of all a well-designed laboratory. A microbiological laboratory shares many of the same features of a standard chemical laboratory. It has means of egress in conformance with fire and safety codes, and the layout is conducive to free movement of personnel in an emergency. It is easily cleaned and maintained. Adequate ventilation is available and well maintained. Appropriate equipment for operations within the laboratory is available and maintained in good condition. Required special safety equipment is present and located so that it is always conveniently available.

All of the common specifications for chemistry laboratories are found in the University Safety Manual. All of this information found in that manual applies to microbiological laboratories, except where they are superseded by more stringent requirements in this handbook, or where they are superseded by additional requirements established by the Animal Care Committee of the University or federal/state regulations.

Biosafety Levels

Microbiological laboratories are designated as one of four different levels. Those meant for working with materials posing the least risk are designated Biosafety Level 1 and those at the most risk, Biosafety Level 4. A combination of laboratory practices, techniques, safety equipment, and design features characterize each level for the operations performed and the degree of hazard posed by the infectious agents employed.

Biosafety Level 1 (BSL-1)

Biosafety Level 1 is suitable for work involving well-characterized agents not known to consistently cause disease in healthy adult humans, and of minimal potential hazard to laboratory personnel and the environment. The laboratory is not necessarily separated from the general traffic patterns in the building. Work is generally conducted on open bench tops using standard microbiological practices. Special containment equipment or facility design is neither required nor generally used. Laboratory personnel have specific training in the procedures conducted in the laboratory and are supervised by a scientist with general training in microbiology or a related science.
The following standard and special practices, safety equipment and facilities apply to agents assigned to Biosafety Level 1:

A. Standard Microbiological Practices

1. Access to the laboratory is limited or restricted at the discretion of the laboratory director when experiments or work with cultures and specimens are in progress.

2. Persons wash their hands after they handle viable materials, after removing gloves, and before leaving the laboratory.

3. Eating, drinking, smoking, handling contact lenses, applying cosmetics, and storing food for human use are not permitted in the work areas. Persons who wear contact lenses in laboratories should

also wear goggles or a face shield. Food is stored outside the work area in cabinets or refrigerators designated and used for this purpose only.

4. Mouth pipetting is prohibited; mechanical pipetting devices are used.

5. Policies for the safe handling of sharps are instituted.

6. All procedures are performed carefully to minimize the creation of splashes or aerosols.

7. Work surfaces are decontaminated at least once a day and after any spill of viable material.

8. All cultures, stocks, and other regulated wastes are decontaminated before disposal by an approved decontamination method such as autoclaving. Materials to be decontaminated outside of the immediate laboratory are to be placed in a durable, leak proof container and closed for transport from the laboratory. Materials to be decontaminated outside of the immediate laboratory are packaged in accordance with applicable local, state, and federal regulations before removal from the facility.

9. A biohazard sign can be posted at the entrance to the laboratory whenever infectious agents are present. The sign may include the name of the agent(s) in use and the name and phone number of the investigator.

10. An insect and rodent control program is in effect (see Appendix G).

B. Special Practices (None)

C. Safety Equipment (Primary Barriers)

1. Special containment devices or equipment such as a biological safety cabinet are generally not required for manipulations of agents assigned to Biosafety Level 1.

2. It is recommended that laboratory coats, gowns, or uniforms be worn to prevent contamination or soiling of street clothes.

3. Gloves should be worn if the skin on the hands is broken or if a rash is present. Alternatives to powdered latex gloves should be available.

4. Protective eye wear should be worn for conduct of procedures in which splashes of microorganisms or other hazardous materials is anticipated.

D. Laboratory Facilities (Secondary Barriers)

1. Laboratories should have doors for access control.

2. Each laboratory contains a sink for hand washing.

3. The laboratory is designed so that it can be easily cleaned. Carpets and rugs in laboratories are not appropriate.

4. Bench tops are impervious to water and are resistant to moderate heat and the organic solvents, acids, alkalis, and chemicals used to decontaminate the work surface and equipment.

5. Laboratory furniture is capable of supporting anticipated loading and uses. Spaces between benches, cabinets, and equipment are accessible for cleaning.

6. If the laboratory has windows that open to the exterior, they are fitted with fly screens.

Biosafety Level 2 (BSL-2)

Biosafety Level 2 is similar to Biosafety Level 1 and is suitable for work involving agents of moderate potential hazard to personnel and the environment. It differs from BSL-1 in that (1) laboratory personnel have specific training in handling pathogenic agents and are directed by competent scientists; (2) access to the laboratory is limited when work is being conducted; (3) extreme precautions are taken with contaminated sharp items; and (4) certain procedures in which infectious aerosols or splashes may be created are conducted in biological safety cabinets or other physical containment equipment.
The following standard and special practices, safety equipment, and facilities apply to agents assigned to Biosafety Level 2:

A. Standard Microbiological Practices

1. Access to the laboratory is limited or restricted at the discretion of the laboratory director when experiments are in progress.

