

CLSI Biosafety

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1.0 PURPOSE

The Canadian Light Source Inc. (CLSI) is committed to providing a safe and healthful working environment for all staff, contractors, users, students and visitors. This document provides guidelines for working safely with biological materials. For CLSI purposes, biological materials may include infectious and non-infectious microorganisms, recombinant DNA, genetically modified organisms and microorganisms, cell lines, human tissues/fluids, animal tissues/fluids, and plants.

2.0 BACKGROUND

The CLS facility maintains a Public Health Agency of Canada (PHAC) Pathogen and Toxin License, as well as an operating licence from the Canadian Nuclear Safety Commission (CNSC). All personnel requiring access to the facility must comply with the Human Pathogens and Toxins Act (HPTA), the Canada Labour Code, and all other applicable acts and regulations, including but not limited to, the CNSC Act and regulations, and the operating licence conditions. The most recent versions of CLSI licences are available in CLSI document control.

The HPTA was established to “promote safety and security with respect to human pathogens and toxins” [18]. The CLS facility is registered as a facility that handles Risk Group level 2 human pathogens and toxins with PHAC as defined by the Act. As such, the CLS facility requires the use of all pathogens and toxins to comply with this document which is based on the *Canadian Biosafety Standard and the Canadian Biosafety Handbook*, as amended from time to time.

The Canadian Food Inspection Agency (CFIA) maintains the importation of soils, plants and animal pathogens. Applications for import must be applied prior to importation occurring. Biannually, a CFIA facility/lab inspection must occur to ensure compliance with regulations.

The Canada Labour Code Part II [13] states that the employer has a responsibility to protect the health and safety of the staff, contractors, users, students and visitors, from hazardous substances and activities that could cause personal injury or damage to the environment. Every individual who conducts an activity with any biohazardous material must take all reasonable precautions to protect the health and safety of the public against the risks posed by that activity.

All experiments conducted at the CLS facility shall be reviewed by the CLSI HSE Department for health, safety and environmental concerns [9]. During the review, all hazards and subsequent controls and precautions are identified. A permit is created, identifying the organisms and the controls required to work safely. The permit is electronic and visible with the e-USO system. The permit must be signed on by the user prior to commencing.

2.1 BIOSAFETY

Biosafety is the application of knowledge, techniques and equipment to prevent personal, laboratory and environmental exposure to biohazardous material. Biosafety also defines the containment conditions under which biological material can be safely manipulated. The objective of containment is to confine biological material and to reduce the potential exposure of the laboratory worker, persons outside the laboratory, and the environment to potentially infectious agents.

The following controls must be in place to ensure Biosafety issues identified in a risk assessment are minimized:

- **Elimination** (removing the hazard)
- **Substitution** (using a less hazardous option)
- **Engineering Controls** (Lab/facility design, containment levels, Biological Safety Cabinets, etc.)
- **Administrative Controls** (Training, Records, etc.)
- **Procedural Controls** (Standard Operating Procedures, Exposure Controls Plan, Emergency Response Plan, etc.)

2.2 DEFINITIONS

Animal Pathogens: A biological agent that causes disease or illness in animals. Containment standards are described in *the Canadian Biosafety Standard and the Canadian Biosafety Handbook*, as amended from time to time [19].

Biohazard: Workplace Hazardous Materials Information System (WHMIS) regulations [16] define biohazardous materials as an organism and the toxins of organisms that have been shown to cause disease or are reasonably believed to cause disease in persons or animals. These organisms are also known as infectious organisms. WHMIS 1988 assigns these materials to Class D, Division 3. WHMIS 2015 assigns these materials within the Health Hazard Group, Biohazardous Infectious Materials Class (Category 1). An inventory must be maintained of all such organisms and material safety data sheets made available.

Biological Material: Material that includes, but is not limited to microorganisms, recombinant DNA, cell lines, animals, plants, and any materials derived from animals, plants or humans.

