UNIVERSITY OF NORTH DAKOTA

INSTITUTIONAL BIOSAFETY MANUAL

July 2016

Prepared by the University of North Dakota Institutional Biosafety Committee and the Office of Safety

UND EMERGENCY PHONE NUMBERS

For Emergency Services
You may always dial 911 for Emergency Assistance*

UND Police	701-777-3491
Operations Call Center	701-777-2591

OFFICE OF SAFETY

Associate Director of Safety	701-777-3759
Biological Safety Officer Biological spills	701-777-2444
Environmental Health & Safety Manager Hazardous Chemical/Radioisotope Spills	701-777-5931
Environmental Health & Safety Technician Fire Safety	701-777-6044

PUBLIC HEALTH AND SAFETY

Chief of Police	701-777-3391
Associate Director for Emergency Management	701-777-2030

FACILITIES MANAGEMENT

Facilities Main Desk	701-777-4137

MEDICAL SERVICES

Occupational Health – Altru Health System	701-780-1546

PREFACE

The Institutional Biosafety Manual is part of the University of North Dakota's (UND) biosafety program, which was established to accomplish the following goals:

- ✓ Protect personnel from exposure to infectious agents
- ✓ Prevent environmental contamination
- ✓ Provide an environment for high quality research while maintaining a safe work place
- ✓ Comply with applicable federal, state and local requirements

The biosafety manual provides university-wide safety guidelines, policies and procedures for the use and manipulation of biohazards. Although the implementation of these procedures is the responsibility of the Principal Investigator (PI), its success depends largely on the combined efforts of laboratory supervisors and employees. Planning for and implementation of biological safety must be part of every laboratory activity in which biohazardous materials are used. In general, the handling and manipulation of hazardous biological agents and toxins, as well as recombinant DNA molecules, requires the use of various precautionary measures depending on the material(s) involved. This manual will provide assistance in the evaluation, containment and control of biohazards. However, it is imperative that all parties involved or working with these materials seek additional advice and training when necessary. The Office of Safety and the Institutional Biosafety Committee are available at UND to assist in this endeavor.

Your comments and suggestions concerning the Manual are welcomed and can be emailed to the Institutional Biosafety Committee Chair (rdc@research.UND.edu) or the Biological Safety Officer (und.safety@email.UND.edu).

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A. INTRODUCTION

A. Purpose

The primary objective of this manual is to provide guidance to employees assigned to work with, or in the vicinity of, potentially infectious or otherwise hazardous materials deriving from plant, animal or human sources. In general, the handling and manipulation of biohazardous materials requires the use of various precautionary measures depending on the material(s) involved (biohazardous materials include all infectious agents, toxins, as well as recombinant DNA molecules). This manual will provide assistance in the evaluation, containment and control of biohazards.
The manual has been tailored for the needs of University of North Dakota (UND) researchers by assembling important information from the following sources:

The Centers for Disease Control and Prevention Biosafety in Microbiological and Biomedical Laboratories, 5th Edition, 2009
http://www.cdc.gov/biosafety/publications/bmbl5/index.htm

NIH guidelines for research involving recombinant or synthetic nucleic acid molecules (NIH GUIDELINES)
http://osp.od.nih.gov/sites/default/files/resources/NIH_Guidelines.pdf

WHO Laboratory Biosafety Manual-Third Edition
http://www.who.int/csr/resources/publications/biosafety/Biosafety7.pdf?ua=1

Guide for the Care and Use of Laboratory Animals
http://grants.nih.gov/grants/olaw/guide-for-the-care-and-use-of-laboratory-animals.pdf

Guidelines for the Safe transport of Infectious substances and Diagnostic specimens
http://www.absa.org/pdf/who97.pdf

Guidance on regulations for the Transport of Infectious Substances 2015-2016
http://apps.who.int/iris/bitstream/10665/149288/1/WHO_HSE_GCR_2015.2_eng.pdf

The Biosafety manuals of the University of Chicago, Arizona State University, Michigan State University, and Emory University were also used as references.

The Biosafety Manual will be readily available to employees through their Principal Investigator or Primary Supervisor and is accessible from the UND Office of Safety website: http://und.edu/finance-operations/office-of-safety/index.cfm and the Institutional Biosafety Committee (IBC) website: https://und.edu/research/resources/institutional-biosafety-committee.cfm. The Biosafety Manual shall be reviewed and updated at least annually and whenever necessary to reflect new or modified tasks and procedures and to reflect or revised procedures.

B. Scope

This Biosafety Program applies to all UND personnel whose occupational tasks or responsibilities include the handling and manipulation of biohazardous materials. This includes occupations with non-routine exposure.

C. Management

Biosafety is a cooperative effort between UND and its employees. The Institutional Biosafety Committee (IBC), the Biological Safety Officer, Principal Investigators and laboratory personnel must work in concert to

minimize the risk of injury and illness associated with research involving potentially biohazardous materials. The Biosafety Program is managed through oversight provided by the IBC and the Office of Safety. The Biological Safety program at UND developed from the University's commitment to address and comply with the NIH Guidelines regarding safe research with recombinant DNA and associated viral materials. The IBC and Office of Safety are responsible for implementation of biosafety policies throughout the University. Following is a list of individuals and/or organizations and their assigned responsibilities that will ensure the Biosafety Program is effectively implemented:

- ✓ Principal Investigators / Primary Supervisors
- ✓ Laboratory Managers
- ✓ Students and Employees
- ✓ Institutional Biosafety Committee (IBC)
- ✓ Research Development and Compliance (RD&C)
- ✓ Office of Safety
- ✓ Biological Safety Officer (BSO)
- ✓ Deans, Directors, Chairpersons
- ✓ Licensed Healthcare Provider
- ✓ Attending Veterinarian
- ✓ Other Committees [Human Subjects (IRB), Institutional Animal Care and Use Committee (IACUC), Radiation Safety and Hazardous Materials Committee]

The roles and responsibilities of each are described below:

Principal Investigators / Primary Supervisors/Instructors

The Principal Investigators/Primary Supervisors/Instructors are responsible for biosafety in their laboratory, work space or classrooms. They shall:

- Ensure that all work is conducted in accordance with established policies and guidelines described in this document.
- Ensure that all employees and/or students under their supervision are adequately trained in good aseptic techniques and have received required training.
- Develop, review and approve laboratory-specific and/or protocol-specific procedures, consulting with the BSO when necessary.
- Provide training/information to all employees under their supervision regarding laboratory-specific or protocol-specific hazards and document such training.
- Ensure that all at-risk employees have been informed of risk assessments and/or provisions for any recommended precautionary medical practices, such as vaccinations and any special health or handling requirements regarding potentially biohazardous materials or toxins used or stored in the laboratory or work area.
- Ensure prompt reporting of any job-related injuries, exposures or illnesses.
- Inform the Supervisor and BSO of any serious, or potentially serious, accidents/incidents or situations involving exposure to biohazardous materials. This would include any accidental releases, illnesses or diseases to workers, plants or animals involved in or potentially exposed to the activity, and any possible adverse personnel exposure.
- Act upon requests and/or directives from the IBC and/or Office of Safety and correct any unsafe laboratory conditions.
- Ensure that appropriate containment devices and other engineering controls are in place and appear to be operating correctly, are current with certifications (ensures Biosafety Cabinets are certified) and are used according to established procedures.
- Conduct regular laboratory safety inspections and participate in audits and evaluations as necessary.

- Ensure that appropriate personal protective equipment (PPE) are available, used and that staff is adequately trained on the use and limitations of PPE equipment.
- Keep self and staff informed of new criteria, guidelines, directives or procedures that may be developed or which become applicable to activities in which they are engaged.
- Ensure proper decontamination of the laboratory or animal facility and equipment necessary to ensure safety during any needed inspection, calibration, certification, disposal or termination of use.
- Ensure proper disposal of all infectious material or toxins.
- Provide adequate storage of materials and security based on risk categorization.
- Maintain proper biohazard labeling of premises under their control.

Laboratory Managers

When delegated by the PI, Laboratory Managers who have a supervisory role are responsible for:

- Ensuring that all University and laboratory practices and protocols are followed. Lab managers are responsible for identifying any unsafe lab practices or workers and reporting them to the PI.

Students and Employees

All students and employees performing work with biohazardous materials must accept a shared responsibility for operating in a safe manner. Ultimately, each individual is responsible for his/her own safety. They also shall:

- Ensure that all work is conducted in accordance with established policies and guidelines described in this document or specific laboratory standard operating procedures (SOPs).
- Report all hazardous conditions to the PI and /or BSO.
- Promptly report any job related injuries, exposures or illnesses to the PI and/or BSO and seek medical treatment immediately.
- Refrain from operating any equipment or instrument without proper instruction.
- Request information and training when unsure how to handle potentially hazardous materials.
- Wear and maintain PPE necessary to perform each task.
- Use engineering controls properly-Example Biosafety Cabinet.
- Practice good microbiological techniques.
- Participate in all required training programs.

Institutional Biosafety Committee (IBC)

- Develop policy and procedures that provide guidance for activities involving potentially biohazardous materials.
- Follow the guidelines for membership defined by the NIH.
- Ensure that UND's biosafety policies, practices and facilities meet regulatory requirements and follow University-accepted practice.
- Review and/or approve risk assessments for specific biohazardous agents. When warranted, ask whether the scientific aims of the proposed research can be sought by means involving lower biohazard potential, and when appropriate, bring to executive management's attention the risks associated with a particular experiment.
- Report any significant problems with or violations of the *NIH Guidelines* and any significant research-related accidents or illness to the appropriate Institutional Office and to the NIH Office of Biotechnology Activities (OBA) within 30 days.
- Ensure that an inventory of potentially biohazardous materials and toxins is maintained. Ensure accurate current inventory for each Select Agent (including viral genetic elements, recombinant nucleic acids, and recombinant organisms) held in long term storage and all agents stored in BSL-3 labs.

Research Development and Compliance (RD&C)

- Initiates the registration of biological research (IBC Application process) by providing departments with the application material.
- Accepts all Applications and Annual Reviews for research proposals submitted by Principal Investigators and departments and coordinates their review by the IBC.
- Accepts research proposals involving the use of humans and coordinates their review by the Institutional Review Board (IRB).

Biological Safety Officer (BSO)

The Biological Safety Officer provides expertise in developing the UND Biosafety Program and supports BSL-1, BSL-2, BSL-3 Laboratories, and ABSL-1, ABSL-2, ABSL-3 spaces. The BSO develops, implements, and updates biosafety policies, and procedures that are necessary for an effective, compliant, and effective biosafety program.

The BSO plays an important role in:

- Providing technical support to the IBC and PIs on campus as well as working closely with researchers to provide necessary training on biosafety procedures and proper use of containment equipment.
- Conducting periodic laboratory inspections of all areas on campus involved in research utilizing biohazardous agents to assure appropriate safety controls, containment, and compliance.
- Reviewing activities and facilities for proper biohazard control; apply relevant laws, standards and guidelines; and be aware of community attitudes and health and environmental considerations.
- Report any significant problems, trends and/or violations of regulations or policies and practices to the IBC and appropriate management.
- Take measures necessary to ensure that all biohazardous activities comply with the policies and practices established by the IBC.

When accidents, exposures, or spills happen in the Lab, the Office of Safety and the BSO also respond to, investigate, and follow up with suggestions and strategies for a resolution to prevent reoccurrences.

Office of Safety

The Office of Safety works closely with the IBC to ensure that operations for which the Office of Safety has responsibility are conducted in accordance with the criteria and guidelines established by the IBC. These include:

- Disposal of medical waste.
- Selection of appropriate protective clothing for individuals working with hazards, including biohazardous, materials.
- Development and implementation of emergency response and preparedness plans.
- Monitoring work areas, including the presence of allergens.

Deans, Directors, Chairpersons

They are responsible for all the students, employees, and visitors in the spaces under their control. They must be aware of what research is happening in these spaces, the risks associated with that research, and the control methods proposed by the PIs.

Licensed Healthcare Provider

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

Attending Veterinarian

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

Other committees (IRB, IACUC, Radiation Safety and Hazardous Materials Committee)

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

Failure of any personnel to recognize this responsibility or to comply with established procedures/policies is cause for disciplinary action.

D. Rules, Regulations, and Guidelines

The University assures its compliance with pertinent government regulations, laws, and required guidelines, including but not limited to, the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines), as implemented by the National Institutes of Health, a division of the United States Department of Health and Human Services (HHS); the Select Agent Final Rule, as implemented by the United States Department of Health and Human Services' Centers for Disease Control and Prevention (CDC) and the United States Department of Agriculture's (USDA) Animal and Plant Health Inspection Service (APHIS) via Title 42 Code of Federal Regulations Part 73 (42 CFR 73 "Possession, Use, and Transfer of Select Agents and Toxins; Final Rule), Title 7 Code of Federal Regulations Part 331, and Title 9 Code of Federal Regulations Part 121 (7 CFR 331 and 9 CFR 121 Agricultural Bioterrorism Protection Act of 2002; Possession, Use, and Transfer of Biological Agents and Toxins; Final Rule); the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (Public Law 107-188); and the Uniting and Strengthening America by Providing Appropriate Tools Required to Intercept and Obstruct Terrorism Act of 2001 (USA PATRIOT Act, Public Law 107-56). Additionally, the University adheres to the Department of Commerce's (DOC) Bureau of Industry and Standards (BIS) Title 15 Code of Federal Regulations Parts 730-777 (15 CFR 730-774 "Commerce Control List") and the Department of Transportation's (DOT) Research and Special Programs Administration's Title 49 Code of Federal Regulations Parts 171-180 (49 CFR 171-80 "Hazardous Materials: Revision to Standards for Infectious Substances; Final Rule).

Additionally, in 1984, the CDC/NIH published the first edition of the Biosafety in Microbiological and Biomedical Laboratories (BMBL). This document describes combinations of standard and special microbiological practices, safety equipment, and facilities that constitute Biosafety Levels 1-4, which are recommended for working with a variety of infectious agents in various laboratory settings. This document also outlines requirements for animal biosafety levels. The BMBL has been revised several times and is commonly seen as the standard for biosafety. UND is using the BMBL (current edition) as the basis for this biosafety manual and for revisions of this manual.

II. BIOHAZARDOUS RESEARCH PROJECT REGISTRATION AND APPROVAL

A. Biohazards

Biohazards include infectious or etiologic (disease causing) agents of humans, animals and plants, toxins of biological origin, human-derived materials, recombinant DNA and any materials potentially containing infectious agents or biohazards. Biohazardous agents may include but are not limited to: Certain bacteria, fungi, viruses, rickettsiae, chlamydiae, parasites, recombinant products, allergens, cultured human or animal cells and the potentially infectious agents these cells may contain (viroids, prions and other infectious agents as outlined in laws, regulations, or guidelines). Each Principal Investigator (PI) is responsible for the preparation of an IBC Registration Document for all research involving biological materials or agents including the assignment of the required Biosafety Level to the proposed research. This includes research involving:

- ✓ Recombinant DNA, including experiments that are specifically exempt under the NIH Guidelines, including PCR, or Extraction of DNA
- ✓ Infectious Agents (Bacteria, Eukaryotic Pathogens, Protozoa or Viruses pathogenic to plants and animals)
- ✓ Toxins
- ✓ Tumorigenic Material
- ✓ Human Blood/Tissue/Cell Lines
- ✓ Vertebrate Animal Usage
- ✓ Plant or Animal Pathogens (bacterial, viral, fungal, parasitic, protozoan, etc), viral vectors, naturally-occurring plant or animal toxins, or other potentially infectious agents
- ✓ Plants/Plant Parts/Algae
- ✓ Radioisotopes with biohazardous agents

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

B. Registration and Approval Process

All faculty or staff who plan on using recombinant DNA or biohazardous materials for research, teaching, or other activities must submit a completed signed registration document to the IBC. The IBC will then consider the application at its earliest convenience. Any changes to an approved project with respect to recombinant DNA or biohazardous materials must receive IBC approval prior to their use. Copies of the IBC Registration Document can be downloaded from the IBC website https://und.edu/research/resources/institutional-biosafety-committee.cfm. To determine the appropriate Biosafety Level for the proposed research, the PIs can utilize the Agent Summary Statements in the BMBL (http://www.cdc.gov/biosafety/publications/bmbl5/BMBL.pdf, section VIII), consult the Pathogen Safety Data Sheets and Risk Assessment maintained by The Public Health Agency of Canada (http://www.phac-aspc.gc.ca/lab-bio/res/psds-ftss/index-eng.php), or consult the Control of Communicable Diseases Manual (published by the American Public Health Association).

C. Additional Approvals and Requirements

Select Biological Agents and Toxins: The US Department of Health and Human Services (HHS) and the US Department of Agriculture (USDA) have developed a list of select biological agents and toxins that have the potential to pose a severe biosecurity threat to public health, animals, and agricultural crops. As directed by the US Patriot Act, HHS and USDA have adopted strict regulations for the obtaining, possession, use, or transfer of any of these selected agents. Failure to comply with the established regulations can result in significant civil and criminal penalties. Therefore, any plans for obtaining such materials must be discussed with the University Biological Safety Officer and approved by the IBC well in advance of any planned use. Also, anyone contemplating select agent use should understand that a decision to use Select Biological Agents and Toxins requires accepting a significant level of personal responsibility for meeting all aspects of the requirements

mandated by the federal rules and failure to meet the federal mandates could result in personal criminal and civil penalties. HHS regulations in 42 CFR Part 73 Possession, Use, and Transfer of Select Agents and Toxins and the companion USDA regulations in 9 CFR Part 121 require federal registration and inspection; restricted lab access; development of written and strictly followed safety and security plans; personnel background checks (including fingerprinting) and training; accurate records and/or reporting of agent use, transfer, loss, or destruction. Further information about the Select Agents Program and regulations can be found on the Federal Select Agent Program web page www.selectagents.gov.

Toxins of Biological Origin

Any biological toxin with a median lethal dose, or LD_{50}, of less than 100 micrograms per kilogram body weight in vertebrates, must be approved by the UND Institutional Biosafety Committee prior to beginning research. Research with recombinant or synthetic nucleic acid molecules containing genes for the biosynthesis of toxin molecules lethal for vertebrates at an LD_{50} of less than 100 nanograms per kilogram body weight requires pre-approval from the National Institutes of Health's Office of Biotechnology Activities. Examples of biological toxins with an LD_{50} of less than 100 nanograms per kilogram include the botulinum toxins, tetanus toxin, and diphtheria toxin.