2. Persons wash their hands after they handle viable materials, after removing gloves, and before leaving the laboratory.

3. Eating, drinking, smoking, handling contact lenses, and applying cosmetics are not permitted in the work areas. Food is stored outside the work area in cabinets or refrigerators designated for this purpose only.

4. Mouth pipetting is prohibited; mechanical pipetting devices are used.

5. Policies for the safe handling of sharps are instituted.

6. All procedures are performed carefully to minimize the creation of splashes or aerosols.

7. Work surfaces are decontaminated on completion of work or at the end of the day and after any spill or splash of viable material with disinfectants that are effective against the agents of concern.

8. All cultures, stocks, and other regulated wastes are decontaminated before disposal by an approved decontamination method such as autoclaving. Materials to be decontaminated outside of the immediate laboratory are placed in a durable, leak proof container and closed for transport from the laboratory. Materials to be decontaminated off-site from the facility are packaged in accordance with applicable local, state, and federal regulations, before removal from the facility.

9. An insect and rodent control program is in effect (see Appendix G).

B. Special Practices

1. Access to the laboratory is limited or restricted by the laboratory director when work with infectious agents is in progress. In general, persons who are at increased risk of acquiring infection, or for whom infection may have serious consequences, are not allowed in the laboratory or animal rooms. For example, persons who are immunocompromised or immunosuppressed may be at increased risk of acquiring infections. The laboratory director has the final responsibility for assessing each circumstance and determining who may enter or work in the laboratory or animal room.

2. The laboratory director establishes policies and procedures whereby only persons who have been advised of the potential hazards and meet specific entry requirements (e.g., immunization) may enter the laboratory.

3. A biohazard sign must be posted on the entrance to the laboratory when etiologic agents are in use. Appropriate information to be posted includes the agent(s) in use, the biosafety level, the required immunizations, the investigator's name and telephone number, any personal protective equipment that must be worn in the laboratory, and any procedures required for exiting the laboratory.

4. Laboratory personnel receive appropriate immunizations or tests for the agents 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 for laboratory and other at-risk personnel are collected and stored. Additional serum specimens may be collected periodically, depending on the agents handled or the function of the facility.

6. Biosafety procedures are incorporated into standard operating procedures or in a biosafety manual adopted or prepared specifically for the laboratory by the laboratory director. Personnel are advised of special hazards and are required to read and follow instructions on practices and procedures.

7. The laboratory director ensures that laboratory and support personnel receive appropriate training on the potential hazards associated with the work involved, the necessary precautions to prevent exposures, and the exposure evaluation procedures. Personnel 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.

a. Needles and syringes or other sharp instruments should be restricted in the laboratory for use only when there is no alternative, such as parenteral injection, phlebotomy, or aspiration of fluids from laboratory animals and diaphragm bottles. Plasticware should be substituted for glassware whenever possible.

b. Only needle-locking syringes or disposable syringe-needle units (i.e., needle is integral to the syringe) are used for injection or aspiration of infectious materials. Used disposable needles

must not be bent, sheared, broken, recapped, removed from disposable syringes, or otherwise 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.

c. Syringes which re-sheathe the needle, needleless systems, and other safety devices are used when appropriate.

d. 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 are decontaminated before disposal, according to any local, state, or federal regulations. Contact OES for assistance with disposal.

9. Cultures, tissues, specimens of body fluids, or potentially infectious wastes are placed in a container with a cover that prevents leakage during collection, handling, processing, storage, transport, or shipping.

10. Laboratory equipment and work surfaces should be decontaminated with an effective 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 any 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 are immediately reported to the laboratory director. Medical evaluation, surveillance, and treatment are provided as appropriate and written records are maintained.

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

C. Safety Equipment (Primary Barriers)

1. Properly maintained biological safety cabinets, preferably Class II, or other appropriate personal protective equipment or physical containment devices are used whenever:

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

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

2. Face protection (goggles, mask, face shield or other splatter guard) is used for anticipated splashes or sprays of infectious or other hazardous materials to the face when the microorganisms must be manipulated outside the BSC.