Canadian Food Inspection Agency (CFIA): Federal agency which maintains information and Pathogen Safety Data Sheets (PSDS) for animal and plant pathogens.

Contact Time: Period of time that a surface treated with disinfectant remains wet. An effective contact time depends on the disinfectant and the microorganism present.

ECP: Experimental Control Plan

Genetically Modified Microorganism (GMMOs): Any microorganism in which the genetic material has been altered.

Genetically Modified Organisms (GMOs): Any organism whose genetic material has been altered using recombinant DNA technology.

Human Pathogen: Any microorganism or parasite that causes disease in humans. This includes zoonotics. Human pathogens may be contained in cultures, diagnostic specimens, or tissues.

Laboratory Acquired Infection (LAI): Infection acquired through laboratory or laboratory-related activities. May be symptomatic or asymptomatic in nature.

Safety Data Sheet (SDS): Compilation of information on the identity of hazardous materials including information on health hazards, physical hazards, exposure limits and precautions. The Public Health Agency of Canada (PHAC) has drafted SDSs for human pathogens [21], whereas the Canadian Food Inspection Agency (CFIA) has drafted Pathogen Safety Data Sheets (PSDS) for animal pathogens [1].

Personal Protective Equipment (PPE): Specialized clothing or equipment (such as gloves, eye protection, respirators, etc.) worn by a worker for protection against a hazard.

Public Health Agency of Canada (PHAC): Federal agency which regulates the use of and maintains information and MSDS for human pathogens.

Recombinant DNA: Altered DNA resulting from the insertion by chemical, enzymatic, or biological means, of a sequence not originally present.

SOP: Standard Operating Procedure

Toxins: Biological toxins consist of any toxic substance produced by an organism. They can cause acute toxic disease as well as long-term effects. Toxins are non-replicating and are not communicable between individuals. They are capable of eliciting pathologic effects associated with infectious diseases, and are one of the key virulence factors.

Transgenic Organism: Any animal or plant that has had DNA from any other source (most often a complete gene) put into its genome.

Universal Precautions: Prevention strategy where all blood and potentially infectious materials are treated as if infectious regardless of the health status of the source individual.

Zoonosis: An infectious disease in animals that can be transmitted to people. The natural reservoir for the infectious agent is an animal.

3.0 ROLES AND RESPONSIBILITIES

Descriptions of roles and responsibilities while at the CLS are outlined in the CLSI *Health, Safety and Environment Manual* [9]. The following sections outline roles and responsibilities specific to biosafety at the CLS. All individuals working with biological materials must adhere to administrative procedures, operational practices, and rules outlined by the CLSI for the acquisition, use, storage, transport and disposal of biohazardous materials.

The Biosafety program, including all support documentation for the program is reviewed on an annual basis, at minimum. As new regulations, trends in non-compliance, and gaps within the program are identified, additional reviews shall occur.

Financial resources required for the biosafety program are included within the Health, Safety and Environment budget and are allotted by the Health, Safety, and Environment Manager, as required.

3.1 CLSI HSE DEPARTMENT

The CLSI HSE Department provides consultation on operation of the CLS facility to ensure compliance with PHAC, CFIA, CNSC and other applicable regulatory requirements. It provides information on regulations that apply to the CLS facility and advises on safe methods for new procedures. The HSE department reviews all applications for research involving hazardous material, including biohazardous material. In addition, HSE advises on the suspension of access privileges for beamline scientists, users and other researchers found to be in violation of policies and procedures governing facility use.

The CLSI Biological, Chemical and OHS Lead is responsible for the development, implementation and maintenance of a comprehensive biosafety and biosecurity program and ensuring compliance with all applicable federal, provincial and municipal regulations. The Biological, Chemical and OHS Lead also acts as the facility Biosafety Officer. The Biological, Chemical and OHS Lead has the authority to take any action deemed appropriate or to stop any activity deemed unsafe in consultation with the CLSI HSE Manager.