Environmental Samples

Environmental samples, such as water, air, soil, or plants, may contain pathogens (e.g., bacteria, viruses, spores) that could present a health hazard to people, animals, or the environment. Using appropriate personal protective equipment when collecting environmental samples will reduce exposure to potential pathogens and minimize transfer of pathogens in the environment. Use care when handling environmental samples, especially if the sample will be enhanced in the laboratory by culturing or other growing mechanisms, including greenhouses. Techniques used to enhance and/or culture environmental samples should be conducted at BSL-2 or higher levels in an appropriate containment device, such as a biological safety cabinet. If the environmental sample is sterilized prior to experimentation, then the sample may be manipulated in a BSL-1 rated laboratory. All other environmental samples must be registered with the UND Institutional Biosafety Committee.

Human Blood Tissue

In any laboratory where work involves the use of and/or exposure to human blood, other body fluids, or unfixed human tissue, there is the danger of exposure to bloodborne pathogens. Work with any of these materials in a laboratory setting usually requires that workers take the Bloodborne Pathogens Training. The BBP Program ensures compliance with the Federal Occupational Health and Safety Administration (OSHA) Bloodborne Pathogens Standard (29 CFR 1910.1030).

All laboratories that work with human blood, other body fluids, or unfixed human tissue need to be enrolled in the UND Bloodborne Pathogens Exposure Control Plan (https://und.edu/finance-operations/_files/docs/6-27-bloodborne-pathogens-ecp.pdf). Specifically, the Plan:

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

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

- Use appropriate personal protective equipment and follow established safe work practices.

NOTE: A copy of the UND Bloodborne Pathogens Exposure Control Plan is available on the IBC website (https://und.edu/finance-operations/_files/docs/6-27-bloodborne-pathogens-ecp.pdf). Each laboratory needs to send a copy of Appendix 1 and Appendix 4 to the Office of Safety to complete enrollment in the UND Bloodborne Pathogens Exposure Control Plan.

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

- Submit the research proposal through Research Development & Compliance (RD&C) to the Institutional Review Board (IRB).
- Get assurance that, when human blood or blood products are received from sources outside the University, donors (or blood products) have been tested for HIV and hepatitis B and C and found to be negative. When such testing is impractical or impossible, requests for exemptions to this requirement are to be made to the IBC Committee.

III. BIOLOGICAL RISK ASSESSMENT

A. Risk Assessment

Risk assessment is an important responsibility for Supervisors and Principal Investigators of microbiological and biomedical laboratories. Institutional biosafety committees, animal care and use committees, biological safety professionals, and laboratory animal veterinarians share in this responsibility. Risk assessment is a process used to examine the various factors associated with a procedure involving biological materials in order to identify the hazardous characteristics of the material, the activities that can result in a person's exposure to an infectious agent, the likelihood that exposure will cause a laboratory acquired infection, and the probable consequences of an infection. The information identified by risk assessment will provide a guide for the selection of biosafety levels, microbiological practices, safety equipment, and facility safeguards that can prevent laboratory acquired infections (LAIs) and reduce environmental contamination risk.

Factors to consider in a risk assessment include both agent hazards and laboratory factors.

Agent Hazards

- ✓ Capability to infect and cause disease in a susceptible host
- ✓ Virulence as measured by the severity of disease
- ✓ Availability of preventive measures and effective treatments for the disease
- ✓ Probable routes of transmission of laboratory infection
  - The predominant routes of transmission in the laboratory include mucous membrane exposure, parenteral inoculation, ingestion and inhalation of infectious aerosols
- ✓ Infective dose
- ✓ Stability in the environment
- ✓ Host range
- ✓ Its endemic nature
- ✓ Reports of laboratory acquired infections
- ✓ Origin of the agent

Laboratory Procedure Hazards

- ✓ Parenteral inoculations
- ✓ Injection of potentially hazardous materials can occur by a needle, other contaminated sharp or by bites from infected animals or arthropod vectors
- ✓ Spills and splashes into skin and mucous membranes
- ✓ Mucous membranes include the eyes, nose and mouth
- ✓ Ingestion through mouth pipetting
- ✓ Animal bites and scratches
- ✓ Inhalation exposures to infectious aerosols

Aerosols, or respirable sized particles, are extremely hazardous because they are generated in many lab procedures and are usually undetected. The creation of infectious aerosols places the person carrying out the procedure and others in the laboratory at risk. Any procedure that breaks the surface tension of a liquid will produce aerosols. ***Pipetting, blenders, non-self-contained centrifuges, sonicators and vortex mixers all produce aerosols.*** Procedures and equipment that create aerosols also create larger droplets that rapidly settle out of the air. These droplets can settle on surfaces and therefore contaminate gloved hands, work spaces and mucous membranes.

NOTE: University of North Dakota Laboratory Risk Assessment tool is available on the Office of Safety website (http://und.edu/public-safety/campus-safety/biological.cfm).

B. Risk Groups

Risk groups (RG) are a method used by the World Health Organization (WHO) and by the National Institutes of Health (NIH) to classify human etiological agents based on hazard to both the individual and to the community. ***There are four risk groups.*** These correlate to but are not equivalent to biosafety levels. Determining the risk group of a biological agent can be part of the biosafety risk assessment and helps in assigning the correct biosafety level for containment. In general, RG-2 agents are handled at BSL- 2, and RG-3 agents at BSL-3. However, the use of certain RG-2 agents in large quantities might require BSL-3 conditions, while some RG-3 agents may be safely manipulated at a BSL-2 level under certain conditions. Refer to **Table 1** for the basis of classification of Biohazardous Agents by Risk Group:

TABLE 1. Basis for the Classification of Biohazardous Agents by Risk Group

Risk Group Classification	NIH Guidelines for Research Involving Recombinant DNA Molecules, 2016	World Health Organization Laboratory Biosafety Manual 3rd Edition, 2004
Risk Group 1	Agents not associated with disease in healthy adult humans	**(No or low individual and community risk)** A microorganism unlikely to cause human or animal disease.
Risk Group 2	Agents associated with human disease that is rarely serious and for which preventive or therapeutic interventions are often available.	**(Moderate individual risk; low community risk)** A pathogen that can cause human or animal disease but is unlikely to be a serious hazard to laboratory workers, the community, livestock or the environment. Laboratory exposures may cause serious infection, but effective treatment and preventive measures are available and the
Risk group 3	Agents associated with serious or lethal human disease for which preventive or therapeutic interventions may be available (high individual risk but low community risk).	**(High individual risk; low community risk)** A pathogen that usually causes serious human or animal disease but does not ordinarily spread from one infected individual to another. Effective treatment and preventive measures are available
Risk Group 4	Agents likely to cause serious or lethal human disease for which preventive or therapeutic interventions are not usually available (high individual risk and high community risk).	**(High individual and community risk)** A pathogen that usually causes serious human or animal disease and can be readily transmitted from one individual to another, directly or indirectly. Effective treatment and preventive measures are not

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C. Hazards of Genetically-Modified Agents

When conducting a risk assessment of genetically modified agents, consideration of the same factors used in risk assessment of the wild-type organism should be done. However, it is important to address the possibility that the genetic modification could alter (i.e., increase or decrease) the pathogenicity of the agent or affect its susceptibility to antibiotics or other treatments. Sometimes, important information may not be available for a newly engineered agent and the risk assessment may be difficult or incomplete. In these cases, due diligence should be practiced and the biosafety level assignment should be made conservatively. Once the information is available another risk assessment should be completed.

D. Hazards of Cell Cultures

Human and animal cells and tissues have the potential to harbor latent infectious agents and personnel who handle these materials are at risk for possible exposure. For additional information and requirements for working with human cell cultures please refer to the **UND Bloodborne Pathogens Exposure Control Plan** (https://und.edu/finance-operations/_files/docs/6-27-bloodborne-pathogens-ecp.pdf).

E. Storage and Labeling of Biohazardous Agents

Biohazardous agents must be stored using leak proof and sealed container. Containers must be clearly labeled with the identity of the agent and should include the universal biohazard symbol **(see Figure 1)** as physical space on the container permits. At a minimum, secondary (or outside) containers must include the universal biohazard symbol (identity of contents is also desirable).

Certain other areas and pieces of equipment within a laboratory may also require signs. Refrigerators, freezers, cabinets, and other storage facilities require the biohazard symbol whenever they are used to store infectious agents; human blood or blood products; unfixed tissues; cell or organ cultures; body fluids; or excreta. Large pieces of equipment for handling such materials (e.g., centrifuges, biological safety cabinets) must be similarly labeled.

Figure 1
Biohazard Symbol

F. Laboratory Door Signs

Each laboratory must have a sign at the entrance that provides safety information to visitors and service personnel. Room door signs must contain designations for all laboratory hazards in use within the laboratory (carcinogens, acutely toxic agents, reproductive hazards, biohazards, radioactive materials, lasers, and magnetic fields). The door sign are available on the Office of Safety website (https://und.edu/public-safety/_files/docs/safety-information-card.pdf).

Biohazard signs will be posted at the following:

- ✓ Entrances to laboratories and animal rooms that use agents classified as BSL-1, BSL-2 or BSL-3.
- ✓ Cages or animal rooms used for housing animals infected with BSL-1, BSL-2 or BSL-3 agents.

IV. PRINCIPLES OF BIOSAFETY AND STANDARD LABORATORY BIOSAFETY LEVELS

A. Biological Safety in Laboratories

Biological Safety is the application of knowledge, techniques and equipment to prevent personal, laboratory and environmental exposure to potentially infectious agents or biohazards. Biosafety defines the containment conditions under which infectious agents can be safely manipulated. The objective of containment is to confine biohazards and to reduce the potential exposure of the laboratory worker, persons outside of the laboratory, and the environment to potentially infectious agents. It can be accomplished through the following means:

Primary Containment: Protection of personnel and the immediate laboratory environment through good microbiological techniques (laboratory practices) and the use of appropriate safety equipment.

Secondary Containment: Protection of the environment external to the laboratory from exposure to infectious materials through a combination of facility design and operational practices.

Combinations of laboratory practices, containment equipment, and special laboratory design can be made to achieve different levels of physical containment. Currently ***four biosafety levels (1- 4)*** define the levels of containment necessary to protect personnel and the environment. A biosafety level 1 (BSL-1) is the least restrictive, while biosafety level 4 (BSL-4) requires a special containment laboratory or facility. This Institutional Biosafety Manual is tailored for BSL-1 and BSL-2 laboratories at UND. **For more information on Biosafety level 3 and 4 requirements refer to the appropriate literature or contact the Biological Safety Officer at 777-2444.** UND cannot accommodate BSL-4 level work.

The most important element in maintaining a safe work environment is strict adherence to good microbiological and laboratory practices and techniques. Everyone working with infectious agents or potentially infectious materials must be aware of the potential risks. In addition, they must be trained and proficient in the practices and techniques required for handling such material. It is the responsibility of the Principal Investigator or person in charge of the laboratory to provide or arrange for appropriate training of all personnel.

Standard Microbiological Practices to be followed at both BSL-1 and BSL-2 Laboratories (BMBL Current edition)

Laboratories under all biosafety levels are required to adhere to the following Standard Microbiological Practices:

- ✓ The laboratory supervisor must enforce the institutional policies that control access to the laboratory.
- ✓ Persons must wash their hands after working with potentially hazardous materials and before leaving the laboratory.
- ✓ Eating, drinking, smoking, handling contact lenses, applying cosmetics, and storing food for human consumption must not be permitted in laboratory areas. Food must be stored outside the laboratory area in cabinets or refrigerators designated and used for this purpose.
- ✓ Mouth pipetting is prohibited; mechanical pipetting devices must be used.
- ✓ Policies for the safe handling of sharps, such as needles, scalpels, pipettes, and broken glassware must be developed and implemented. Whenever practical, laboratory supervisors should adopt improved engineering and work practice controls that reduce risk of sharps injuries. Precautions, including those listed below, must always be taken with sharp items. These include:
    a. Careful management of needles and other sharps are of primary importance. Needles must not be bent, sheared, broken, recapped, removed from disposable syringes, or otherwise manipulated by hand before disposal.
    b. Used disposable needles and syringes must be carefully placed in conveniently located puncture-resistant containers used for sharps disposal.

c. Non-disposable sharps must be placed in a hard walled container for transport to a processing area for decontamination, preferably by autoclaving.
d. Broken glassware must not be handled directly. Instead, it must be removed using a brush and dustpan, tongs, or forceps. Plastic ware should be substituted for glassware whenever possible.

- ✓ Perform all procedures to minimize the creation of splashes and/or aerosols.
- ✓ Decontaminate work surfaces after completion of work and after any spill or splash of potentially infectious material with appropriate disinfectant.
- ✓ Decontaminate all cultures, stocks, and other potentially infectious materials before disposal using an effective method. Depending on where the decontamination will be performed, the following methods should be used prior to transport.
    a. Materials to be decontaminated outside of the immediate laboratory must be placed in a durable, leak proof container and secured for transport.
    b. Materials to be removed from the facility for decontamination must be packed in accordance with applicable local, state, and federal regulations.
- ✓ A sign incorporating the universal biohazard symbol must be posted at the entrance to the laboratory when infectious agents are present. The sign may include the name of the agent(s) in use, and the name and phone number of the laboratory supervisor or other responsible personnel.
- ✓ An effective integrated pest management program is required.
- ✓ The laboratory supervisor must ensure that laboratory personnel receive appropriate training regarding their duties, the necessary precautions to prevent exposures, and exposure evaluation procedures. Personnel must receive annual updates or additional training when procedural or policy changes occur. Personal health status may impact an individual's susceptibility to infection, ability to receive immunizations or prophylactic interventions. Therefore, all laboratory personnel and particularly women of childbearing age should be provided with information regarding immune competence and conditions that may predispose them to infection. Individuals having these conditions should be encouraged to self-identify to the institution's licensed healthcare provider for appropriate counseling and guidance.

B. Biosafety Level 1 (BSL-1)

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

Laboratory Biosafety Level Criteria (BSL-1)

Special practices: None Required

Safety Equipment (Primary Barriers and Personal Protective Equipment)

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

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

Laboratory Facilities (Secondary Barriers)

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

C. Biosafety Level 2 (BSL-2)

Biosafety level 2 build upon BSL-1. BSL-2 is suitable for work involving agents that pose moderate hazards to personnel and the environment. It differs from BSL-1 in that:

- ✓ Laboratory personnel have specific training in handling pathogenic agents and are supervised by scientists competent in handling infectious agents and associated procedures;
- ✓ Access to the laboratory is restricted when work is being conducted; and
- ✓ All procedures in which infectious aerosols or splashes may be created are conducted in BSCs or other physical containment equipment.

Laboratory Biosafety Level Criteria (BSL-2)

Special practices:

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

- ✓ Animal and plants not associated with the work being performed must not be permitted in the laboratory.
- ✓ All procedures involving the manipulation of infectious materials that may generate an aerosol should be conducted within a BSC or other physical containment devices.

Safety Equipment (Primary Barriers and Personal Protective Equipment)

- ✓ Properly maintained BSCs, other appropriate PPE, or other physical containment devices must be used whenever:
    a. Procedures with a potential for creating infectious aerosols or splashes are conducted. These may include pipetting, centrifuging, grinding, blending, shaking, mixing, sonicating, opening containers of infectious materials, inoculating animals intranasally, and harvesting infected tissues from animals or eggs.
    b. High concentrations or large volumes of infectious agents are used. Such materials may be centrifuged in the open laboratory using sealed rotor heads or centrifuge safety cups.
- ✓ Protective laboratory coats, gowns, smocks, or uniforms designated for laboratory use must be worn while working with hazardous materials. Remove protective clothing before leaving for non-laboratory areas, e.g., cafeteria, library, and administrative offices). Dispose of protective clothing appropriately, or deposit it for laundering by the institution. It is recommended that laboratory clothing not be taken home.
- ✓ Eye and face protection (goggles, mask, face shield or other splatter guard) is used for anticipated splashes or sprays of infectious or other hazardous materials when the microorganisms must be handled outside the BSC or containment device. Eye and face protection must be disposed of with other contaminated laboratory waste or decontaminated before reuse. Persons who wear contact lenses in laboratories should also wear eye protection.
- ✓ Gloves must be worn to protect hands from exposure to hazardous materials. Glove selection should be based on an appropriate risk assessment. Alternatives to latex gloves should be available. Gloves must not be worn outside the laboratory. In addition, BSL-2 laboratory workers should:
    a. Change gloves when contaminated, glove integrity is compromised, or when otherwise necessary.
    b. Remove gloves and wash hands when work with hazardous materials has been completed and before leaving the laboratory.
    c. Do not wash or reuse disposable gloves. Dispose of used gloves with other contaminated laboratory waste. Hand washing protocols must be rigorously followed.
- ✓ Eye, face and respiratory protection should be used in rooms containing infected animals as determined by the risk assessment.

Laboratory Facilities (Secondary Barriers)

- ✓ Laboratory doors should be self-closing and have locks in accordance with the institutional policies.
- ✓ Laboratories must have a sink for hand washing. The sink may be manually, hands-free, or automatically operated. It should be located near the exit door.
- ✓ The laboratory should be designed so that it can be easily cleaned and decontaminated. Carpets and rugs in laboratories are not permitted.
- ✓ Laboratory furniture must be capable of supporting anticipated loads and uses. Spaces between benches, cabinets, and equipment should be accessible for cleaning.
    a. Bench tops must be impervious to water and resistant to heat, organic solvents, acids, alkalis, and other chemicals.
    b. Chairs used in laboratory work must be covered with a non-porous material that can be easily cleaned and decontaminated with appropriate disinfectant.
- ✓ Laboratory windows that open to the exterior are not recommended. However, if a laboratory does have windows that open to the exterior, they must be fitted with screens.