3. Protective laboratory coats, gowns, smocks, or uniforms designated for lab use are worn while in the laboratory. This protective clothing is removed and left in the laboratory before leaving for non-laboratory areas (e.g., cafeteria, library, administrative offices). All protective clothing is either disposed of in the laboratory or laundered by the institution; it should never be taken home by personnel.

4. Gloves are worn when hands may contact potentially infectious materials, contaminated surfaces or equipment. Wearing two pairs of gloves may be appropriate. Gloves are disposed of when overtly contaminated, and removed when work with infectious materials is completed or when the integrity of the glove is compromised. Disposable gloves are not washed, reused, or used for touching "clean" surfaces (keyboards, telephones, etc.), and they should not be worn outside the lab. Alternatives to powdered latex gloves should be available. Hands are washed following removal of gloves.

D. Laboratory Facilities (Secondary Barriers)

1. Provide lockable doors for facilities that house restricted agents (as defined in 42 CFR 72.6).

2. Consider locating new laboratories away from public areas.

3. Each laboratory contains a sink for hand washing.

4. The laboratory is designed so that it can be easily cleaned. Carpets and rugs in laboratories are inappropriate.

5. Bench tops are impervious to water and are resistant to moderate heat and the organic solvents, acids, alkalis, and chemicals used to decontaminate the work surfaces and equipment.

6. Laboratory furniture is capable of supporting anticipated loading and uses. Spaces between benches, cabinets, and equipment are accessible for cleaning. Chairs and other furniture used in laboratory work should be covered with a non-fabric material that can be easily decontaminated.

7. Install *biological* safety cabinets in such a manner that fluctuations of the room supply and exhaust air do not cause the biological safety cabinets to operate outside their parameters for containment. Locate biological safety cabinets away from doors, from windows that can be opened, from heavily traveled laboratory areas, and from other potentially disruptive equipment so as to maintain the biological safety cabinets' air flow parameters for containment.

8. An eyewash station is readily available.

9. Illumination is adequate for all activities, avoiding reflections and glare that could impede vision.

10. There are no specific ventilation requirements. However, planning of new facilities should consider mechanical ventilation systems that provide an inward flow of air without recirculation to spaces outside of the laboratory. If the laboratory has windows that open to the exterior, they are fitted with fly screens.

Biosafety Level 3 (BSL-3)

Biosafety Level 3 is applicable to clinical, diagnostic, teaching, research, or production facilities in which work is done with indigenous or exotic agents which may cause serious or potentially lethal disease as a result of exposure by the inhalation route. Laboratory personnel have specific training in handling pathogenic and potentially lethal agents, and are supervised by competent scientists who are experienced in working with these agents.
All procedures involving the manipulation of infectious materials are conducted within biological safety cabinets or other physical containment devices, or by personnel wearing appropriate personal protective clothing and equipment. The laboratory has special engineering and design features.

It is recognized, however, that some existing facilities may not have all the facility features recommended for Biosafety Level 3 (i.e., double-door access zone and sealed penetrations). In this circumstance, an acceptable level of safety for the conduct of routine procedures, (e.g., diagnostic procedures involving the propagation of an agent for identification, typing, susceptibility testing, etc.), may be achieved in a Biosafety Level 2 facility, providing 1) the exhaust air from the laboratory room is discharged to the outdoors, 2) the ventilation to the laboratory is balanced to provide directional airflow into the room, 3) access to the laboratory is restricted when work is in progress, and 4) the recommended Standard Microbiological Practices, Special Practices, and Safety Equipment for Biosafety Level 3 are rigorously followed. The decision to implement this modification of Biosafety Level 3 recommendations should be made only by the laboratory director.

The following standard and special safety practices, equipment and facilities apply to agents assigned to Biosafety Level 3:

A. Standard Microbiological Practices

1. Access to the laboratory is limited or restricted at the discretion of the laboratory director when experiments are in progress.

2. Persons wash their hands after handling infectious materials, after removing gloves, and when they leave the laboratory.

3. Eating, drinking, smoking, handling contact lenses, and applying cosmetics are not permitted in the laboratory. Persons who wear contact lenses in laboratories should also wear goggles or a face shield. Food is stored outside the work area in cabinets or refrigerators designated for this purpose only.

4. Mouth pipetting is prohibited; mechanical pipetting devices are used.

5. Policies for the safe handling of sharps are instituted.

6. All procedures are performed carefully to minimize the creation of aerosols.

7. Work surfaces are decontaminated at least once a day and after any spill of viable material.

8. All cultures, stocks, and other regulated wastes are decontaminated before disposal by an approved decontamination method, such as autoclaving. Materials to be decontaminated outside of the immediate laboratory are placed in a durable, leak proof container and closed for transport from the laboratory. Infectious waste from BSL-3 laboratories should be decontaminated before removal for off-site disposal.