- ✓ BSCs must be installed so that fluctuations of the room air supply and exhaust do not interfere with proper operations. BSCs should be located away from doors, windows that can be opened, heavily traveled laboratory areas, and other possible airflow disruptions.
- ✓ Vacuum lines should be protected with liquid disinfectant traps.
- ✓ An eyewash station must be readily available.
- ✓ There are no specific requirements for ventilation systems. However, planning of new facilities should consider mechanical ventilation systems that provide an inward flow of air without recirculation to spaces outside of the laboratory.
- ✓ HEPA filtered exhaust air from a Class II BSC can be safely recirculated back into the laboratory environment if the cabinet is tested and certified at least ***annually*** and operated according to manufacturer's recommendations. BSCs can also be connected to the laboratory exhaust system by either a thimble (canopy) connection or directly exhausted to the outside through a hard connection. Provisions to assure proper safety cabinet performance and air system operation must be verified.
- ✓ A method for decontaminating all laboratory wastes should be available in the facility (e.g., autoclave, chemical disinfection, incineration, or other validated decontamination method).

V. BIOSAFETY LEVELS IN ANIMAL LABORATORIES

A. Biological Safety in Animal Facilities

Animal biosafety levels (ABSL) are also derived directly from the CDC's BMBL, and provide containment recommendations for both experimentally infected animals and those that may naturally harbor zoonotic infectious agents. The animal room can present unique hazards not found in a standard laboratory. Animals can generate aerosols, they may introduce agents through bites or scratches, and their wastes present another source of infectious or zoonotic agents. The co-application of biosafety levels, and animal biosafety levels are determined by protocol-driven risk assessment and, as a general principle, the BSL recommended for working with the infectious agent *in vivo* and *in vitro* are similar. Large animal ABSL-2, as well as ABSL-3, and ABSL-4 work is currently not possible at UND due to the lack of appropriate animal containment facilities. Therefore, these ABSL descriptions apply to rodent/small animal work on campus.

Standard Microbiological Practices applied to both ABSL-1 and ABSL-2

- ✓ The animal facility veterinarian and the IACUC chair establishes and enforces policies, procedures, and protocols for institutional policies and emergencies.
    b. Each organization must assure that worker safety and health concerns are addressed as part of the animal protocol review.
    c. Prior to beginning a study, animal protocols must also be reviewed and approved by the IACUC and the IBC.
- ✓ A safety manual specific to the animal facility is prepared or adopted in consultation with the animal facility veterinarian and appropriate safety professionals.
    a. The safety manual must be available and accessible. Personnel are advised of potential hazards, and are required to read and follow instructions on practices and procedures.
    b. Consideration should be given to specific biohazards unique to the animal species and protocol in use.
- ✓ The supervisor must ensure that animal care, laboratory, and support personnel receive appropriate training regarding their duties, animal husbandry procedure, potential hazards, manipulations of infectious agents, necessary precautions to prevent hazard or exposures, and hazard/exposure evaluation procedures (physical hazards, splashes, aerosolization, etc.).
- ✓ Personnel must receive annual updates or additional training when procedures or policies change. Records are maintained for all hazard evaluations, employee training sessions and staff attendance.
- ✓ An appropriate medical surveillance program is in place, as determined by risk assessment. The need for an animal allergy prevention program should be considered.
    a. Facility supervisors should ensure that medical staff is informed of potential occupational hazards within the animal facility, to include those associated with research, animal husbandry duties, animal care and manipulations.
    b. Personal health status may impact an individual's susceptibility to infection, ability to receive immunizations or prophylactic interventions. Therefore, all personnel and particularly women of childbearing age should be provided information regarding immune competence and conditions that may predispose them to infection. Individuals having these conditions should be encouraged to self-identify to the institution's healthcare provider for appropriate counseling and guidance.
    c. Personnel using respirators must be enrolled in an appropriately constituted respiratory protection program. **NOTE:** University of North Dakota Respiratory Protection Policy is available on the Finance and Operations website (https://und.edu/finance-operations/_files/docs/6-30-respiratory-protection-program.pdf).
- ✓ A sign incorporating the universal biohazard symbol must be posted at the entrance to areas where infectious materials and/ or animals are housed or are manipulated when infectious agents are present. The sign must include the animal biosafety level, general occupational health requirements, PPE

requirements, the supervisor's name (or names of other responsible personnel), telephone number, and required procedures for entering and exiting the animal areas. Identification of all infectious agents is necessary when more than one agent is being used within an animal room.

a. Security-sensitive agent information and occupational health requirements should be posted in accordance with the institutional policy.
b. Advance consideration should be given to emergency and disaster recovery plans, as a contingency for man-made or natural disasters.

- ✓ Access to the animal room is limited. Only those persons required for program or support purposes are authorized to enter the animal facility and the areas where infectious materials and/or animals are housed or manipulated.
    a. All persons including facility personnel, service workers, and visitors are advised of the potential hazards (physical, naturally occurring, or research pathogens, allergens, etc.) and are instructed on the appropriate safeguards.
- ✓ Protective laboratory coats, gowns, or uniforms are recommended to prevent contamination of personal clothing.
    a. Gloves are worn to prevent skin contact with contaminated, infectious and hazardous materials and when handling animals.
    b. Gloves and personal protective equipment should be removed in a manner that prevents transfer of infectious materials outside of the areas where infectious materials and/or animals are housed or are manipulated.
    c. Persons must wash their hands after removing gloves, and before leaving the areas where infectious materials and/or animals are housed or are manipulated.
    d. Eye, face and respiratory protection should be used in rooms containing infected animals, as dictated by the risk assessment.
- ✓ Eating, drinking, smoking, handling contact lenses, applying cosmetics, and storing food for human consumption must not be permitted in laboratory areas. Food must be stored outside of the laboratory in cabinets or refrigerators designated and used for this purpose.
- ✓ All procedures are carefully performed to minimize the creation of aerosols or splatters of infectious materials and waste.
- ✓ Mouth pipetting is prohibited. Mechanical pipetting devices must be used.
- ✓ Policies for the safe handling of sharps, such as needles, scalpels, pipettes, and broken glassware must be developed and implemented. When applicable, laboratory supervisors should adopt improved engineering and work practice controls that reduce the risk of sharps injuries. Precautions must always be taken with sharp items. These include:
    a. The use of needles and syringes or other sharp instruments in the animal facility is limited to situations where there is no alternative such as parenteral injection, blood collection, or aspiration of fluids from laboratory animals and diaphragm bottles.
    b. Disposable needles must not be bent, sheared, broken, recapped, removed from disposable syringes, or otherwise manipulated by hand before disposal. Used, disposable needles must be carefully placed in puncture-resistant containers used for sharps disposal. Sharps containers should be located as close to the work site as possible.
    c. Non-disposable sharps must be placed in a hard-walled container for transport to a processing area for decontamination, preferably by autoclaving.
    d. Broken glassware must not be handled directly; it should be removed using a brush and dustpan, tongs, or forceps. Plastic ware should be substituted for glassware whenever possible.
    e. Use of equipment with sharp edges and corners should be avoided.
- ✓ Equipment and work surfaces are routinely decontaminated with an appropriate disinfectant after work with an infectious agent, and after any spills, splashes, or other overt contamination.

- ✓ Animals and plants not associated with the work being performed must not be permitted in the areas where infectious materials and/ or animals are housed or manipulated.
- ✓ An effective integrated pest management program is required.
- ✓ All wastes from the animal room (including animal tissues, carcasses, and bedding) are transported from the animal room in leak-proof containers for appropriate disposal in compliance with applicable institutional, local and state requirements.

B. Animal Biosafety Level 1 (ABSL-1)

Animal Biosafety Level 1 is suitable for work in animals involving well-characterized agents that are not known to cause disease in immunocompetent adult humans, and present minimal potential hazard to personnel and the environment. ABSL-1 facilities should be separated from the general traffic patterns of the building and restricted as appropriate. Personnel must have specific training in animal facility procedures and must be supervised by an individual with adequate knowledge of potential hazards and experimental animal procedures. The use of PPE and any specific entry/exit procedures for the animal space is determined by animal species used, and the protocol specific risk assessment.

Special Practices - None Required

Safety Equipment (Primary and Personal Protective Equipment)

- ✓ A risk assessment should determine the appropriate type of PPE to be utilized.
- ✓ Special containment devices or equipment may not be required as determined by appropriate risk assessment.
- ✓ Protective laboratory coats, gowns, or uniforms may be required to prevent contamination of personal clothing.
    a. Protective outer clothing is not worn outside areas where infectious materials and/or animals are housed or manipulated. Gowns and uniforms are not worn outside the facility
- ✓ Protective eyewear is worn when conducting procedures that have the potential to create splashes of microorganisms or other hazardous materials. Persons who wear contact lenses should also wear eye protection when entering areas with potentially high concentrations or airborne particulates.
    a. Persons having contact with nonhuman primates (NHPs) must assess risk of mucous membrane exposure and wear protective equipment (e.g., masks, goggles, face shields, etc.) as appropriate for the task to be performed.
- ✓ Gloves are worn to protect hands from exposure to hazardous materials.
    a. A risk assessment should be performed to identify the appropriate glove for the task and alternatives to latex gloves should be available.
    b. Change gloves when contaminated, glove integrity is compromised, or when otherwise necessary.
    c. Gloves must not be worn outside the animal rooms.
    d. Gloves and personal protective equipment should be removed in a manner that prevents transfer of infectious materials.
    e. Do not wash or reuse disposable gloves. Dispose of used gloves with other contaminated waste.
- ✓ Persons must wash their hands after handling animals and before leaving the areas where infectious materials and/or animals are housed or are manipulated. Hand washing should occur after the removal of gloves.

Laboratory Facilities (Secondary Barriers)

- ✓ The animal facility is separated from areas that are open to unrestricted personnel traffic within the building. External facility doors are self-closing and self-locking.
    a. Access to the animal facility is restricted.
    b. Doors to areas where infectious materials and/or animals are housed, open inward, are self-closing, are kept closed when experimental animals are present, and should never be propped

open. Doors to cubicles inside an animal room may open outward or slide horizontally or vertically.

- ✓ The animal facility must have a sink for hand washing.
    a. Sink traps are filled with water, and/or appropriate liquid to prevent the migration of vermin and gases.
- ✓ The animal facility is designed, constructed, and maintained to facilitate cleaning and housekeeping. The interior surfaces (walls, floors and ceilings) are water resistant. Floors must be slip resistant, impervious to liquids, and resistant to chemicals.
    a. It is recommended that penetrations in floors, walls and ceiling surfaces be sealed, including openings around ducts, doors and doorframes, to facilitate pest control and proper cleaning.
- ✓ Cabinets and bench tops must be impervious to water and resistant to heat, organic solvents, acids, alkalis, and other chemicals.
- ✓ Spaces between benches, cabinets, and equipment should be accessible for cleaning.
- ✓ Chairs used in animal area must be covered with a non-porous material that can be easily cleaned and decontaminated. Furniture must be capable of supporting anticipated loads and uses. Sharp edges and corners should be avoided.
- ✓ External windows are not recommended; if present windows must be resistant to breakage. Where possible, windows should be sealed. If the animal facility has windows that open, they are fitted with fly screens. The presence of windows may impact facility security and therefore should be assessed by security personnel.
- ✓ Ventilation should be provided in accordance with the Guide for Care and Use of Laboratory Animals. No recirculation of exhaust air may occur. It is recommended that animal rooms have inward directional airflow.
    a. Ventilation system design should consider the heat and high moisture load produced during the cleaning of animal rooms and the cage wash process.
- ✓ Internal facility appurtenances, such as light fixtures, air ducts, and utility pipes, are arranged to minimize horizontal surface areas to facilitate cleaning and minimize the accumulation of debris or fomites.
- ✓ If floor drains are provided, the traps are filled with water, and/or appropriate disinfectant to prevent the migration of vermin and gases.
- ✓ Cages are washed manually or preferably in a mechanical cage washer. The mechanical cage washer should have a final rinse temperature of at least 180°F. If manual cage washing is utilized, ensure that appropriate disinfectants are selected.
- ✓ Illumination is adequate for all activities, avoiding reflections and glare that could impede vision.
- ✓ Emergency eyewash and shower are readily available; location is determined by risk assessment.

C. Animal Biosafety Level 2 (ABSL-2)

Animal Biosafety Level 2 builds upon the practices, procedures, containment equipment, and facility requirements of ABSL-1. ABSL-2 is suitable for work involving laboratory animals infected with agents associated with human disease and pose moderate hazards to personnel and the environment. It also addresses hazards from ingestion as well as from percutaneous and mucous membrane exposure. ABSL-2 requires that:

- ✓ Access to the animal facility is restricted;
- ✓ Personnel must have specific training in animal facility procedures, the handling of infected animals and the manipulation of pathogenic agents;
- ✓ Personnel must be supervised by individuals with adequate knowledge of potential hazards, microbiological agents, animal manipulations and husbandry procedures; and
- ✓ BSCs or other physical containment equipment is used when procedures involve the manipulation of infectious materials, or where aerosols or splashes may be created. Appropriate PPE must be utilized to

reduce exposure to infectious agents, animals, and contaminated equipment. Implementation of employee occupational health programs should be considered.

Laboratory Biosafety Level Criteria-ABSL-2

Special practices:

- ✓ Animal care staff, laboratory and routine support personnel must be provided a medical surveillance program as dictated by the risk assessment and administered appropriate immunizations for agents handled or potentially present, before entry into animal rooms.
- ✓ When appropriate, a base line serum sample should be stored.
- ✓ Procedures involving a high potential for generating aerosols should be conducted within a biosafety cabinet or other physical containment device. When a procedure cannot be performed within a biosafety cabinet, a combination of PPE and other containment devices must be used.
- ✓ Restraint devices and practices that reduce the risk of exposure during animal manipulations (e.g., physical restraint devices, chemical restraint medications) should be used whenever possible.
- ✓ Decontamination by an appropriate method (e.g. autoclave, chemical disinfection, or other approved decontamination methods) is necessary for all potentially infectious materials and animal waste before movement outside the areas where infectious materials and/or animals are housed or are manipulated. This includes potentially infectious animal tissues, carcasses, contaminated bedding, unused feed, sharps, and other refuse.
- ✓ A method for decontaminating routine husbandry equipment, sensitive electronic and medical equipment should be identified and implemented.
- ✓ Materials to be decontaminated outside of the immediate areas where infectious materials and/or animals are housed or are manipulated must be placed in a durable, leak proof, covered container and secured for transport. The outer surface of the container is disinfected prior to moving materials. The transport container must have a universal biohazard label.
- ✓ Develop and implement an appropriate waste disposal program in compliance with applicable institutional, local and state requirements. Autoclaving of content prior to incineration is recommended.
- ✓ Equipment, cages, and racks should be handled in a manner that minimizes contamination of other areas.
- ✓ Equipment must be decontaminated before repair, maintenance, or removal from the areas where infectious materials and/or animals are housed or are manipulated.
- ✓ Spills involving infectious materials must be contained, decontaminated, and cleaned up by staff properly trained and equipped to work with infectious material.
- ✓ Incidents that may result in exposure to infectious materials must be immediately evaluated and treated according to procedures described in the safety manual. All such incidents must be reported to the animal facility supervisor or personnel designated by the institution. Medical evaluation, surveillance, and treatment should be provided as appropriate and records maintained.

Safety Equipment (Primary Barriers and Personal Protective Equipment)

- ✓ Properly maintained BSCs, PPE (e.g., gloves, lab coats, face shields, respirators, etc.) and/or other physical containment devices or equipment, are used whenever conducting procedures with a potential for creating aerosols, splashes, or other potential exposures to hazardous materials. These include necropsy of infected animals, harvesting of tissues or fluids from infected animals or eggs, and intranasal inoculation of animals.
- ✓ When indicated by risk assessment, animals are housed in primary biosafety containment equipment appropriate for the animal species, such as solid wall and bottom cages covered with filter bonnets for rodents or other equivalent primary containment systems for larger animal cages.
- ✓ A risk assessment should determine the appropriate type of PPE equipment to be utilized.

- ✓ Scrub suits and uniforms are removed before leaving the animal facility. Reusable clothing is appropriately contained and decontaminated before being laundered. Laboratory and protective clothing should never be taken home.
- ✓ Gowns, uniforms, laboratory coats and PPE are worn while in the areas where infectious materials and/or animals are housed or manipulated and removed prior to exiting. Disposable PPE and other contaminated waste are appropriately contained and decontaminated prior to disposal.
- ✓ Eye and face protection (mask, goggles, face shield or other splatter guard) are used for manipulations or activities that may result in splashes or sprays from infectious or other hazardous materials and when the animal or microorganisms must be handled outside the BSC or containment device. Eye and face protection must be disposed of with other contaminated laboratory waste or decontaminated before reuse. Persons who wear contact lenses should also wear eye protection when entering areas with potentially high concentrations or airborne particulates.
- ✓ Persons having contact with NHPs should assess risk of mucous membrane exposure and wear protective equipment (e.g., masks, goggles, face shields) appropriate for the task to be performed. Respiratory protection is worn based upon risk assessment.
- ✓ Gloves are worn to protect hands from exposure to hazardous materials. A risk assessment should be performed to identify the appropriate glove for the task and alternatives to latex gloves should be available.
- ✓ Gloves are changed when contaminated, glove integrity is compromised, or when otherwise necessary.
- ✓ Gloves must not be worn outside the animal rooms.
- ✓ Gloves and personal protective equipment should be removed in a manner that prevents transfer of infectious materials.
- ✓ Do not wash or reuse disposable gloves. Dispose of used gloves with other contaminated waste.
- ✓ Persons must wash their hands after handling animals and before leaving the areas where infectious materials and/or animals are housed or are manipulated. Hand washing should occur after the removal of gloves.

Laboratory Facilities (Secondary barriers)

- ✓ The animal facility is separated from areas that are open to unrestricted personnel traffic within the building. External facility doors are self-closing and self-locking.
- ✓ Doors to areas where infectious materials and/or animals are housed, open inward, are self-closing, are kept closed when experimental animals are present, and should never be propped open. Doors to cubicles inside an animal room may open outward or slide horizontally or vertically.
- ✓ A hand-washing sink is located at the exit of the areas where infectious materials and/or animals are housed or are manipulated. Additional sinks for hand washing should be located in other appropriate locations within the facility.
- ✓ If the animal facility has segregated areas where infectious materials and/or animals are housed or manipulated, a sink must also be available for hand washing at the exit from each segregated area.
- ✓ Sink traps are filled with water, and/or appropriate disinfectant to prevent the migration of vermin and gases.
- ✓ The animal facility is designed, constructed, and maintained to facilitate cleaning and housekeeping. The interior surfaces (walls, floors and ceilings) are water resistant.
- ✓ Penetrations in floors, walls and ceiling surfaces are sealed, including openings around ducts, doors and doorframes, to facilitate pest control and proper cleaning.
- ✓ Floors must be slip-resistant, impervious to liquids, and resistant to chemicals.
- ✓ Cabinets and bench tops must be impervious to water and resistant to heat, organic solvents, acids, alkalis, and other chemicals. Spaces between benches, cabinets, and equipment should be accessible for cleaning.

- ✓ Furniture should be minimized. Chairs used in animal area must be covered with a non-porous material that can be easily cleaned and decontaminated. Furniture must be capable of supporting anticipated loads and uses. Sharp edges and corners should be avoided.
- ✓ External windows are not recommended; if present, windows must be sealed and resistant to breakage. The presence of windows may impact facility security and therefore should be assessed by security personnel.
- ✓ Ventilation should be provided in accordance with the Guide for Care and Use of Laboratory Animals.
    a. The direction of airflow into the animal facility is inward; animal rooms maintain inward directional airflow compared to adjoining hallways.
    b. A ducted exhaust air ventilation system is provided. Exhaust air is discharged to the outside without being recirculated to other rooms.
- ✓ Ventilation system design should consider the heat and high moisture load produced during the cleaning of animal rooms and the cage wash process.
- ✓ Internal facility appurtenances, such as light fixtures, air ducts, and utility pipes, are arranged to minimize horizontal surface areas, to facilitate cleaning and minimize the accumulation of debris or fomites.
- ✓ Floor drains must be maintained and filled with water, and/or appropriate disinfectant to prevent the migration of vermin and gases.
- ✓ Cages should be autoclaved or otherwise decontaminated prior to washing. Mechanical cage washer should have a final rinse temperature of at least 180°F. The cage wash area should be designed to accommodate the use of high-pressure spray systems, humidity, strong chemical disinfectants and 180°F water temperatures during the cage/equipment cleaning process.
- ✓ Illumination is adequate for all activities, avoiding reflections and glare that could impede vision.
- ✓ If BSCs are present, they must be installed so that fluctuations of the room air supply and exhaust do not interfere with proper operations. BSCs should be located away from doors, heavily traveled laboratory areas, and other possible airflow disruptions.
- ✓ HEPA filtered exhaust air from a Class II BSC can be safely re-circulated back into the laboratory environment if the cabinet is tested and certified at least ***annually*** and operated according to manufacturer's recommendations. BSCs can also be connected to the laboratory exhaust system by either a thimble (canopy) connection or directly to the outside through an independent, hard connection. Provisions to assure proper safety cabinet performance and air system operation must be verified. BSCs should be recertified at least once a year to ensure correct performance.
- ✓ All BSCs should be used according to manufacturer's specifications to protect the worker and avoid creating a hazardous environment from volatile chemicals and gases.
- ✓ If vacuum service (i.e., central or local) is provided, each service connection should be fitted with liquid disinfectant traps and an in-line HEPA filter placed as near as practicable to each use point or service cock. Filters are installed to permit in-place decontamination and replacement.
- ✓ An autoclave should be present in the animal facility to facilitate decontamination of infectious materials and waste.
- ✓ Emergency eyewash and shower are readily available; location is determined by risk assessment.

Refer to Appendix A and B for a good summary of requirements at each biosafety level (laboratory and animal facility).

VI. LABORATORY EQUIPMENT AND PROCEDURES

A. Biological Safety Cabinets

A biological safety cabinet (BSC) is used as a primary barrier against exposure to infectious biological agents. A BSC has High Efficiency Particulate Air (HEPA) filters. The airflow in a BSC is laminar, i.e. the air moves with uniform velocity in one direction along parallel flow lines. A BSC must be used in conjunction with safe laboratory techniques, because potentially dangerous aerosols can still escape. Depending on the design, a BSC may be vented to the outside or the air may be exhausted into the room. **BSCs are not chemical fume hoods**. A percentage of the air is re-circulated in most types of BSCs. Therefore, the levels of explosive, flammable, or toxic materials will be concentrated within the cabinet. HEPA filters only trap particulates, allowing any containment in non-particulate form to pass through the filter.

Class I BSCs

In Class I BSCs, the exhaust air is HEPA filtered so the user and the environment are protected, but the product inside the cabinet is not. With a Class I cabinet, the user's hands and arms while inside the cabinet are exposed to the infectious materials. The Class I BSC is designed for general microbiological research with low to moderate risk agents, and is useful for containment of mixers, blenders, and other equipment.

Class II BSCs

There are different types of Class II BSCs, but they all offer HEPA filtered supply and exhaust air. This type of cabinet will protect the user, environment, and the product and is suitable for work assigned to Biosafety Levels 1, 2, or 3. Class II cabinets are the class most commonly used.

Class III BSCs

These cabinets are often referred to as Gloveboxes. The Class III cabinet is gas-tight and under negative pressure. All work in the cabinet is performed through rubber gloves attached to entry portals. The Class III cabinet offers the highest level of protection from infectious aerosols. Class III cabinets are most suitable for work with agents that require BSL-3 or BSL-4 containment.

B. Utilization of Biological Safety Cabinets

In general, the following guidelines are recommended when using biological safety cabinets (BSCs):

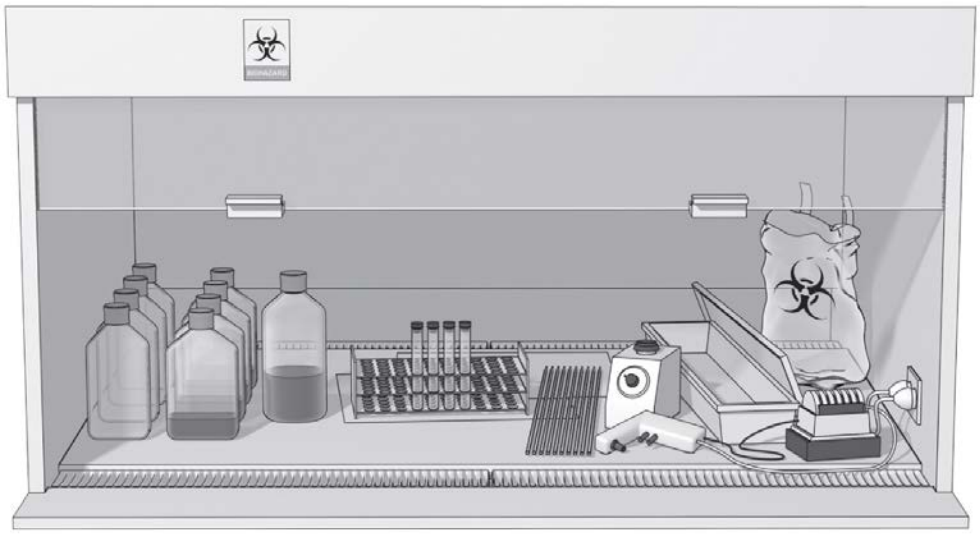
- ✓ The magnehelic gauge should be checked regularly. This gauge will normally run at a relatively fixed value. When it deviates significantly, the cabinet should not be used until the cause of the deviation has been identified and fixed.
- ✓ Personnel should understand how the BSC works.
- ✓ Personnel should be familiar with the safe and effective use of any UV lamps inside the BSC and use appropriate precautions to avoid UV-related injuries.

NOTE: The NIH, CDC, NSF/ANSI, and the American Biological Safety Association all agree that UV lamps are not recommended nor are they necessary (NSF/ANSI 49 Standard and BMBL 5th edition). If installed, UV lamps must be cleaned weekly to remove any dust and dirt that may block the germicidal effectiveness of the ultraviolet light. The lamps should be checked weekly with a UV meter to ensure that the appropriate intensity of UV light is being emitted. UV lamps must be turned off when the room is occupied to protect eyes and skin from UV exposure, which can burn the cornea and cause skin cancer. If the cabinet has a sliding sash, close the sash when operating the UV lamp.

- ✓ The BSC's protective airflow pattern should not be disrupted. Rapid arm movement, nearby workers, and open laboratory doors may disrupt the airflow pattern and reduce the cabinet's effectiveness.
- ✓ Work and the necessary materials should be planned to minimize the need to exit and reenter the work space.

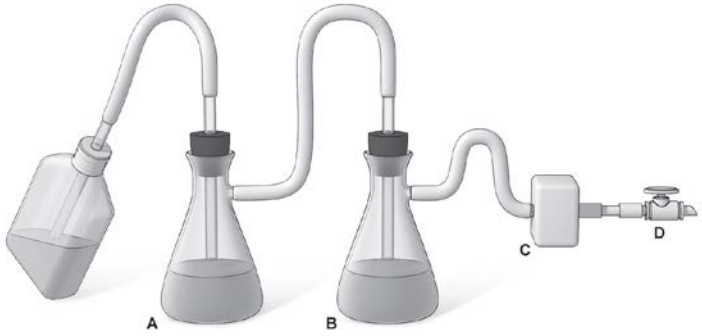
- ✓ Accumulation of materials in the BSC work volume should be minimized to reduce turbulence and ensure proper laminar air flow.
- ✓ The BSC should be left running whenever the cabinet is in use.
- ✓ Proper disinfectants that avoid damaging the cabinet's interior should be used.
- ✓ Work surface should be wiped with 70% alcohol before use. Each item needed for the planned procedures should be wiped off and placed in the cabinet.
- ✓ After the work space is set up, the BSC should run for at least 5 minutes to allow for stabilization of air flow before any procedures are begun.
- ✓ If a piece of equipment, such as a centrifuge or blender, will create air turbulence in the BSC, it should be placed in the back one-third of the cabinet. All other work should be stopped while this equipment is operating.
- ✓ Open flames should be avoided in the work space because they create air flow turbulence that may compromise sterility. In addition, the heat buildup may damage the HEPA filters. If a flame is necessary, a bacti-cinerator should be used.
- ✓ A pan with disinfectant and/or a sharps container should be placed inside the BSC for pipette/sharps disposal. Vertical pipette discard canisters on the floor outside the cabinet should be avoided.
- ✓ Contaminated and clean items should be segregated, and personnel should work from "clean to dirty." The biohazardous waste collection bag should be in a rigid container. Do not block air flow into the front and rear exhaust grilles.

Figure 1. A typical layout for working "clean to dirty" within a Class II BSC. Clean cultures (left) can be inoculated (center); contaminated pipettes can be discarded in the shallow pan and other contaminated materials can be placed in the biohazard bag (right). This arrangement is reversed for left-handed persons.
(Source: Biosafety in Microbiological and Biomedical Laboratories 5th Edition)



- ✓ Move arms slowly when removing items from or introducing items into the cabinet work volume.
- ✓ Protect the facility vacuum system from biohazards by using dual aspirator flasks in series (A & B) and placing an in-line hydrophobic HEPA filter (C) between the vacuum trap and the source valve in the cabinet:

Figure 2. A method to protect a house vacuum system during aspiration of infectious fluids
(Source: Biosafety in Microbiological and Biomedical Laboratories 5th Edition)



NOTE: Office of Safety requires that the flasks are placed in a secondary container, such as a Nalgene tub.

- ✓ All spills in the cabinet should be cleaned immediately. Work should not resume for 20 minutes.
- ✓ When work is complete, all materials should be removed from the BSC and all interior surfaces should be wiped with 70% alcohol, or other appropriate disinfectants.
- ✓ Laboratory coat and gloves must be removed and hands thoroughly washed before leaving laboratory.

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

C. Certification of BSCs

Certification is a series of performance tests on the BSC to confirm that it will provide the user and experimental material the protection for which it is designed. The air flows, filters, and cabinet integrity are checked to ensure that the cabinet meets minimum performance standards. A BSC must be ***certified annually*** and after it has been newly installed, moved, or had a filter replaced according to NSF requirements and UND Biological Safety Cabinet Policy (http://und.edu/finance-operations/_files/docs/6-25-biological-safety-cabinet.pdf). A NSF certified technician does the annual certification of the BSCs at UND. For further information, contact Office of Safety at 777-3341. BSC's that are potentially contaminated with infectious agents may require decontamination. BSC decontamination (using the paraformaldehyde gas production process) is also provided by an outside vendor and needs to be done:

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

D. Animal Hazards and Exposures

Good housekeeping practices and sanitation are essential to reducing the risk of physical hazard injuries. It is important to keep work surfaces clean and clear of obstructions, waste, and other materials. All boxes, hoses, or bags of bedding material should be routinely removed from the work area. Mop floors and clean work surfaces with the appropriate cleaning and disinfectant solutions. Keep in mind that poor housekeeping is unprofessional and will increase the risk of accidents and injuries.

Bites and Scratches

The risk of animal bites and scratches is associated with handling of animals and is best avoided by proper handling techniques and wearing appropriate PPE. Knowledge of animal behavior and how animals respond to their immediate physical environment is important in reducing risk of injury to the individual and the animal. Animals respond to sights, sounds, and smells as people do, but they also may hear, smell, and react to things

that people do not detect. For example, if an animal hears a high-pitched sound, it may become frightened and react defensively. Many animals have a flight zone, and, if approached by another animal or the handler, the affected animal may try to escape. Unsuccessful escape may cause the animal to act aggressively. Of course, inappropriate handling of an animal can cause discomfort, pain, and distress and provoke an animal to bite or scratch. Animal bites and scratches that cause minor skin damage are sometimes disregarded by animal workers who are unfamiliar with the number of diseases that can be spread by such injuries. Even minor bites and/or scratches can result in infections and illnesses if they are not properly treated. Scrapes and injuries from contaminated equipment associated with animal care and housing, such as cages, can be as great a risk as direct animal contact and should be addressed similarly. Most animals used in research are bred specifically for that purpose and do not have the potential for transmitting the kinds of pathogenic organisms that those in the wild do; however, there are some illnesses and infections that can be passed from animals to people (i.e., zoonosis). With research animals, biological hazards are of most concern when the animals are naturally infected or if animals are infected with bacteria, virus or human cells (e.g., tumorigenic cell lines) as part of the experimental work. Under these conditions and when doing field research with wild species, it is of critical importance that appropriate PPE and other appropriate protective measures be used to prevent infection. The most important step to prevent infection following any bite, scratch (or puncture from sharps exposure) is to immediately and thoroughly wash the injury with soap and water. Inform a supervisor and record the injury to the Office of Safety using the UND incident reporting form (https://und.edu/public-safety/_files/docs/incident-reporting-form.pdf). Contact the UND Occupational Health provider or Licensed Healthcare provider for medical consultation or treatment.

Physical Hazards

Sharps such as needles, broken glass, syringes, pipettes, and scalpels are all commonly found in animal facilities and laboratories and present a physical hazard. Use extra care to avoid inadvertent contact and injury. Needlestick injuries represent substantial risk of becoming infected especially when injecting animals with microbial agents or drawing blood. The animal facility should have puncture-resistant and leak-proof containers for disposal of sharps. To prevent needle sticks, it is critical to always place used needles directly into the sharps container without recapping or attempting to bend, shear, break, or remove the needle from the syringe. Animal care operations involve a number of activities that can cause physical stress when handling and moving heavy loads. The use of proper lifting techniques can help prevent back and shoulder injuries when moving cages, bags of feed and bedding, pieces of equipment, and supplies. Poor physical fitness, obesity, poor posture, smoking, and medical/physical deficiencies are personal factors that may contribute to back pain. When lifting heavy loads, every attempt should be made to avoid sudden movements and use a two-handed lifting technique. Keep your back straight, feet positioned apart with one slightly ahead of the other, and knees bent as the lift is completed. Reduce loads where possible and get help when lifting awkward loads or those that cannot be handled safely by one person.

Chemical Hazards

Personnel involved in the care and use of research animals must be familiar with the chemical hazards associated with the animal care and laboratory environment. Chemical properties may include flammability, corrosiveness, reactivity, or the potential to be explosive. Potentially hazardous chemicals used in animal laboratories include solvents (e.g., xylene, acetone, dimethyl sulfoxide), acids (hydrochloric, sulfuric), bases (e.g., sodium hydroxide, quaternary disinfectants), fixatives (e.g., formaldehyde, osmium tetroxide), sterilants (e.g., peracetic acid, chlorine dioxide, peroxides, gluteraldehyde), and anesthetics (e.g., isoflurane, tribromoethanol, methane sulfonate, nitrous oxide, urethane, barbiturates). Each chemical product should be handled carefully using the label directions and recommended PPE in accordance with University guidelines and lab training. Safety Data Sheets (SDS) are also available in each animal facility. These provide additional

information on the hazards and precautions related to a chemical's use. Users must be certain that they understand the proper use of the chemical material before they use it.

Animal Allergies

Allergic reaction to animals is among the most common conditions that adversely affects worker health. The estimated prevalence of allergic symptoms among workers exposed to animals is from 10% to 40%. Workers who are continually exposed to animal allergens tend to have progressively more frequent and severe symptoms, and an estimated 10% develop asthma. Hence, it is critical that all workers seek to minimize their exposure to animal allergens. Additionally, once animal allergy develops, the affected worker should minimize any additional allergen exposure to prevent progression of allergy symptoms. Allergy is most often manifested by nasal symptoms (e.g., allergic rhinitis), itchy eyes (e.g., allergic conjunctivitis), and rashes (e.g., contact urticaria, atopy). Symptoms usually evolve over a period of 1-2 years and may lead to acute anaphylaxis in a small number of patients. In rodents, the allergen protein is of urinary origin and in rabbits it is contained in the fur, dander, and, to a lesser degree, the saliva and urine. In Guinea pigs, urine is the main allergen with dander, fur, and saliva contributing. Exposure to birds can cause rhinitis and asthma symptoms. Multiple bird proteins have been identified as allergens and can be found in serum and fecal droppings that contain serum. Fish proteins can be an inhalation allergen for those who are sensitized. Prudent efforts to prevent allergen exposure and reduce the frequency of sensitization in animal workers require strict work practices and consistent use of PPE. Housing animals in filter-top cages, working in well-ventilated areas, and using ventilated hoods for soiled bedding disposal will minimize exposure to animal allergens. The work area must be maintained clean to prevent inhalant and contact exposure. Procedures should be adopted that minimize release of airborne materials, including bedding dust and antibiotic aerosols, and the contamination of hands, arms, body, and face. Workers should adopt the use of PPE during each and every animal contact or allergen exposure. Wearing PPE "just some of the time" will not prevent exposure. Of particular importance is wearing a facemask to reduce inhalation and hand-to-face spread of allergens and covering all exposed skin (e.g., gloves, lab coat, sleeve protectors, and hair cover) to prevent allergen contact. It is also important that once animal procedures are complete, all contaminated PPE and clothing are removed and properly disposed of to prevent repeated exposure while performing subsequent duties. Supervisors or Office of Safety can provide further information and access to approved PPE devices.