9. An insect and rodent control program is in effect (see Appendix G).

B. Special Practices

1. Laboratory doors are kept closed when experiments are in progress.

2. The laboratory director controls access to the laboratory and restricts access to persons whose presence is required for program or support purposes. Persons who are at increased risk of acquiring infection or for whom infection may have serious consequences are not allowed in the laboratory or animal rooms. For example, persons who are immunocompromised or immunosuppressed may be at risk of acquiring infections. The director has the final responsibility for assessing each circumstance and determining who may enter or work in the laboratory. No minors should be allowed in the laboratory.

3. The laboratory director establishes policies and procedures whereby only persons who have been advised of the potential biohazard, who meet any specific entry requirements (e.g., immunization), and who comply with all entry and exit procedures, enter the laboratory or animal rooms.

4. When infectious materials or infected animals are present in the laboratory or containment module, a hazard warning sign, incorporating the universal biohazard symbol, is posted on all laboratory and animal room access doors. The hazard warning sign identifies the agent, lists the name and telephone number of the laboratory director or other responsible person(s), and indicates any special requirements for entering the laboratory, such as the need for immunizations, respirators, or other personal protective measures.

5. Laboratory personnel receive the appropriate immunizations or tests for the agents handled or potentially present in the laboratory (e.g., hepatitis B vaccine or TB skin testing), and periodic testing as recommended for the agent being handled.

6. Baseline serum samples are collected as appropriate and stored for all laboratory and other at-risk personnel. Additional serum specimens may be periodically collected, depending on the agents handled or the function of the laboratory.

7. A biosafety manual specific to the laboratory is prepared or adopted by the laboratory director and biosafety precautions are incorporated into standard operating procedures. Personnel are advised of special hazards and are required to read and follow instructions on practices and procedures.

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

9. The laboratory director is responsible for ensuring that, before working with organisms at Biosafety Level 3, all personnel demonstrate proficiency in standard microbiological practices and techniques, and in the practices and operations specific to the laboratory facility. This might include prior experience in handling human pathogens or cell cultures, or a specific training program provided by the laboratory director or other competent scientist proficient in safe microbiological practices and techniques.

10. A high degree of precaution must always be taken with any contaminated sharp items, including needles and syringes, slides, pipettes, capillary tubes, and scalpels.

a. Needles and syringes or other sharp instruments should be restricted in the laboratory for use only when there is no alternative, such as parenteral injection, phlebotomy, or aspiration of fluids from laboratory animals and diaphragm bottles. Plasticware should be substituted for glassware whenever possible.

b. Only needle-locking syringes or disposable syringe-needle units (i.e., needle is integral to the syringe) are used for injection or aspiration of infectious materials. Used disposable needles must not be bent, sheared, broken, recapped, removed from disposable syringes, or otherwise 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.

c. Syringes which re-sheathe the needle, needleless systems, and other safe devices are used when appropriate.

d. 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, and disposed of according to any local, state, or federal regulations. Contact OES for assistance with disposal.

11. All open manipulations involving infectious materials are conducted in biological safety cabinets or other physical containment devices within the containment module. No work in open vessels is conducted on the open bench. Clean-up is facilitated by using plastic-backed paper toweling on non-perforated work surfaces within biological safety cabinets.

12. Laboratory equipment and work surfaces should be decontaminated routinely with an effective disinfectant, after work with infectious materials is finished, and especially after overt spills, splashes, or other contamination with infectious materials.

a. Spills of infectious materials are decontaminated, contained and cleaned up by appropriate professional staff, or others properly trained and equipped to work with concentrated infectious material. Spill procedures are developed and posted.

b. Contaminated equipment must be decontaminated before removal from the facility for repair or maintenance or packaging for transport, in accordance with applicable local, state, or federal regulations.

13. Cultures, tissues, specimens of body fluids, or wastes are placed in a container that prevents leakage during collection, handling, processing, storage, transport, or shipping.

14. All potentially contaminated waste materials (e.g., gloves, lab coats, etc.) from laboratories are decontaminated before disposal or reuse.

15. Spills and accidents that result in overt or potential exposures to infectious materials are immediately reported to the laboratory director. Appropriate medical evaluation, surveillance, and treatment are provided and written records are maintained.

16. Animals and plants not related to the work being conducted are not permitted in the laboratory.

C. Safety Equipment (Primary Barriers)

1. Protective laboratory clothing such as solid-front or wrap-around gowns, scrub suits, or coveralls are worn by workers when in the laboratory. Protective clothing is not worn outside the laboratory. Reusable clothing is decontaminated before being laundered. Clothing is changed when overtly contaminated.