All staff, faculty, visiting researchers, and students who have direct contact with animals must enroll in the University of North Dakota's Occupational Health Plan (http://und.edu/finance-operations/_files/docs/6-28-occupational-health-plan.pdf. Enrollment is initiated by the individual reviewing the Occupational Health Plan and completing the Occupational Health Risk Assessment Questionnaire. Completion of the form will be recorded by the Office of Safety and Center for Biomedical Research (CBR) offices. Review of the program and completion of the form must occur before the individual will be provided access to the animal facility. Personnel also receive training by the attending veterinarian in biomethodology and safe handling techniques for those animals with which they will have contact. All research involving the care and handling of animals is reviewed and approved by the Institutional Animal Care and Use Committee (IACUC). Hazards associated with animal exposure are addressed through this committee. IACUC protocols forms must to be completed and submitted to IACUC. The necessary forms can be obtained by contacting the Research Development and Compliance (rdc@mail.und.nodak.edu).

Latex Gloves and Related Allergies

Allergic reactions to natural rubber latex have been increasing since 1987, when the CDC recommended the use of universal precautions to protect against potentially infectious materials, bloodborne pathogens, and HIV. Increased glove demand also resulted in higher levels of allergens due to changes in the manufacturing process.

In addition to skin contact with the latex allergens, inhalation is another potential route of exposure. Latex proteins may be released into the air along with the powders used to lubricate the interior of the glove.
In June 1997, the National Institute of Occupational Safety and Health (NIOSH) issued an alert, "Preventing Allergic Reactions to Latex in the Workplace" (publication number DHHS (NIOSH) 97-135). NIOSH studies indicate that 8-12% of healthcare workers regularly exposed to latex are sensitized, compared to 1-6% of the general population. Latex exposure symptoms include skin rash and inflammation, respiratory irritation, asthma, and shock. The amount of exposure needed to sensitize an individual to natural rubber latex is not known, but when exposures are reduced, sensitization decreases.

NIOSH recommends the following actions to reduce exposure to latex:

- ✓ If latex gloves must be used, choose reduced-protein, powder-free latex gloves.
- ✓ Whenever possible, substitute another glove material.
- ✓ Wash hands with mild soap and water after removing latex gloves

When using antibiotic materials, procedures should be adopted that minimize release of airborne materials and skin contamination. Of particular concern are releases of penicillin-type (or other) antibiotics during syringe-loading from multi-dose vials. Persons who have had previous exposures and have developed sensitivity can quickly go into anaphylactic shock after inhaling a mist of antibiotic material. Be sure to handle these materials with caution and according to use directions. Use and caution inserts for each antibiotic are provided in the product packaging and should be read and understood prior to use. Investigators inexperienced in conducting these types of experiments should seek help in designing their experiments from individuals who are experienced in this special work.

VII. EMERGENCY RESPONSE PROCEDURES

A. Decontamination

Decontamination is a process or treatment that renders an instrument or environmental surface safe to handle. A decontamination procedure can be as simple as clean-up with detergent and water or as thorough as sterilization. Sterilization and disinfection are two ways to address microbial contamination.

- ✓ Sterilization is the use of physical or chemical processes to destroy all viable forms of microbial life, such as bacterial spores.
- ✓ Disinfection is a chemical or physical treatment that destroys the most resistant vegetative microbes or viruses, but not the spores, in or on inanimate surfaces. Effectiveness is influenced by a number of factors, including the type and number of organisms, amount of organic matter, the object being disinfected, the disinfectant being used, concentration, temperature, and exposure time.
- ✓ Antisepsis is the application of a liquid antimicrobial to skin or other living tissue to inhibit or destroy microorganisms. Examples include hand washing with germicidal solutions or swabbing skin with alcohol before an injection.

Sterilization, disinfection, and antisepsis are all forms of decontamination.

When to Decontaminate

In most UND laboratories, it is recommended that decontamination be accomplished by steam heat sterilization in an autoclave or by surface application of or placement in a chemical disinfectant solution, such as 1:10 bleach solution or an EPA-registered disinfectant and applied per manufacturer instructions. All material and equipment contaminated with or containing potentially biohazards should be decontaminated:

- ✓ Upon completion of procedures involving the use of biohazardous material;
- ✓ In the event of spills of biohazards;
- ✓ Before being washed, stored, or discarded; and
- ✓ At least daily

Autoclave Use

Autoclaving (saturated steam under pressure of approximately 15 pounds per square inch (psi) to achieve a chamber temperature of at least 121°C [250˚F] for a designated time) is the preferred and most convenient method to rapidly destroy all forms of microbial life. However, to do this, the autoclave process must reach proper temperature, pressure, and time, and also prevent the entrapment of air in the bag or container of treated material. The following procedures should be followed during autoclave use:

- ✓ Material to be sterilized must come into contact with steam.
- ✓ Bags or containers should be left open during autoclaving or water (~200 ml) should be added to sealed bags to generate steam.
- ✓ Heat indicator tape should be used outside the bag or container with each autoclave load to indicate that sterilization has been completed.
- ✓ Autoclave sterility monitoring should be conducted on a regular basis using biological indicators (such as *B. stearothermophilus* spore strips) placed among treated materials and at locations throughout the autoclave. The spores, which are more resistant to heat than most other biological materials, provide validation of general microbial destruction when they are effectively inactivated by autoclave operation (typically 250˚F for 30 minutes).
  Note: The type and frequency of sterility monitoring varies and is based on usage, cycle type, and autoclave type. Contact Office of Safety (777-3341) for more information.

Chemical Disinfectant Use

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

Liquid Decontamination

- ✓ Add liquid chlorine bleach to provide a final 1:10 dilution (made fresh or within one week of use);
- ✓ Let stand at least 20 minutes; and
- ✓ Discard the solution appropriately.

NOTE: No waste down the drain unless approval has been obtained from the Office of Safety.

Surface Decontamination

- ✓ Wipe with 1:10 dilution of chlorine bleach; or
- ✓ Wipe with iodophor disinfectant (per label concentration); or
- ✓ Wipe with another EPA registered disinfectant following manufacturer guidelines.

See Appendix C for additional information on disinfectants.

An understanding of the resistance of organisms to chemical germicides should also be considered when selecting the disinfection methods and disinfectants. Table 1 shows the resistance of selected organisms to decontamination, from most to least resistant.

Table. 1
Descending Order of Organism Resistance to Germicidal Chemicals
Source: BMBL, fifth edition

Bacterial Spores *Bacillus subtilis, Clostridium sporogenes*
▼
Mycobacteria *Mycobacterium tuberculosis* var. *bovis*, Nontuberculous mycobacteria
▼
Nonlipid or Small Viruses Poliovirus, Coxsackievirus, Rhinovirus
▼
Fungi *Trichophyton* spp., *Cryptococcus* spp., *Candida* spp.
▼
Vegetative Bacteria *Pseudomonas aeruginosa, Staphylococcus aureus, Salmonella choleraesuis*, Enterococci
▼
Lipid or Medium-size Viruses Herpes simplex virus, CMV, Respiratory syncytial virus, HBV, HCV, HIV, Hantavirus, Ebola virus

NOTE: There are exceptions to this list. *Pseudomonas* spp. are sensitive to high-level disinfectants, but if they grow in water and form biofilms on surfaces, the protected cells can approach the resistance of bacterial spores to the same disinfectant. The same is true for resistance to glutaraldehyde by some nontuberculous mycobacteria, some fungal ascospores of *Microascus cinereus* and *Cheatomium globosum*, and the pink-pigmented *Methylobacterium.* Prions are also resistant to most liquid chemical germicides.

Decontamination in Animal Facilities

In UND animal facilities, decontamination is accomplished by use of the provided disinfectants applied to surfaces and equipment; by chemical sterilants; by steam heat sterilization in an autoclave (particularly for surgical equipment and for bedding, animal feed, and other materials used in the barrier animal facility); by gas sterilization; or by use of the cage-washing machine. All animal users should be familiar with the safe and proper use of all chemical decontamination materials and equipment that they need to use as part of their animal lab responsibilities.

B. Spills of Biohazards

UND does not have a centralized biological spill response team. Therefore, each laboratory working with potentially hazardous biological material must be prepared and trained to handle its own biological spills. Office of Safety is available for assistance if necessary.

The quantities of biohazardous materials should be limited so they can be easily contained, cleaned, or destroyed. If respiratory protection is required, the UND Respiratory Protection Program must be followed. A simple spill kit with the following supplies should be available and used by trained personnel:

- ✓ Bleach or other EPA-registered disinfectant
- ✓ Biohazard bag
- ✓ Disposable lab coat
- ✓ Disposable shoe covers
- ✓ Hand sanitizing wipes
- ✓ Nitrile gloves (4 pair)
- ✓ Mini brush and dustpan (or something to scoop spilled materials)
- ✓ Paper towels
- ✓ Safety goggles
- ✓ Tong or forceps to pick up broken glass
- ✓ Spray bottle (to make fresh bleach solution)
- ✓ "Biohazard Spill" sign

The following procedures are provided as guideline to biohazardous spill cleanup and will need to be modified for specific situations. As with emergency situation, stay calm and proceed with common sense. If the spill requires assistance contact the Office of Safety at 777-3341. If the spill outgrows the resources in the laboratory dial 911 to request assistance.

Spills inside a Biological Safety Cabinet

1. Remain calm and secure research samples.
2. Alert the other laboratory employees of the spill.
3. Leave the cabinet turned on.
4. Evacuate the room for at least 30 min. Close door. Discard potentially contaminated PPE and remove any contaminated clothing. Wash hands thoroughly.
5. Notify PI.
6. Don fresh PPE: lab coat or gown, gloves, mask, eye protection. While wearing gloves, spray or wipe cabinet walls, work surfaces and equipment with disinfectant equivalent to 1:10 bleach solution. If

necessary, flood the work surface, as well as drain-pans and catch basins below the work surface, with disinfectant for a contact time of at least 20 minutes.
7. Soak up disinfectant and spill with paper towels.
8. Pick up any pieces of broken glass with forceps or tongs and place in sharps container. Never use hands.
9. Drain catch basin into a container. Lift front exhaust grill and tray and wipe all surfaces. Ensure that no paper towels or solid debris are blown into the area beneath the grill.
10. Dispose cleanup materials in the biohazard waste container.
11. Wash hands and any exposed surfaces thoroughly after the cleanup procedure.
12. Report the spill to the laboratory's Principal Investigator and the Office of Safety (777-3341) if there was a potential for any material escaping the Biological Safety Cabinet.
13. Resume work if deemed safe by supervisor/manager.

Small Spill (<500 mL) Outside a Biological Safety Cabinet

1. Remain calm and make note of whether your person has been contaminated.
2. Alert other laboratory employees in the area and block off the area.
3. Evacuate the room for at least 30 min. Close door. Discard potentially contaminated PPE and remove any contaminated clothing. Wash hands thoroughly.
4. Notify PI.
5. Don fresh PPE: lab coat or gown, gloves, mask, eye protection.
6. Wearing gloves, safety glasses, and a lab coat, cover the spill with paper towels and gently apply disinfectant, proceeding from the outer edge of the spill to its center. Leave in place for 20 minutes.
7. Pick up the towels and discard into a biohazard container.
8. Pick up any pieces of broken glass with forceps or tongs and place in sharps container. Never use hands.
9. Re-wipe the spill area with disinfectant and thoroughly wash hands after glove removal.
10. Report the spill to the laboratory's principal investigator and/or to Office of Safety (777-3341) immediately.
11. Resume work if deemed safe by supervisor/manager.

Large Spill (>500 ml) Outside a Biological Safety Cabinet

1. Remain calm and hold your breath and leave the room immediately if no other workers are present. Otherwise:
   - Warn others to stay out of the spill area to prevent spread of contamination.
2. Post a sign stating: "DO NOT ENTER, BIOHAZARD SPILL, contact (name and phone #) for information" and block off area as possible.
3. Remove any contaminated clothing, ensuring that clothing is not pulled over the face, and put into a biohazard bag for later autoclaving.
4. Wash hands, eyes and exposed skin.
5. Notify the principal investigator, supervisor, and Office of Safety immediately.
6. Wait 30 minutes before re-entering the contaminated area to allow for dissipation of aerosols.
7. Meanwhile, put on protective clothing (lab coat, gloves and, if indicated, respirator, eye protection, shoe covers) and assemble clean-up materials.
8. Cover the spill with paper towels and gently apply disinfectant, proceeding from the outer edge of the spill to its center. Leave in place for 20 minutes.
9. Collect all treated material and discard in a biohazard container.
10. Pick up any broken glass with forceps and place them into a sharps container. Never use hands
11. Re-wipe the spill area with disinfectant and wash hands thoroughly at completion of clean-up.

Spill of Biohazards in a Centrifuge

A single centrifuge spill or release can lead to multiple infections in a laboratory. Aerosols are created when fluid escapes from the rotor or cup while the centrifuge is operating at high speed. Therefore, whenever opening a centrifuge, it must be performed slowly.

Unsealed Buckets

1. If a centrifuge tube breaks while the centrifuge is running, turn off motor. Allow the machine to be at rest for 30 minutes before opening.
2. Unplug centrifuge before initiating clean up.
3. Put on two pairs of nitrile gloves and other PPE before proceeding with clean up.
4. Flood centrifuge bowl with a disinfectant (e.g., 10% bleach solution or other EPA registered disinfectant).
5. Place paper towels soaked in a disinfectant over the entire spill area. Allow 20 minutes' contact time.
6. Remove broken tubes and glass fragments using tongs or forceps. Place fragments in a sharps container for autoclaving and disposal as infectious waste.
7. Remove buckets, trunnions, and rotor and place in disinfectant for 20 minutes or autoclave.
8. Unbroken, capped tubes may be placed in disinfectant and recovered after 20 minutes' contact time or autoclaved.
9. Remove remaining disinfectant soaked materials from centrifuge bowl and discard as infectious waste.
10. Place paper towels soaked in a disinfectant in the centrifuge bowl and allow it to soak overnight, wipe down again with disinfectant, wash with water and dry. Discard disinfectant soaked materials as infectious waste. **NOTE:** Household bleach is a corrosive. Use caution when immersing or having metal components in contact with bleach (sodium hypochlorite) for extended periods of time.
11. Remove protective clothing used during cleanup and place in a biohazard bag for autoclaving. Wash hands whenever gloves are removed.
12. Notify principal investigator, supervisor, and/or Office of Safety.

Sealed Buckets (Safety Cups)

1. If breakage is suspected, remove the sealed bucket to a biological safety cabinet before opening.
2. If breakage occurred, replace the cap on the safety cup loosely and autoclave.
3. Notify principal investigator, supervisor, and Office of Safety if there was a potential for any material escaping the centrifuge.

Biohazardous Radioactive Material Spills

Procedures for spill cleanup of a radioactive biological material require emergency procedures which protect the person from exposure to the radiochemical while disinfecting the biological material.

1. Avoid inhaling airborne material, notify other room occupants, and quickly leave the area.
2. Remove all contaminated clothing by turning exposed areas inward. Place in a biohazard bag.
3. Wash all exposed skin areas with a disinfectant soap. Rinse for a minimum of 15 minutes.
4. Inform the laboratory supervisor.
5. Post a spill sign and do not reenter the lab for at least 30 minutes.
6. Contact the Radiation Safety Officer at 777-5931, to confirm safe entry into the laboratory.
7. Utilize appropriate protective clothing and reenter the spill area. The use of respirators requires special training. Call the Office of Safety if a respirator trained individual is required but not available for spill cleanup.
8. Cover the area with disinfectant soaked towels. Pour the disinfectant around the perimeter of the spill area. As the spill becomes diluted with disinfectant, increase the concentration of the disinfectant. Allow 20 minutes for disinfection. Please note that the use of bleach on iodinated material may cause the

release of radioiodine gas. An alternative such as, phenolic compounds or an iodophor should be used when radioactive iodine has been spilled.

9. Collect any broken glass with forceps and place in an appropriate broken glass collection container. To clean splashed material, spray with disinfectant solution and wipe clean or saturate a paper towel with disinfectant solution and wipe clean.
10. PPE must be disinfected with bleach solution and disposed of as radioactive waste. Place the used PPE on absorbent paper. Spray the PPE with 10% bleach solution and allow a 20 minutes' contact time.
11. Place all decontaminated waste materials in an approved container for radiation and label appropriately.
12. Wash hands and potentially exposed areas with a disinfectant.
13. Monitor laboratory occupants for contamination of radioactive materials.
14. Decontaminate under the advisement of the Radiation Safety Officer.
15. All contaminated persons must seek medical assistance after decontamination procedures have been completed.
16. Monitor the area for residual activity.

C. Reporting Exposures

In the event of an exposure to a biohazard:

1. Report to an Occupational Health Provider or Licensed Medical Provider.
2. Complete an Accident/Illness Report Form and submit to Office of Safety within 24 hours of incident. **NOTE:** The incident reporting form can be found on the Office of Safety website: http://und.edu/finance-operations/office-of-safety/_files/docs/incident-reporting-form.pdf
3. For all accidents related to biohazards submit an IBC adverse event reporting form (http://und.edu/research/resources/_files/docs/ibc-adverse-event-report.pdf) within 24 hours of incident. **NOTE:** This form is different from the Incident reporting form.
4. If exposure or incident occurs with Synthetic/Recombinant Nucleic Acid, work with the principal investigator, supervisor, and Biological Safety Officer to report accident to the NIH Office of Biotechnology Activities as required by the *NIH Guidelines* (http://www.osp.od.nih.gov/office-biotechnology-activities/biosafety/institutional-biosafety-committees/incident-reporting).

D. Fires

Laboratory workers must know building evacuation routes in case of fire. It is the laboratory supervisor's responsibility to provide this information. In the event of a fire, immediate evacuation is essential. On the way out of the building remember these safety precautions:

- ✓ Never enter a room containing a fire.
- ✓ Never enter a room that is smoke filled.
- ✓ Never enter a room in which the top half of the door is hot to the touch.
- ✓ Never use the elevator.

Small Fires

- ✓ Pull the fire alarm and call the UND Campus Operations Call Center at 777-2591 to report the fire.
- ✓ Alert people in the area to evacuate. Assist those individuals with disabilities.
- ✓ Turn off gas main.
- ✓ If you have been trained to use a fire extinguisher, do so while maintaining a clear exit path behind you.
- ✓ Operate the extinguisher using the P-A-S-S method:
  - P – Pull the pin located on the extinguishers handle.
  - A – Aim the nozzle at the base of the fire.
  - S – Squeeze or press the handles together.
  - S – Sweep from side to side at the base of the fire until it is out.

Large Fires

- ✓ Pull the fire alarm, when in a safe area, call Campus Operations Call Center at 777-2591.
- ✓ Alert people in the area to evacuate. Assist those individuals with disabilities.
- ✓ Turn off gas mains, only if time permits.
- ✓ Close the doors to confine the fire.
- ✓ Move to a designated assembly area away from and upwind from the building.
- ✓ Persons having knowledge about the incident and location must provide this information to emergency response personnel.

E. Weather Alerts

- ✓ When a severe weather notification is announced from the UND-ALERT system, immediately request all persons in the laboratory to turn off any gases, hotplates, and pressure reactive experiments.
- ✓ Immediately leave the area in an orderly manner. Use the innermost stairway and take cover in the lowest most internal compartment of the building.

VIII. GENERAL LABORATORY SAFETY GUIDELINES

A. Food and Beverages in the Laboratory

In order to reduce potential exposures and to ensure compliance with prudent laboratory operations, regulations, and other best management practices, UND prohibits the storage and consumption of food and drink in all designated laboratory space. The only exception is for food and beverages used in research and teaching projects. These materials must be labeled, "Not for Human Consumption."

In order to prevent potential exposure to hazardous materials:

- ✓ Do not eat, drink, smoke, chew gum, apply cosmetics, or take medicine in laboratories where hazardous materials are handled or stored.
- ✓ Do not store food, beverages, cups, or other drinking and eating utensils in areas where hazardous materials are handled or stored.
- ✓ Do not use glassware for laboratory operations to prepare or consume food or beverages.
- ✓ Do not use laboratory refrigerators, ice chests, cold rooms, and ovens for food storage or preparation.
- ✓ Do not use laboratory water sources or deionized laboratory water for drinking water.

B. Protective Clothing beyond the Laboratory

The improper use or lack of protective clothing in a laboratory can lead to chemical burns, biological exposures, or other potential dangers. To help reduce the risk of exposure, personnel in UND laboratories are required to wear gloves, safety glasses (when required by experimental protocol), lab coats and other personal protective clothing. However, in public areas, such as hallways and lounges, wearing personal protective clothing is not recommended. This is because contaminated clothing may present a hazard, and the perception of contaminated protective clothing in a public area may project a careless image to both colleagues and visitors. Hazardous materials should be transported from place to place on a cart, in a clean secondary container, or in a bottle carrier with secure handles. When this is not an option, personnel should use a clean, ungloved hand to touch common surfaces and a gloved hand to carry the items: the one-glove rule. **Alternatively, the material should be packaged so the outer container may be transported without the need for personal protective equipment. This is what the Office of Safety and the Institutional Biosafety Committee recommends.** Protective gloves should never come into contact with door handles, elevator buttons, telephones, lavatory faucets, vending machines, bottled water dispensers, ice-making machines, or other surfaces outside the laboratory. Also, please be aware that strict federal and state regulations address the transport of hazardous (e.g., biological, chemical, radiological) materials on public roads. For the sake of safety, appearances, and courtesy, personnel are asked not to wear contaminated, stained, or potentially contaminated lab coats and other research clothing and equipment in any public area, especially dining areas, lounges, auditoriums, conference rooms, or other non-hazardous areas.

C. Security

Laboratory security is an integral part of an effective safety program. Follow these steps to ensure a secure working environment in your laboratory:

- ✓ Keep laboratory doors closed and locked when unoccupied.
- ✓ Keep stocks of organisms and hazardous chemicals locked when the laboratory is unoccupied.
- ✓ Keep an accurate record of chemicals, stocks, cultures, project materials, growth media, and those items that support project activities.
- ✓ Notify UND police (777-3491) if materials are damaged or missing from laboratories.
- ✓ Inspect all packages arriving into the laboratory.
- ✓ When research is completed for the day, ensure that chemicals and biological materials have been stored properly and securely.
- ✓ Decontaminate materials and work surfaces after completing work and at least daily.

- ✓ Turn off equipment, flames, steam supply, and electrical appliances after completing work.
- ✓ Ask strangers (someone you do not recognize as a co-worker or support staff person) to exit the room if they are not authorized to be there.
- ✓ Discuss other security-specific requirements with your supervisor and colleagues.

D. Laundering Laboratory Clothing

Laboratory coats/gowns and contaminated clothing or clothing suspected to be contaminated with chemicals or biohazards are never be taken home or to a public laundry facility.

UND Laundry Facility

UND has a laundry facility on campus. Follow departmental procedures for cleaning mild to moderately contaminated clothing. The UND laundry facility utilizes the following standard operating procedure for cleaning contaminated items:

- ✓ Use gloves and gown (additional PPE if determined necessary)
- ✓ Wash at 150 degrees Fahrenheit (hot)
- ✓ Use bleach if uncertain of the temperature
- ✓ Dry at 200 degrees Fahrenheit (hot)
- ✓ Discard any blood or OPIM-contaminated plastic bags
- ✓ Laundry is to be handled only by trained employees

Professional Laundering Services

Where UND laundry facility is not available, contaminated clothing must be laundered by a professional laundry service. Laboratory managers shall ensure that all laundry sent off-site is containerized in leak-proof bags or boxes marked with the biohazard symbol and shall advise the vendor that the laundry is contaminated with blood and/or potentially infectious bodily fluids for textiles that are mildly contaminated.

Laundering of Personal Clothing

Clothing contaminated with biohazardous material must be autoclaved prior to laundering at home. Documentation of effective autoclaving must be maintained.
NOTE: Personal laundering is not acceptable for clothing contaminated with chemicals, blood, blood products, or other bodily fluids.

Overtly Contaminated Clothing

Clothing that is overtly contaminated with chemicals must be disposed as hazardous waste. Clothing contaminated with radiological material must be disposed as radiological waste. Clothing that is contaminated with blood, blood products, or other bodily fluids must be removed and containerized in leak-proof bags or boxes at the location where it was used. Containers or bags must be marked with the biohazard symbol

E. Working Alone

All faculty, staff, students, and visitors working in an area (e.g., laboratory, animal holding room) where hazardous conditions exist should have knowledge of the following:

- ✓ Emergency Contacts
- ✓ Emergency Response Procedures
- ✓ Evacuation Routes
- ✓ First Aid Procedures
- ✓ Health and Safety Training Requirements
- ✓ Personal Protective Equipment Requirements
- ✓ Procedures to Report Unhealthy and Unsafe Conditions

- ✓ Safety Policies and Procedures
- ✓ Spill Response Equipment and Procedures

All personnel working alone‡ in a laboratory where hazardous conditions exist should:

- ✓ Obtain written permission (e.g., e-mail, letter) from the Principal Investigator or Laboratory Supervisor to work alone in the laboratory;
- ✓ Ensure that a means to contact emergency response personnel is available when working alone in the laboratory; and
- ✓ Require that individuals working alone during weekends contact their supervisor before beginning work and upon completion.

NOTE: According to the National Safety Council, the term “alone” means that a person is beyond the visual or auditory range of any other individual for more than a few minutes at a time.

IX. BIOLOGICAL WASTE HANDLING

A. Biohazardous Waste (Regulated Infectious Waste/Medical Waste)

Some wastes associated with biological materials must be disposed of in special ways because they may have been contaminated with infectious organisms or agents. These potentially infectious or biohazardous materials are defined by ND regulations as Regulated Infectious Waste (Chapter 33-20-12 of the North Dakota Administrative Code). These wastes include the following:

- ✓ **Cultures and stocks**: Cultures and stocks of infectious agents and associated biologicals, including cultures from medical and pathological laboratories; cultures and stocks of infectious agents from research and industrial laboratories; wastes from the production of biologicals; discarded live and attenuated vaccines; and culture dishes and devices used to transfer, inoculate, and mix cultures.
- ✓ **Pathological waste:** Human pathological waste, including tissues, organs, and body parts and body fluids that are removed during surgery or autopsy, or other medical procedures, and specimens of body fluids and their containers.
- ✓ **Human blood and blood products**: Liquid waste human blood; products of blood; items saturated or dripping with human blood; or items that were saturated or dripping with human blood that are now caked with dried human blood (including serum, plasma, and other blood components, and their containers).
- ✓ **Sharps:** Sharps that have been used in animal or human patient care or treatment or in medical, research, or industrial laboratories, including hypodermic needles, syringes (with or without the attached needle), Pasteur pipettes, scalpel blades, blood vials, needles with attached tubing, and culture dishes (regardless of presence of infectious agents). Also included are other types of broken or unbroken glassware that were in contact with infectious agents, such as used slides and cover slips.
- ✓ **Animal waste**: Contaminated animal carcasses, body parts, and bedding of animals that were known to have been exposed to infectious agents during research (including research in veterinary hospitals), production of biological, or testing of pharmaceuticals.
- ✓ **Isolation waste:** Biological waste and discarded materials contaminated with blood, excretion, exudates, or secretions from humans who are isolated to protect others from highly communicable diseases, or isolated animals known to be infected with highly communicable diseases.
- ✓ **Unused sharps**: Unused, discarded sharps, hypodermic needles, suture needles, and scalpel blades.

For disposal of these wastes, the lab personnel:

a. Sterilize or disinfect waste materials associated with viral, bacterial or other agents infectious to humans (by autoclave or chemical treatment equivalent to 1:10 bleach solution). Note: Autoclaved waste can be disposed for removal by housekeeping (After autoclaving cross the biohazard symbol or put in a black trash bag)
b. Place all biohazardous wastes, except for sharps, directly into the red bag-lined biohazard boxes.
c. When the biohazard box is filled, seal the bag liner and box and notify Office of Safety for pick-up.
d. Place sharps into labeled sharps containers. When containers are full, submit a waste manifest form to the Office of Safety for pick-up and disposal through a licensed vendor.

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

B. Animal Bedding waste

Animal bedding is bagged by animal care personnel in red biohazard bags and placed in specially provided carts for movement to the autoclave facility. Bags should be filled only to a depth and weight that will allow for

effective tying of the bag by animal facility staff and for ease of handling by one person. For example, several partially-filled bags should be tied and placed in the carts rather than one or two full bags (bag weight should not exceed 50 pounds). This will help to prevent repetitive motion injury to staff and help to prevent bags from being ripped open while being handled. The carts are maintained clean and in sanitary condition by the animal facility staff.

C. Animal Carcasses and Non-regulated biological waste

Freezers are provided in the CBR animal facility for storage of carcasses that have been bagged and sealed. Freezers are cleaned and defrosted as necessary by animal laboratory personnel to keep them in a sanitary condition.

Non-regulated biological waste cannot include animal tissues containing pharmaceuticals or toxins and cannot include animal tissue used in the following:

- In the diagnosis, treatment or immunization of humans or animals
- In research pertaining to the above
- In the production or testing of biologicals. Biologicals are preparations made from living organisms and their products, including vaccines, cultures etc. intended for use in diagnosing, immunizing or treating of humans or animals, or in research pertaining thereto.

All non-regulated biological waste for disposal in the local landfill must be sealed in plastic bags which are then sealed inside cardboard boxes or other sturdy, opaque containers.

Contact the Office of Safety at 777-3341 if you have questions about your waste being non-regulated. The waste should not be placed in a dumpster.

D. Animal Waste from BSL-2 Animal Rooms

Rodents housed in BSL-2 space are considered to be potentially infectious because as part of the research protocol they are infected with Biosafety Level 2 (BSL-2) animal and/or human infectious agents. Animal bedding, carcasses, and tissue are placed in biohazard bags by the research staff. All animal bedding is autoclaved before disposal by animal care staff. Bagged animal carcasses and tissue are placed in the provided CBR storage freezers. These are disposed through a licensed vendor.

Refer to Appendix D for biohazard waste disposal chart.

X. TRANSPORTATION, PACKAGING, AND SHIPPING OF INFECTIOUS AGENTS

A. Definitions

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

The definitions below apply to the packaging and shipping instructions that follow:
Etiologic agent means a viable microorganism or its toxin which causes, or may cause, human disease.

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

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

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

B. Packaging, Transporting, and Shipping

Shipping biological materials is a highly regulated activity. A large number of people will handle or be in proximity to your package as it travels to its destination and all that protects these people from any hazard within the package is the information you provide on or with your package and the packaging itself. To meet International Air Transport Association (IATA) regulations, anyone who ships biological materials must be certified to do so and renew the certification every two years or when regulations change. U.S. Department of Transportation (DOT) hazardous materials shipping training must be obtained every three years, or within 90 days of when regulation revisions are issued.
Regulations that apply to the packaging and shipment of biological materials:

- ✓ U.S. Department of Transportation, 49 CFR Parts 171-180 and amendments
- ✓ U.S. Public Health Service, 42 CFR Part 72, Interstate Shipment of Etiologic Agents
- ✓ U.S. Department of Labor, OSHA, 29 CFR Part 1910.1030, Bloodborne Pathogens
- ✓ IATA, Dangerous Goods Regulations
- ✓ U.S. Postal Service, 39 CFR Part 111, Mailability of Etiologic Agents, Mailability of Sharps and Other Medical Devices, and Publication 52, Acceptance of Hazardous, Restricted or Perishable Matter
- ✓ International Civil Aviation Organization, Technical Instructions for the Safe Transport of Dangerous Goods by Air
- ✓ United Nations, Recommendations of the Committee of Experts on the General DOT Packaging Requirements for Transport of Infectious Substances by Aircraft *(Source: Biosafety in Microbiological and Biomedical Laboratories 5th Edition, Appendix C).*

The DOT packaging's for transporting infectious substances by aircraft are required by domestic and international aircraft carriers, and are the basis for infectious substance packaging's for motor vehicle, railcar, and vessel transport. The following is a summary of each packaging type and related transportation requirements.

C. Shipping of Select Agents

The transferring, packing, and shipping of **select agents and toxins is <u>HIGHLY REGULATED</u>.** No select agent or toxin shall be transferred, packed, or shipped without the express approval from the Responsible Official. Please contact the UND Biological Safety Officer for more information. For materials that are not

Select Agents, each principal investigator must develop procedures for transferring or shipping from the laboratory. The principal investigator must ensure the following:

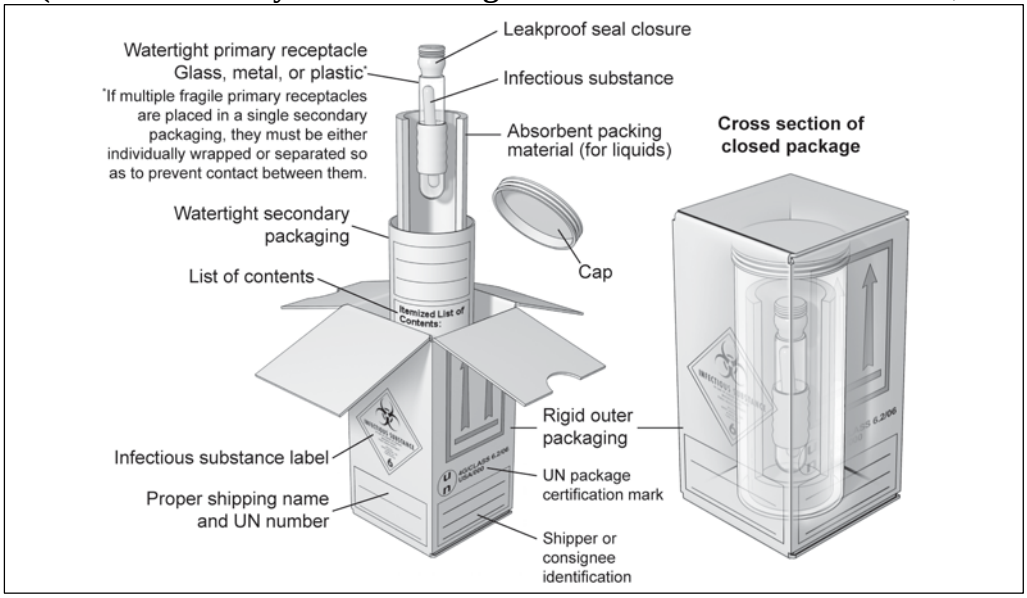
- Personnel who package, handle, and ship non-select agents and biohazardous materials (including import and export) are subject to all applicable training. The Responsible Official must be notified of all select agent transfers; internal or external.
- Standard operating procedures should be in place for all import and export activities.
- Package, label, and transport biohazards in compliance with all applicable local, federal, and international transportation and shipping regulations, including U.S. DOT regulations. Materials that are transported by airline carrier should also comply with packaging and shipping regulations set by the IATA.
- Required permits (e.g., granted by the U.S. Public Health Service, USDA, DOT, U.S. Department of Commerce, and IATA) are obtained before biohazards are prepared for transport.
- Decontaminate contaminated or potentially contaminated materials before they are removed from the laboratory area.
- Avoid hand-carrying biohazards when transferring them to other external facilities. If biohazards are to be hand-carried on common carriers, all applicable packaging, transport, and training regulations should be followed. Develop and follow a protocol for intra-facility transfer (between laboratories on UND campuses) of all biological and biohazards. Contact Office of Safety for assistance.
- Packaging and shipping of biological materials must be completed in a way that ensures the contents will not leak and that the package will arrive in good condition.