2. Gloves must be worn when handling infectious materials, infected animals, and when handling contaminated equipment.

3. Frequent changing of gloves accompanied by hand washing is recommended. Disposable gloves are not reused.

4. All manipulations of infectious materials, necropsy of infected animals, harvesting of tissues or fluids from infected animals or embryonate eggs , etc., are conducted in a Class II or Class III biological safety cabinet (see Appendix A).

5. When a procedure or process cannot be conducted within a biological safety cabinet, then appropriate combinations of personal protective equipment (e.g., respirators, face shields) and physical containment devices (e.g., centrifuge safety cups or sealed rotors) are used.

6. Respiratory and face protection are used when in rooms containing infected animals.

D. Laboratory Facilities (Secondary Barriers)

1. The laboratory is separated from areas that are open to unrestricted traffic flow within the building, and access to the laboratory is restricted. Passage through a series of two self-closing doors is the basic requirement for entry into the laboratory from access corridors. Doors are lockable (see Appendix F). A clothes change room may be included in the passageway.

2. Each laboratory room contains a sink for hand washing. The sink is hands-free or automatically operated and is located near the room exit door.

3. The interior surfaces of walls, floors, and ceilings of areas where BSL-3 agents are handled are constructed for easy cleaning and decontamination. Seams, if present, must be sealed. Walls, ceilings, and floors should be smooth, impermeable to liquids and resistant to the chemicals and disinfectants normally used in the laboratory. Floors should be monolithic and slip-resistant. Consideration should be given to the use of coved floor coverings. Penetrations in floors, walls, and ceiling surfaces are sealed or capable of being sealed to facilitate decontamination. Openings such as around ducts and the spaces between doors and frames are capable of being sealed to facilitate decontamination.

4. Bench tops are impervious to water and are resistant to moderate heat and the organic solvents, acids, alkalis, and those chemicals used to decontaminate the work surfaces and equipment.

5. Laboratory furniture is capable of supporting anticipated loading and uses. Spaces between benches, cabinets, and equipment are accessible for cleaning. Chairs and other furniture used in laboratory work should be covered with a non-fabric material that can be easily decontaminated.

6. All windows in the laboratory are closed and sealed.

7. A method for decontaminating all laboratory wastes is available in the facility and utilized, preferably within the laboratory (i.e., autoclave, chemical disinfection, incineration, or other approved decontamination method). Consideration should be given to means of decontaminating equipment. If waste is transported out of the laboratory, it should be properly sealed and not transported in public corridors.

8. Biological safety cabinets are required and are located away from doors, from room supply louvers, and from heavily-traveled laboratory areas.

9. A ducted exhaust air ventilation system is provided. This system creates directional airflow which draws air into the laboratory from "clean" areas and toward "contaminated" areas. The exhaust air is not recirculated to any other area of the building. Filtration and other treatments of the exhaust air are not required, but may be considered based on site requirements, and specific agent manipulations and use conditions. The outside exhaust must be dispersed away from occupied areas and air intakes, or the exhaust must be HEPA-filtered. Laboratory personnel must verify that the direction of the airflow (into the laboratory) is proper. It is recommended that a visual monitoring device that indicates and confirms directional inward airflow be provided at the laboratory entry. Consideration should be given to installing an HVAC control system to prevent sustained positive pressurization of the laboratory. Audible alarms should be considered to notify personnel of HVAC system failure.

10. HEPA-filtered exhaust air from a Class II biological safety cabinet can be recirculated into the laboratory if the cabinet is tested and certified at least annually. When exhaust air from Class II safety cabinets is to be discharged to the outside through the building exhaust air system, the cabinets must be connected in a manner that avoids any interference with the air balance of the cabinets or the building exhaust system (e.g., an air gap between the cabinet exhaust and the exhaust duct). When Class III biological safety cabinets are used they should be directly connected to the exhaust system. If the Class III cabinets are connected to the supply system, it is done in a manner that prevents positive pressurization of the cabinets (see Appendix A).

11. Continuous flow centrifuges or other equipment that may produce aerosols are contained in devices that exhaust air through HEPA filters before discharge into the laboratory. These HEPA systems are tested at least annually. Alternatively, the exhaust from such equipment may be vented to the outside if it is dispersed away from occupied areas and air intakes.

12. Vacuum lines are protected with liquid disinfectant traps and HEPA filters, or their equivalent. Filters must be replaced as needed. An alternative is to use portable vacuum pumps (also properly protected with traps and filters).

13. An eyewash station is readily available inside the laboratory.

14. Illumination is adequate for all activities, avoiding reflections and glare that could impede vision.

15. The Biosafety Level 3 facility design and operational procedures must be documented. The facility must be tested for verification that the design and operational parameters have been met prior to operation. Facilities should be re-verified, at least annually, against these procedures as modified by operational experience.

16. Additional environmental protection (e.g., personnel showers, HEPA filtration of exhaust air, containment of other piped services and the provision of effluent decontamination) should be considered if recommended by the agent summary statement, as determined by risk assessment, the site conditions, or other applicable federal, state, or local regulations.

Note that at this time the University has no research requiring Biosafety Level 4, and there are no facilities that are adequate for such research.

Vertebrate Animal Biosafety Level Criteria

If experimental animals are used, institutional management must provide facilities and staff and establish practices which reasonably assure appropriate levels of environmental quality, safety, and care. Laboratory animal facilities in many ways are extensions of the laboratory. As a general principle, the biosafety level (facilities, practices, and operational requirements) recommended for working with infectious agents in vivo and in vitro are comparable. It is well to remember, however, that the animal room is not the laboratory, and can present some unique problems. In the laboratory, hazardous conditions are caused by personnel or the equipment that is being used. In the animal room the activities of the animals

themselves can introduce new hazards. Animals may produce aerosols, and they may also infect and traumatize animal handlers by biting and scratching.

These recommendations presuppose that laboratory animal facilities, operational practices, and quality of animal care meet applicable standards and regulations and that appropriate species have been selected for animal experiments (e.g., Guide for the Care and Use of Laboratory Animals, HEW Publication No. (NIH) 86-23, Rev. 1985, and Laboratory Animal Welfare Regulations - 9 CFR, Subchapter A, Parts 1, 2 and 3).

Ideally, facilities for laboratory animals used for studies of infectious or noninfectious disease should be physically separate from other activities such as animal production and quarantine, clinical laboratories, and especially from facilities that provide patient care. Animal facilities should be designed and constructed to facilitate cleaning and housekeeping. Traffic flow that will minimize the risk of cross contamination should be considered in the plans. A "clean/dirty hall" layout is useful in achieving this. Floor drains should be installed in animal facilities only on the basis of clearly defined needs. If floor drains are installed, the drain trap should always contain water or a suitable disinfectant.

These recommendations describe four combinations of practices, safety equipment, and facilities for experiments on animals infected with agents which produce, or may produce, human infection. These four combinations provide increasing levels of protection to personnel and to the environment, and are recommended as minimal standards for activities involving infected laboratory animals. These four combinations, designated Animal Biosafety Levels (ABSL) 1-4, describe animal facilities and practices applicable to work on animals infected with agents assigned to corresponding Biosafety Levels 1-4.

Facility standards and practices for invertebrate vectors and hosts are not specifically addressed in standards written for commonly used laboratory animals. "Laboratory Safety for Arboviruses and Certain other Viruses of Vertebrates," (178) prepared by the Subcommittee on Arbovirus Laboratory Safety of the American Committee on Arthropod-Borne Viruses, serves as a useful reference in the design and operation of facilities using arthropods.

Animal Biosafety Level 1

A. *Standard Practices*

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

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

3. Eating, drinking, smoking, handling contact 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 are carefully performed to minimize the creation of aerosols.

5. Work surfaces are decontaminated after use or after any spill of viable materials.

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

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

8. An insect and rodent control program is in effect.

B. *Special Practices*

1. The laboratory or animal facility director limits 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 work is in progress. In general, persons who may be at increased risk of acquiring infection, or for whom infection might be unusually hazardous, are not allowed in the animal room.

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

3. Bedding materials from animal cages are removed in such a manner as to minimize the creation of aerosols, and are disposed of in compliance with applicable institutional or local requirements.

4. Cages are washed manually or in a cage washer. Temperature of final rinse water in a mechanical washer should be 180 degrees F.

5. The wearing of laboratory coats, gowns, or uniforms in the animal facility is recommended. It is further recommended that laboratory coats worn in the animal facility not be worn in other areas.

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

C. *Safety Equipment* (Primary Barriers)

Special containment equipment is not required for animals infected with agents assigned to Biosafety Level 1.

D. *Animal Facilities* (Secondary Barriers)

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

2. A handwashing sink is available in the animal facility.

3. If the animal facility has windows that open, they are fitted with fly screens.

4. Exhaust air is discharged to the outside without being recirculated to other rooms, and it is recommended, but not required, that the direction of airflow in the animal facility is inward.