D. Shipping of Category A and Category B Substances

Category A Infectious Substance (UN 2814 and UN 2900): Figure 1. A Category A material is an infectious substance that is transported in a form that is capable of causing permanent disability or life-threatening or fatal disease to otherwise healthy humans or animals when exposure to it occurs. An exposure occurs when an infectious substance is released outside of its protective packaging, resulting in physical contact with humans or animals. Category A infectious substance are assigned to identification number “UN 2814” for substances that cause disease in humans or in both humans and animals, or “UN 2900” for substances that cause disease in animals only.

Figure 1 shows an example of the UN standard triple packaging system for materials known or suspected of being a Category A infectious substance. The package consists of a watertight primary receptacle or receptacles; a watertight secondary packaging; for liquid materials, the secondary packaging must contain absorbent material in sufficient quantities to absorb the entire contents of all primary receptacles; and a rigid outer packaging of adequate strength for its capacity, mass, and intended use. Each surface of the external dimension of the packaging must be 100 mm (3.9 inches) or more. The completed package must pass specific performance tests, including a drop test and a water-spray test, and must be capable of withstanding, without leakage, an internal pressure producing a pressure differential of not less than 95 kPa (0.95 bar, 14 psi). The completed package must also be capable of withstanding, without leakage, temperatures in the range of -40ºC to +55ºC (-40ºF to 131ºF). The completed package must be marked “Infectious substances, affecting humans, UN 2814” or “Infectious substances, affecting animals, UN 2900” and labeled with a Division 6.2 (infectious substance) label. In addition, the package must be accompanied by appropriate shipping documentation, including a shipping paper and emergency response information.

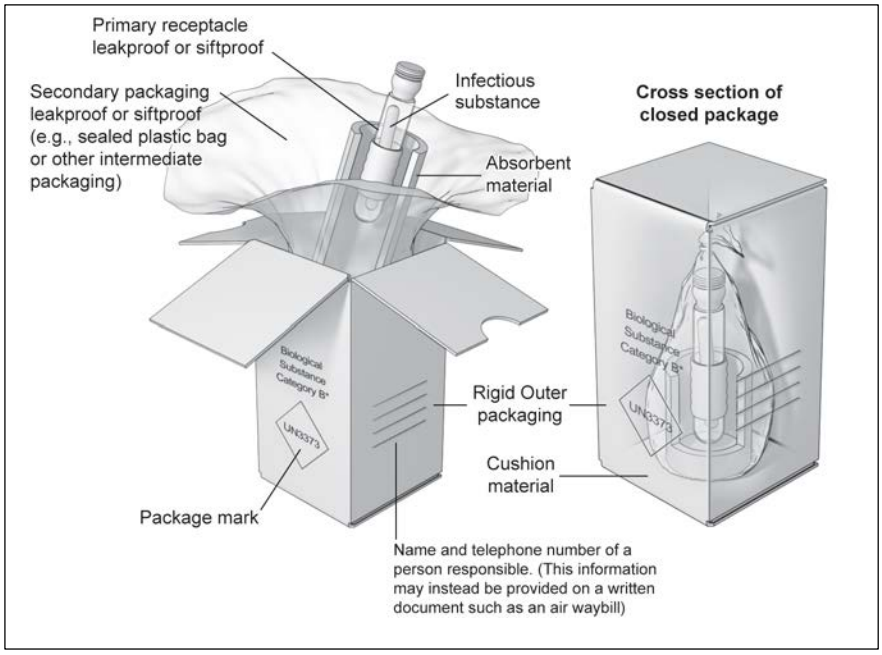
Figure 1. A Category A UN Standard Triple Packaging
(Source: Biosafety in Microbiological and Biomedical Laboratories, 5th Edition)



Biological specimen, Category B (UN 3373): Figure 2. (Previously known as Clinical specimen and Diagnostic Specimen). A Category B infectious substance is one that does not meet the criteria for inclusion in Category A. A Category B infectious substance does not cause permanent disability or life-threatening or fatal disease to humans or animals when exposure to it occurs. The proper shipping name for a Category B infectious substance, "Biological specimen, Category B," is assigned to identification number "UN 3373." The proper shipping names "Diagnostic specimen" and "Clinical specimen" may no longer be used (as of January 1, 2007).

Figure 2 shows an example of the triple packaging system for materials known or suspected of containing a Category B infectious substance. A Category B infectious substance must be placed in a packaging consisting of a leak proof primary receptacle, leak proof secondary packaging, and rigid outer packaging. At least one surface of the outer packaging must have a minimum dimension of 100 mm by 100 mm (3.9 inches). The packaging must be of good quality and strong enough to withstand the shocks and loadings normally encountered during transportation. For liquid materials, the secondary packaging must contain absorbent material in sufficient quantities to absorb the entire contents of all primary receptacles. The primary or secondary packaging must be capable of withstanding, without leakage, an internal pressure producing a pressure differential of 95 kPa. The package must be constructed and closed to prevent any loss of contents that might be caused under normal transportation conditions by vibration or changes in temperature, humidity, or pressure. The completed package must be capable of passing a 1.2-meter (3.9 feet) drop test. The package must be marked with a diamond-shaped marking containing the identification number "UN 3373" and with the proper shipping name "Biological Substance, Category B." In addition, the name, address, and telephone number of a person knowledgeable about the material must be provided on a written document, such as an air waybill, or on the package itself.

Figure 2. A Category B Non-Specification Triple Packaging
(Source: Biosafety in Microbiological and Biomedical Laboratories, 5th Edition)



Packaging Volumes

Volume not exceeding 50 milliliters (ml):

1. Place material in a securely enclosed, watertight primary container (e.g., test tube, vial). Enclose this primary container in a secondary, durable, watertight container. Several primary containers may be enclosed in a single secondary container as long as the total volume of material in all the primary containers enclosed does not exceed 50 ml.
2. Place absorbent non-particulate material (e.g., paper towels, not sawdust or vermiculite) in the spaces at the top, bottom, and sides between the primary and secondary containers. Use enough absorbent material to absorb the entire contents of the primary container(s) in case of breakage or leakage.
3. Enclose each set of primary and secondary containers in an outer shipping container constructed of corrugated fiberboard, cardboard, wood or other material of equal strength. Do not use bags, envelopes, or similar materials.
4. If you package the material with dry ice, see the Packaging with Dry Ice section in this document.

Volume greater than 50 milliliters (ml):

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

Packaging with Dry Ice:

1. If used, place dry ice between the secondary and outside containers.
2. Place shock absorbent material so as to prevent the secondary container from becoming loose inside the outer container as the dry ice sublimates.
3. Use the DOT dry ice label. Guidelines for shipping are available by contacting Office of Safety.

All North American airlines and FedEx, the largest shipper of infectious materials, use the IATA regulation (also referred to as the Dangerous Goods Regulation or DGR) as their standard. Meeting the conditions of this standard will ensure meeting the provisions of the other US regulations. Many biological materials fall into the category of dangerous goods for shipping purposes. All individuals involved in the transport of dangerous goods or the preparation of dangerous goods for transport must be trained to do so properly and safely. If you are in need of shipping biological materials, please contact the Office of Safety at 777-3341 and we will do whatever we can to assist you in this process.
NOTE: Please refer to Biological Material Shipping Manual for more information about shipping procedures at UND (http://und.edu/public-safety/_files/docs/biological-materials-shipping-manual.pdf).

For safe transport of biohazardous agents and materials on campus, these guidelines must be followed:

1. Double contain the items in plastic leak-proof containers within sturdy outer packaging.
2. Include absorbent material within the containers as well as padding to minimize movement of the container(s) within the outer packaging.
3. Wipe the outer container with an appropriate disinfectant before removing it from the laboratory and apply a biohazard sticker if applicable (if the agent poses an infectivity threat to humans).
4. Place your name and contact information on the package.
5. The person doing the transporting must be knowledgeable on how to handle spills.
6. A state car should be used **(Do not use your personal vehicle)**.

XI. DEA CONTROLLED SUBSTANCES

A. Introduction

Due to their abuse potential, items identified by the US Department of Justice, Drug Enforcement Administration (DEA) and the North Dakota Board of Pharmacy as controlled substances are subject to licensing, registration, storage, security, use, and disposal requirements.

Controlled substances are materials containing any quantity of a substance with a stimulant, depressant, or hallucinogenic effect on the higher functions of the central nervous system, and having the tendency to promote abuse or physiological or psychological dependence, as designated in state and federal controlled substance schedules. (See a list of DEA controlled substances at http://www.deadiversion.usdoj.gov/schedules/#list).

Principal Investigators (PIs) using controlled substances in their laboratory research (including animal research) are subject to state and federal regulatory requirements. Please note that these requirements (including licensing/registration) are separate from and in addition to any that apply to medical practitioners, i.e., MDs. MDs/PhDs conducting laboratory research who also must obtain licensure/registration for laboratory use of controlled substances.

B. Licensing and Registration

Since the University cannot, by law, maintain a campus wide registration for controlled substances, it is the responsibility of each PI to obtain appropriate licenses and registration, and to adhere to applicable state and federal regulatory requirements when working with controlled substances. PIs must register their controlled substance(s) with the federal DEA as well as the ND Department of Pharmacy.

NOTE: Copies of all registration and licensing related correspondence must be kept by the PI and additional copies should be sent to Office of Safety.

C. Annual Self-Evaluation

UND requires that each PI complete a Controlled Substances Self-Evaluation annually. The forms, indicating corrective actions taken, should be kept by the PI for at least one year and a copy should be submitted to Office of Safety.

D. Storage and Security Controls

Controlled substances possessed, kept, or otherwise stored in a manner or location not in compliance with state or federal law is subject to seizure by and forfeiture to federal or state officials. Failure to comply with applicable requirements may also result in a suspension of purchasing privileges and disciplinary actions. In order to guard against theft or diversion, all controlled substances regardless of schedule must be kept under lock and key, and accessible only to authorized personnel. The number of authorized staff must be kept to the minimum essential for operation, and the stocks of controlled substances to the smallest quantity needed. All controlled substances must be kept locked in their storage location except for the actual time required for authorized staff to remove, legitimately work with, and replace them.
Controlled substances must be stored in a substantially constructed cabinet. This cabinet must be kept locked at all times. The room in which the cabinet is located must have limited access during working hours and provide security after hours.

E. Disposal

Controlled substances that are expired, surplus, or contaminated must be disposed of according to federal

regulations and DEA policy. Controlled substances and other pharmaceuticals must never be drained disposed or thrown out in the regular garbage. Disposal of controlled substances must be effected through the use of a 'reverse distributor'. A 'reverse distributor' is a DEA registered entity that is legally allowed to handle controlled substance disposal. The UND System has established a reverse distributorship for the disposal of controlled substances. Prior to disposing controlled substances using this program, researchers need to be registered with the DEA. If abandoned controlled substances have been discovered, contact Office of Safety at 701-777-3341 immediately for proper disposal - an alternate set of documentation will be required in this scenario.

On the UND campus, the point of contact for the disposal of controlled substances is the Department of Public Safety - Office of Safety group. If you no longer have a use for your controlled substances or they have become expired, you can start the disposal process by contacting the UND Office of Safety.

Information that will be needed to arrange disposal will include:

- Trade name or chemical name of the compound or solution for disposal.
- The concentration of active ingredients.
- The original quantity of controlled substance acquired and the remaining quantity left for disposal.
- The National Drug Code (NDC) number from each container.
- A copy of your current DEA registration

Disposal of dilutions and mixtures

When a dilution or mixture of a controlled substance is generated, the quantity of controlled substance used in the dilution or mixture should be removed from your controlled substances inventory. Because the quantity of controlled substance that was used to create the dilution or mixture is removed from inventory, the dilution or mixture is no longer considered a controlled substance. Even though a drug dilution or mixture is no longer considered a controlled substance, it must not be poured down a drain for disposal. Disposal of dilutions and mixtures that have not been used or that can no longer be used must be disposed of through the Office of Safety waste program by completing a Waste Disposal Manifest Form https://und.edu/public-safety/_files/docs/waste-disposal-manifest-form.pdf. Unused or expired drug dilutions and mixtures should be consolidated into an existing hazardous waste stream that your lab already generates, if possible. Always ensure the compatibility of each waste before consolidation. Waste streams such as flammable solvents or toxic aqueous waste streams usually make perfect candidates for consolidation of excess drug dilutions and mixtures for disposal. Please be sure to list the proper chemical names of the drugs and any other ingredients added and their approximate concentration to your hazardous waste tag for disposal. If you have any questions about suitable wastestream consolidations contact the Office of Safety.

Disposal of broken or damaged containers

If a container of a controlled substance is inadvertently broken or damaged, document this in your controlled substances inventory as "unintentional destruction" and list the amount of controlled substance lost. Have a witness sign and date this entry, if possible. All spill cleanup residues and materials used in the cleanup must be disposed of through the Office of Safety hazardous waste program by completing a Waste Disposal Manifest Form.

Disposal of stock bottles

Rinse out stock bottles of controlled substances when they have been emptied. Rinse with water and ensure any trace amounts or residues that remain are properly removed. All rinsate must be collected and sent through the hazardous waste program for disposal. Once the stock bottles have been emptied and rinsed, they can be disposed in the regular garbage.

Disposal of medical materials and supplies

Needles, syringes, catheters and other medical devices used in the administration of controlled substances must be disposed through the hazardous waste program for disposal. Unused drugs must not be left behind in syringes or catheters for disposal. Drugs must be emptied as much as reasonably possible, with the excess drugs being consolidated and disposed through the Office of Safety hazardous waste program. Needles must be autoclaved (even if used on "clean animals") and disposed of through the Office of Safety hazardous waste program. See the UND Sharps Policy on segregation and disposal of metal sharps for further guidance https://und.edu/finance-operations/_files/docs/6-29-sharps.pdf).

Disposal of other Pharmaceuticals

All pharmaceutical substances, including those that are not considered controlled substances, must be properly disposed of. Some are considered a regulated hazardous waste by the Environmental Protection Agency (EPA). However, even materials that are not regulated as a hazardous waste can pose hazards when released into the environment. Because many of these materials were not specifically regulated by the EPA or DOT as hazardous materials, when researchers found themselves with unwanted pharmaceutical drugs their approach has traditionally been to flush the unwanted materials down the drain. However, drain disposal of waste pharmaceuticals is illegal and is a violation of the campus wastewater discharge permit.

Unfortunately, pharmaceutical wastes aren't captured and treated by wastewater treatment facility processes. As result, water discharged from these facilities is laced with untreated pharmaceutical drugs which make their way into drinking water supplies and over time have detrimental effects on ecosystems and aquatic life.

As the news media and recent research has highlighted, this pharmaceutical pollution (coupled with the drugs that pass through our digestive systems and also make their way through sewage treatment systems) may have long term health effects that we are only now beginning to study.

To ensure your lab is in compliance with regulations and to avoid polluting the environment and our drinking water, arrange for disposal of unwanted pharmaceuticals the same way you would dispose of any other chemical waste - submit a Waste Disposal Manifest Form to Office of Safety for disposal.

By properly disposing of controlled substances and other pharmaceuticals, you are doing your part to ensure that future generations will have clean water for swimming, fishing, and drinking. You also ensure continued rights to purchase and hold controlled substances and avoid financial penalties or fines from the DEA. If you have any questions, please contact the Office of Safety (777.3341).

F. Reporting of Loss, Destruction, Theft, or Unauthorized Use

Thefts, suspected thefts, unauthorized uses, or other losses of any controlled substance must be reported to the UND Police Department (777.3491) and Office of Safety (777.3341) upon discovery. Registrants must also document the incident to the Grand Forks Police and federal DEA. (See DEA Theft or Loss of Controlled Substances http://www.deadiversion.usdoj.gov/21cfr_reports/theft/).

G. Recordkeeping

PIs are required by law to maintain complete and accurate inventory records for all controlled substances. These records must be kept separately from all other records and documents, in or near the primary work area, and be available for inspection during regular work hours. The use of codes, symbols, or foreign languages in identifying a controlled substance or person in the record is prohibited. In the event that any controlled substances are lost, destroyed, or stolen, the kind and quantity of the material and the date of discovery of such loss must be recorded in detail. All records must be maintained by PIs for a period of at least two years from the date of the last recorded transaction. The recordkeeping system should include the following information:

Receipt of Controlled Substance: A separate and current record on the receipt of controlled substances, indicating date received, name and address of supplier, and the type, strength or concentration, and amount of the controlled substances received. Each record must be signed by the person receiving the controlled substance.

Use of Controlled Substances: A separate and current record for the storage and use of each controlled substance, indicating the date, laboratory building and room, specific research experiment, controlled substance' s application in the research, and type, strength and quantity of each controlled substance use or disposal. By noting starting volume or mass of substance in the container, each use or disposal is a subtraction from the starting quantity, and the running (decreasing) amount should equal the total amount remaining on-hand. Each record of use must be signed by the person working with the controlled substance.

Inventory of Controlled Substances: A complete and accurate inventory of the stock of controlled substances within each registrant's laboratory must be performed initially. The type, strength, and quantity of all controlled substances must be recorded at this time. The person conducting the inventory must also date and sign the record. After the initial inventory is taken, a new inventory of all stocks of controlled substances on hand should be conducted at least every two years. PIs should be sure that the inventory can be reconciled to the records of receipt, use and disposal at all times.

H. Importing and Exporting Controlled Substances

If you plan to import controlled substances into the United States, or export them out of the United States, you must complete additional forms. (See the Import/Export pages of the DEA Office of Diversion Control website for additional information http://www.deadiversion.usdoj.gov/imp_exp/).

XII. PERMITS AND EXPORT CONTROL

A. Permit Requirements

Research with certain infectious agents may require a permit. The Principal Investigator is responsible for obtaining and maintaining valid permits, and supplying a copy to the BSO.

B. CDC

The Centers for Disease Control and Prevention's Import Permit Program (IPP) regulates the importation of infectious biological agents, infectious substances, and vectors of human disease into the United States. Prior to issuing an import permit, IPP reviews all applications to ensure that entities have appropriate safety measures in place for working safely with these imported materials. You can find more information regarding this permitting program here: http://www.cdc.gov/od/eaipp/.

C. USDA-APHIS

APHIS issues permits for the import, transit and release of regulated animals, animal products, veterinary biologics, plants, plant products, pests, organisms, soil, and genetically engineered organisms. You can learn more about this permitting program here:

http://www.aphis.usda.gov/wps/portal/aphis/resources/permits.