Animal Biosafety Level 2

A. *Standard Practices*

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

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

3. Eating, drinking, smoking, handling contact 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 are carefully performed to minimize the creation of aerosols.

5. Work surfaces are decontaminated after use or after any spill of viable materials.

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

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

8. An insect and rodent control program is in effect.

B. *Special Practices*

1. The laboratory or animal facility director limits 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 work is in progress. In general, persons who may be at increased risk of acquiring infection, or for whom infection might be unusually hazardous, are not allowed in the animal room.

2. The laboratory or animal facility director establishes policies and procedures whereby only persons who have been advised of the potential hazard and meet any specific requirements (e.g., 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 hazard warning sign, incorporating the universal biohazard symbol, is posted on the access door to the animal room. The hazard warning sign identifies the infectious agent(s) in use, lists the name and telephone number of the animal facility supervisor or other responsible person(s), and indicates the special requirement(s) for entering the animal room.

4. Laboratory personnel receive appropriate immunizations or tests for the agents handled or potentially present in the laboratory (e.g., hepatitis B vaccine or TB skin testing).

5. When appropriate, considering the agents handled, baseline serum samples from animal care and other at-risk personnel are 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. The program should provide for the testing of serum samples at each collection interval and the communication of results to the participants.

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

7. Laboratory personnel receive appropriate training on the potential hazards associated with the work involved, the necessary precautions to prevent exposures, and the exposure evaluation procedures. Personnel 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 are restricted in the animal facility 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. Plasticware should be substituted for glassware whenever possible.

a. Only needle-locking syringes or disposable syringe-needle units (i.e., needle is integral to the syringe) are used for injection or aspiration of infectious materials. Used disposable needles must not be bent, sheared, broken, recapped, removed from disposable syringes, or otherwise 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.

b. Syringes which re-sheathe the needle, needle-less systems, and other safe devices should be used when appropriate.

c. 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 any local, state, or federal regulations.

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

10. Cages are 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 any 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 which result in overt exposures to infectious materials are immediately reported to the laboratory director. Medical evaluation, surveillance, and treatment are provided as appropriate and written records are maintained.

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

C. *Safety Equipment* (Primary Barriers)

1. Biological safety cabinets, 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 (139). 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 is worn by all personnel entering animal rooms housing nonhuman primates.

3. Laboratory coats, gowns, or uniforms are worn while in the animal room. This protective clothing is removed before leaving the animal facility.

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

D. *Animal Facilities* (Secondary Barriers)

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

2. A handwashing sink is available in the room where infected animals are housed.

3. If the animal facility has windows that open, they are fitted with fly screens.

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

5. Exhaust air is discharged to the outside without being recirculated to other rooms, and it is recommended, but not required, that the direction of airflow in the animal facility is inward.

6. An autoclave which can be used for decontaminating infectious laboratory waste is available in the building with the animal facility.

Animal Biosafety Level 3

A. *Standard Practices*

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

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

3. Eating, drinking, smoking, handling contact 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 are carefully performed to minimize the creation of aerosols.

5. Work surfaces are decontaminated after use or after any spill of viable materials.

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

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

8. An insect and rodent control program is in effect.

B. *Special Practices*

1. The laboratory director or other responsible person restricts 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, are not allowed in the animal room. Persons at increased risk may include children, pregnant women, and persons who are immunodeficient or immunosuppressed. The supervisor has the final responsibility for assessing each circumstance and determining who may enter or work in the facility.

2. The laboratory director or other responsible person establishes 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 hazard warning sign, incorporating the universal biohazard symbol, is posted on the access door to the animal room. The hazard warning sign identifies the infectious agent(s) in use, lists the name and telephone number of the animal facility supervisor or other responsible person(s), and indicates the special requirement(s) for entering the animal room.

4. Laboratory personnel receive appropriate immunizations or tests for the agents 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 should be collected and stored. Additional serum samples may be collected periodically and stored. The serum surveillance program must take into account the availability

of methods for the assessment of antibody to the agent(s) of concern. The program should provide for the testing of serum samples at each collection interval and the communication of results to the participants.

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

7. Laboratory personnel receive appropriate training on the potential hazards associated with the work involved, the necessary precautions to prevent exposures, and the exposure evaluation procedures. Personnel 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 are 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. Plasticware should be substituted for glassware whenever possible.

a. Only needle-locking syringes or disposable syringe-needle units (i.e., needle is integral to the syringe) are used for injection or aspiration of infectious materials. Used disposable needles must not be bent, sheared, broken, recapped, removed from disposable syringes, or otherwise 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.

b. Syringes which re-sheathe the needle, needle-less systems, and other safe devices should be used when appropriate.

c. 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 any local, state, or federal regulations.

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

10. Cages are 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 according to any 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 which result in overt exposures to infectious materials are immediately reported to the laboratory director. Medical evaluation, surveillance, and treatment are provided as appropriate and written records are maintained.

12. All wastes from the animal room are autoclaved before disposal. All animal carcasses are incinerated. Dead animals are transported from the animal room to the incinerator in leakproof covered 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 is used for all activities involving manipulations of infectious materials or infected animals.

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

b. Personnel wear gloves when handling infected animals. Gloves are removed aseptically and autoclaved with other animal room wastes before disposal.

c. Appropriate face/eye and respiratory protection is worn by all personnel entering animal rooms housing nonhuman primates.

d. Boots, shoe covers, or other protective footwear, and disinfectant footbaths are available and used when indicated.

2. Physical containment devices and equipment appropriate for the animal species are 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 is designed and constructed to facilitate cleaning and housekeeping, and is separated from areas which 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 may also be provided by a double-doored clothes change room (showers may be included), airlock, or other access facility which requires passage through two sets of doors before entering the animal room.

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

3. A foot, elbow, or automatically operated handwashing sink is 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 are protected with liquid traps that are always filled with water or disinfectant.

6. Windows in the animal room are non-operating and sealed.

7. Animal room doors are self-closing and are kept closed when infected animals are present.

8. An autoclave for decontaminating wastes is available, preferably within the animal facility. Materials are transferred to the autoclave in a covered leakproof container whose outer surface has been decontaminated.

9. A non-recirculating ventilation system is provided. The supply and exhaust components of the system are balanced to provide for directional flow of air into the animal room. The exhaust air is discharged directly to the outside and clear of occupied areas and air intakes. Exhaust air from the room can be discharged without filtration or other treatment. Personnel must periodically validate that proper directional airflow is maintained.

10. The HEPA filtered exhaust air from Class I or Class II biological safety cabinets or other primary containment devices is discharged directly to the outside or through the building exhaust system. Exhaust air from these primary containment devices may be recirculated within the animal room if the device is tested and certified at least every 12 months. If the HEPA filtered exhaust air from Class I or Class II biological safety cabinets is discharged to the outside through the building exhaust system, it is connected to this system in a manner (e.g., thimble unit connection)134 that avoids any interference with the performance of either the cabinet or building exhaust system.

Recommended Biosafety Levels

The subsections of this part of the manual will contain, for many potentially infectious agents, the Biosafety Level appropriate for typical laboratory scale operations involving these agents (note that the recommendations are for toxigenic strains of these agents).

However, selection of an appropriate safety level for work with a specific agent or animal study depends on a large number of factors. Some of the most important are: the virulence, pathogenicity, biological stability, route of spread, and communicability of the agent; the nature or function of the laboratory; the procedures and manipulations involving the agent, the endemicity of the agent; and the availability of effective vaccines or therapeutic measures. The following sections will not present the rationale for the recommendations. For additional information, the reader should consult the base document from which most the material in this manual is taken: HHS Publication No. (CDC) 84-8395 BIOSAFETY IN MICROBIOLOGICAL AND BIOMEDICAL LABORATORIES. The NIH Guidelines are also to be followed in selecting appropriate biosafety levels for recombinant DNA work.

The risk assessments and Biosafety Levels recommended presuppose a population of immunocompetent individuals. Recommendations for the use of vaccines and toxoids are included where such products are available. Appropriate precautions should be taken in the administration of live attenuated virus vaccines to individuals with altered immunocompetence. However, these specific

recommendations should in no way preclude the routine use of such products as diphtheria-tetanus toxoids, poliovirus vaccine or influenza vaccine.

The basic Biosafety Level assigned to an agent is based on the activities typically associated with the growth and manipulation of quantities and concentrations of infectious agents required to accomplish identification or typing. If activities with clinical materials pose a lower risk to personnel than those activities associated with the manipulation of cultures, a lower Biosafety Level is recommended.

On the other hand, if the activities involve large volumes or highly concentrated preparations (production quantities) or manipulations that are likely to produce aerosols or which are otherwise intrinsically hazardous, additional personnel precautions and increased levels of primary containment may be indicated. It may be possible to adapt Biosafety levels up or down to compensate for the appropriate level of safety.

It is the responsibility of the Laboratory Director to make these decisions based on the information provided in this manual if present or from other sources. Risk assessment is ultimately a subjective process, but it is recommended that decisions should be biased toward more safety rather than less.