D. Fish & Wildlife Service and National Marine Fisheries Service

Fish and Wildlife Service permits are required for importing marine mammals, certain fish, and certain live animals, including bats. Call 1-800-344-WILD for further information.
Contact information:

- ✓ Website: http://www.fws.gov/permits/ImportExport/ImportExport.shtml
- ✓ Permit Division, Office of Protected Resources, National Marine Fisheries Service 301-713-2355 or 713-2289 and/or Fish and Wildlife Service, Office of Management Authority 703-358-2104.

E. Export Control

UND is committed to pursuing its mission in teaching, research, and service in a manner consistent with all U.S. export laws and regulations. The export of etiologic agents of humans, animals, plants, and related materials primarily is regulated by the U.S. Departments of Commerce, State, and Treasury. A wide variety of etiologic agents of human, plant, and animal diseases, including genetic material and products that might be used for culture or production of biological agents, will require an export license(s). Furthermore, physical export of these agents to certain countries is prohibited. In addition, disclosing (including oral or visual 59 disclosure) controlled information or technologies to a non-U.S. person in the U.S. (also known as a deemed export) or abroad – and/or providing certain technical assistance, training, or other defense services for/on behalf of a non-U.S. person, whether in the U.S (deemed export) or abroad – also may implicate export control laws and regulations. For more information on export compliance and biological agents, visit https://und.edu/research/resources/export-controls.cfm or contact UND's Export Control Officer at 701-777-2049.

XIII. AUDITS AND PROGRAM EVALUATION

A. Safety Audits

UND Office of Safety will conduct regular (e.g., annual) audits of each laboratory to ensure compliance with the procedures and protocols of this manual. Any significant concerns will be reported to the Institutional Biosafety Committee. The safety audit typically includes an evaluation of the autoclave, biological safety cabinet, microbiological techniques, emergency and safety equipment, storage of biohazardous material, general housekeeping, and review of the Laboratory Specific Biosafety Manual. Office of Safety will make every attempt to schedule safety audits with faculty members. However, if the principal investigator is unavailable or is unresponsive, Office of Safety will proceed with the safety audit. Office of Safety may also conduct unannounced accident investigations. Please be aware that federal, state, and local inspectors may also conduct unannounced inspections. Following the biological safety survey, a report listing the safety concerns is sent to the faculty member responsible for the laboratory. Additionally, a copy of the safety survey is forwarded to the department chair. The faculty member is responsible for correcting the hazards. If the faculty member fails to correct the hazard, a second notice is sent to the department chair and the dean with a copy to the faculty member. Follow-up audits may be conducted in laboratories with extremely hazardous conditions and/or numerous concerns.

B. Recordkeeping

The principal investigator must maintain the following records and be prepared to present these at the annual laboratory inspection:

- ✓ An accurate, current list of each biological agent or toxin stored in that room stored in freezers, refrigerators, dehydrated storage, or otherwise.
- ✓ A Risk Assessment for each biological agent or toxin stored in that room.
- ✓ Training Documentation Forms.
- ✓ Safety, security, and emergency response plans.
- ✓ Safety and security incident reports

C. Program Evaluation

The review of the elements as noted in the Recordkeeping sections of this document will constitute an evaluation of the UND Biosafety and Biosecurity Program.

APPENDIX A: Summary of Recommended Biosafety Levels for Infectious Agents

BSL	Agents	Practices	Safety Equipment (Primary Barriers)	Facilities (Secondary Barriers)
1	Not known to consistently cause disease in healthy adults	Standard Microbiological Practices	• No primary barriers required • PPE: laboratory coats and gloves; eye, face protection, as needed	Open bench and sink required
2	Associated with human disease Routes of transmission include: Percutaneous injury, ingestion, mucous membrane exposure	BSL-1 practice plus: • Limited access • Biohazard warning signs • "Sharps" precautions • Biosafety manual defining any needed waste decontamination or medical surveillance policies	Primary barriers: • Class I or II BSCs or other physical containment devices used for all manipulations of agents that cause splashes or aerosols of infectious materials • PPEs: laboratory coats; gloves; face protection as needed	BSL-1 plus: • Autoclave available
3	Indigenous or exotic agents that may cause serious or potentially lethal disease through aerosol transmission	BSL-2 practice plus: • Controlled access • Decontamination of all waste • Decontamination of lab clothing before laundering • Baseline serum	Primary barriers: • Class I or II BCSs or other physical containment devices used for all open manipulations of agents • PPEs: Protective lab clothing; gloves; respiratory protection as needed	BSL-2 plus: • Physical separation from access corridors • Self-closing, double-door access • Exhausted air not recirculated • Negative airflow into laboratory • Entry through anteroom or airlock • Hand washing sink near laboratory exit
4	Dangerous/exotic agents which pose high risk of aerosol transmitted life-threatening disease that are frequently fatal, for which there are no vaccines or treatments Agents with a close or identical antigenic relationship to an agent requiring BSL-4 until data are available to redesignate the level	BSL-3 practices plus: • Clothing change before entering • Shower on exit • All material decontaminated on exit from facility	Primary barriers: • All procedures conducted in Class III BSCs or Class I or II BSCs in combination with full-body, air-supplied, positive pressure personnel suit	BSL-3 plus: Separate building or isolated zone Dedicated supply and exhaust, vacuum, and decontamination systems Other requirements outlined in the text of BMBL 5th Edition

APPENDIX B: Summary of Recommended Animal Biosafety Levels

BSL	Agents	Practices	Safety Equipment (Primary Barriers)	Facilities (Secondary Barriers)
1	Not known to consistently cause disease in healthy human adults	Standard animal care and management practices, including appropriate medical surveillance programs	As required for normal care of each species	• Standard animal facility: • No recirculation of exhaust air • Hand washing sink recommended
2	Associated with human disease Routes of transmission include percutaneous exposure, ingestion, and mucous membrane exposure	ABSL-1 practices plus: • Limited access • Biohazard warning signs • Biosafety manual • Decontamination of all infectious wastes and of animal cages prior to washing	ABSL-1 equipment plus primary barriers: • Containment equipment appropriate for animal species • PPES: laboratory coats, gloves, face and respiratory protection as needed.	ABSL-1 facility plus: • Autoclave available • Hand washing sink available in the animal room. • Mechanical cage washer used
3	Indigenous or exotic agents that may cause serious or potentially lethal disease through the inhalation route of exposure	ABSL-2 practices plus: • Controlled access • Decontamination of clothing before laundering • Cages decontaminated before bedding removed	ABSL-2 equipment plus: • Containment equipment for housing animals and cage dumping activities • Class I or II BSCs available for manipulative procedures (inoculation, necropsy) that may create infectious aerosols. • PPEs: appropriate respiratory protection	ABSL-2 facility plus: • Physical separation from access corridors • Self-closing, double-door access • Autoclave available in facility • Entry through ante-room or airlock • Negative airflow into animal and procedure rooms • Hand washing sink near exit
4	Dangerous/exotic agents that pose high risk of aerosol transmitted laboratory infections that are frequently fatal, for which there no vaccines or treatments Agents with a close or identical antigenic relationship to an agent requiring BSL-4 until data are available to redesignate the level	ABSL-3 practices plus: • Entrance through change room where personal clothing is removed and laboratory clothing is put on; shower on exiting • All wastes are decontaminated before removal from the facility	ABSL-3 equipment plus: • Maximum containment equipment (i.e., Class III BSC or partial containment equipment in combination with full body, air-supplied positive-pressure personnel suit) used for all procedures and activities	ABSL-3 facility plus: • Separate building or isolated zone • Dedicated supply and exhaust, vacuum and decontamination systems • Other requirements outlined in the text of BMBL 5th Edition

APPENDIX C: Summary of Practical Disinfectants for use in Biological Research

DISINFECTANTS		PRACTICAL REQUIREMENTS					INACTIVATES						
			CONTACT TIME (MINUTES)										
TYPE	CATEGORY	USE DILUTION	LIPO-VIRUS	BROAD SPECTRUM	TEMP. (°C)	RELATIVE HUMIDITY (%)	VEGETATIVE BACTERIA	LIPOVIRUSES	NON-LIPID VIRUSES	BACTERIAL SPORES	TB	HIV	HBV
LIQUID	Quaternary Ammonium Compounds	0.1-2.0%	10-30	-			+	+	-	-	-	+	-
	Phenolics, Amphyl	1.0-5.0%	10-30	-			+	+	*	-	+	+	*
	Chlorine Bleach	5%	10-30	30			+	+	+	+	+	+	+
	Iodophor, Wescodyne	0.5-10%	10-30	30			+	-	+	+	+	+	*
	Alcohol, Ethyl	70-85%	10-30	-			+	-	*	-	-	+	*
	Alcohol, Isopropyl	70-85%	10-30	-			+	+	*	-	-	+	*
	Formaldehyde	0.2-8.0%	10-30	30			+	+	+	+	+	+	+
	Glutaraldehyde	2.0%	10-30	30			+	+	+	+	+	+	+
GAS	**Ethylene Oxide**	8-23g/ft^3	60-240	60	37	30	+	+	+	+	+	+	+
	Paraformaldehyde	0.3g/ft^3	60-180	60	>23	>60	+	+	+	+	+	+	+

+ Positive Effect; - No Effect; * Variable Effect **Main Reference: NIH Safety Monograph, 1979; BMBL 5th Edition, 2009; WHO Laboratory Safety Manual, 2004**

Disinfectant selection must be based on several factors.

- What is the target organism that you wish to inactivate? (spore-bearing bacteria are very resistant to most disinfectants)
- What are the physical characteristics of the surface that will be disinfected? (Porous surfaces may absorb disinfectants; some disinfectants may corrode metal surfaces)
- How long will the contact time be between the disinfectant and the target organism? (High concentrations of biological organisms may require longer contact times)
- What is the concentration of the disinfectant as it is being applied? (Dilute applications of disinfectants may not lyse or denature cell chemical components)
- How toxic is the disinfectant? (Paraformaldehyde, Formaldehyde, Glutaraldehyde and Ethylene Oxide should not be used without consent of the Office of Safety)
- The chart is designed to illustrate the efficacy of several disinfectants with regard to some of the most commonly used organisms on University of North Dakota campus. Review the effective concentrations provided in the use dilution column and the contact time as well the type of organism prior to disinfectant selection. If you have any questions, call Office of Safety at 777-3341 (M-F 8am - 4.30pm) for more information.
- Contact the Office of Safety (777-3341) if ethylene oxide is to be used.

APPENDIX D: Biohazard Waste Disposal Chart

BIOHAZARD WASTE DISPOSAL CHART

SHARPS

Razor blades, scalpels, lancets, syringes with/without needles, slide covers, specimen tubes, inoculating loops, stirring devices, and broken glass

Collect in Red Plastic Sharps Containers bearing Biohazard Symbol

Fill Waste Disposal Manifest form and call Office of Safety for disposal

RESEARCH LAB/CLINIC PIPETTING

Pipettes

Puncture resistant outer container bearing biohazard symbol lined with orange autoclave bag

Pipette

Small benchtop biohazard bag

Dispose with pipettes or solid waste

Autoclave with test indicator

SOLIDS

Culture dishes & flasks, Petri dishes, solid waste cultures/stocks from the production of biological, gloves, gowns, masks, shoe covers, and any other solid materials potentially contaminated with biohazardous

Biohazard waste collection container (red hard-walled, closeable) lined with an orange autoclave bag bearing the biohazard symbol.

LIQUID

Human Blood, animal blood, human tissue culture, body fluids, liquid growth media

Was liquid waste used for propagating microbes/viral vectors/toxins?

NO

Dispose of down the sink with copious amounts if water

YES

Autoclave or chemical disinfection with appropriate contact time, then dispose of down

Disposal for removal by housekeeping
(After autoclaving cross the biohazard symbol or put in a black trash bag)

APPENDIX E: PRINCIPAL INVESTIGATOR CHECKOUT PROCEDURE
UNIVERSITY OF NORTH DAKOTA
OFFICE OF SAFETY
SECTION: BIOLOGICAL, CHEMICAL, AND RADIATION SAFETY

PURPOSE

All Principal Investigators (PIs) are required to complete this checkout procedure 30 days prior to the completion of their association with the University of North Dakota (UND). PIs must ensure that all hazardous chemical, biological and radioactive materials under their authorization/supervision are properly disposed, transferred to another laboratory, shipped, or removed to storage. Strict adherence to this policy will reduce the likelihood of accumulating orphaned chemicals, some of which may become dangerously unstable. Uncontrolled inventories of hazardous chemical, biological or radioactive materials eventually lead to storage problems, increased waste disposal costs, contamination and other potentially unsafe conditions. The failure of any PI to complete or properly follow this checkout procedure will require that their departmental chairperson assume such responsibility.

PLEASE NOTE:

- **Radioactive material transfer must receive prior approval of the Radiation Safety Officer.**
- **Registrants authorized by DEA to possess Controlled Substances must follow agency guidelines regarding transfer and disposal of controlled drugs. Follow the procedures mentioned in section XI of this manual (DEA CONTROLLED SUBSTANCES).**

1. Office of Safety must be given written notification of a PI's departure from the University of North Dakota by their department at least 30 days prior to his/her exit date. The written notification is to be sent to: Office of Safety or und.safety@email.und.edu. Advance notice is required to allow adequate time for the scheduling of laboratory clean outs and compliance with regulatory requirements. The attached PI Advance Notification form is provided to the PI for completion and submittal to Office of Safety as required.
2. The PI must include the following items in the written notification of departure:
   a. Forwarding mailing address
   b. Department
   c. Departmental chairperson's name
   d. Room numbers for all laboratories under that PI's supervision
   e. Date of departure
   f. Contact telephone number before and after departure
   g. Name of individual who will take responsibility of transferred chemicals, biological materials and/or radioisotopes
3. Chemicals that will remain in the laboratory must have proper labels that include the chemical name, hazards, reactivity and date received or last utilized. Radioactive materials and radioactive samples must also have labels which include the radioisotope, activity, and date. Biological material remaining in the laboratory must be placed in leak proof or breakage resistant receptacles with the name and hazards associated with the microbial agent on the specimen container.

A. Radioactive materials/samples to be taken with the PI to another licensed institution must be properly shipped through Office of Safety. All outstanding radioisotopes still in inventory must be accounted for prior to leaving. Please consult with the Radiation Safety Officer for assistance with shipping of radioactive materials.

B. Chemicals will not be shipped through Office of Safety; outside vendors may be contacted to arrange legal shipments of such materials. However, our department will inspect all chemical hazardous products prior to shipping to ensure that they are properly packaged for transport.

C. All biological materials that need to be shipped or relocated must be packed and transported following the Department of Transportation (DOT) and the International Air Transport Association (IATA) rules and regulations. Please contact Office of Safety so that trained and certified personnel can assist you with the transportation of your biological materials. It is ultimately the responsibility of the department to make sure that all of the hazardous materials are shipped to a licensed institution in accordance to state and federal laws.

D. All equipment and laboratory ware used with radioactive materials must be identified and properly labeled for disposal or transfer to another approved PI. All such equipment and laboratory ware to be taken with the PI to another licensed institution must be adequately decontaminated prior to removal. Documentation of decontamination must be provided to Office of Safety.

E. All radiation laboratories and remaining equipment (i.e. refrigerators, centrifuges, incubators, etc.) must be decontaminated to the approved levels by the PI prior to leaving. Copies of the PI's final surveys and wipe tests must be sent to Office of Safety. Office of Safety will confirm decontamination with their own surveys and wipe tests. All radiation labels and signage will be removed during the Office of Safety closeout procedures and the laboratories will then be released to other PIs for use.

F. All radiation badges must be returned to Office of Safety prior to the PI's departure or the department will be held responsible for financial reimbursement.

G. All containment equipment such as biosafety cabinets, fume hoods, or centrifuges that were used with infectious agents at Biosafety Level 2 must be properly cleaned and decontaminated with an appropriate disinfectant for the agents used.

UNIVERSITY OF NORTH DAKOTA
OFFICE OF SAFETY
PRINCIPAL INVESTIGATOR CHECKOUT CHECKLIST

The PI Checkout Checklist is provided to assist the PI with properly withdrawing from the University of North Dakota.

1. Completed and submitted form for 30 days advance notification ☐
   (Provide accurate and detailed information)

2. Chemicals & samples properly labeled & packaged ☐
   (PI should consider donating unwanted new and reusable chemicals to fellow investigators with the help of Office of Safety)

3. Biologicals materials properly labeled & packaged by Office of Safety staff ☐ trained in shipping infectious agents and diagnostic materials

4. Radioactive materials & samples properly labeled & packaged ☐

5. Submit Office of Safety Waste Disposal Form/Manifest Form online ☐ at the following website: (As needed for radioactive, chemical, and biological waste) ☐
   http://und.edu/finance-operations/office-of-safety/_files/docs/waste-disposal-manifest-form.pdf

6. Laboratory cleanout completed ☐

7. Equipment & laboratory ware properly decontaminated ☐

8. Final radiation laboratory surveys & wipe tests completed ☐

9. Copies of surveys & wipe tests sent to Office of Safety ☐

10. Radiation badges returned to Office of Safety ☐

11. Hazardous Chemicals inspected prior to shipping ☐

12. Radioactive materials properly shipped through Office of Safety ☐

13. Controlled Substance and Dangerous Drugs properly disposed/transferred ☐

Please submit completed checklist to Office of Safety or und.safety@email.und.edu.

UNIVERSITY OF NORTH DAKOTA
OFFICE OF SAFETY
PRINCIPAL INVESTIGATOR 30 DAYS ADVANCE NOTIFICATION PRIOR TO DEPARTURE FROM UND

This is to officially notify the Office of Safety of my intent to leave the University of North Dakota. This written notification is submitted to: Office of Safety or und.safety@email.und.edu, 30 days prior to my departure from UND. The following information is provided as required in the Principal Investigator Checkout Procedure.

PI: _____

Date of Departure: _____

Department: _____

Department Chair: _____

Room Numbers of all laboratories under PI: _____

Contact Phone Numbers:
Before Departure: _____

After Departure: _____

Name of Responsible Individual(s) receiving transferred Chemicals, Biologicals, and/or Radioactive Materials:

_____