In particular, the Biological, Chemical and OHS Lead responsibilities pertaining to CLS biosafety program include:

- Advises the HSE Manager on policy matters concerned with the protection of staff and users from biohazardous agents and recommends procedures and facility use including such matters as safety training and health surveillance.
- Meet regularly with the HSE Manager to provide progress reports and advisement on specific biological safety issues as well as general safety.
- Certify annually in the Annual Compliance Report that the CLS facility, procedures, and practices, and the training and expertise of CLS staff and users meet the CLSI biosafety standards.
- Maintain required registrations of the CLS facility as per the HPTA and other applicable act and regulations.
- Advises facility users on policies related to biosafety and approve containment and procedures to be used.
- Evaluate and inspect the facility and laboratories for work with biohazardous material.
- Identify and update known or potential biohazardous areas at the CLS facility on a regular basis.
- Disseminate information for safety in biological research.
- Consult with the user community in matters pertaining to biosafety.

Details on the roles and responsibilities are found in the CLSI *Health, Safety and Environment Manual* [9].

3.2 SPOKESPERSON

Duties and responsibilities of the spokesperson or designate are to:

- Ensure all required information, including supporting documentation, in the proposal is complete and accurate.
- Ensure any changes to the proposed experiment are submitted as a permit amendment in a timely fashion.
- Ensure all team members that will handle biohazardous materials at the CLS have the appropriate training and experience to handle the materials in compliance with appropriate standards set forth by regulatory agencies and CLSI policies, principles, programs and procedures. *Note: The CLSI HSE department provides basic safety training specific to the CLS. Task or pathogen specific training is to be provided by the Principle Investigators of the Project or their qualified designates.*
- Ensure all team members are informed of the potential risks associated with the work and the necessary precautions to reduce the risk of exposure.
- Obtain required permits to export or import any biohazardous material or notifiable biological substances.

3.3 RESEARCH TEAM MEMBERS

Only research team members with proper biosafety training and experience are authorized to handle biohazardous materials while at the CLS. Duties and responsibilities of the authorized research team members are to:

- Know their responsibilities and conduct work in a safe and responsible manner so as to protect their health and safety, as well as others that may be affected by their acts or negligence.
- Comply with the appropriate standards set forth by regulatory agencies and CLSI policies, principles, programs and procedures.
- Comply with the controls outlined in the CLS experimental permit.
- Ensure they have received and understood any safety training, Standard Operating Procedures and any other relevant safety information from their supervisor and/or CLSI HSE before commencing work that involves hazardous agents. This training must include the proper use and maintenance of safeguards, safety devices, and PPE, so that they may carry out their work in a safe manner. ***Note:** The CLSI HSE department provides basic safety training specific to the CLS. Task or pathogen specific training is to be provided by the Principle Investigators of the Project or their qualified designates.*
- Provide appropriate transport containers and disinfectants for materials in use.
- Ensure that the handling of all hazardous waste follows CLSI *Hazardous Materials Management Plan* [8].
- Ensure work areas are kept clean, neat and tidy and that any spills, or contaminated equipment, trays, floors, and working surfaces are appropriately disinfected during the course of and after the completion of the experiment.
- Exercise proper hygiene to avoid personal exposure.

- Immediately notify the CLSI HSE department of any exposures, accidents, spills, or malfunctions of containment equipment involving biohazardous materials or notifiable biological substances.

3.4 CLSI AUTHORIZED PERSONNEL

Supervisors and Managers must ensure their workers have the required work authorization, safety orientation, PPE and other controls in place to do their work safely. Supervisors and Managers should consult CLSI HSE for guidance on the requirements.

CLSI Authorized Personnel must:

- Be familiar with their responsibilities and conduct their work in a safe and responsible manner so as to protect their health and safety, as well as any others that may be affected by their acts or negligence.
- Co-operate with their supervisor in performing their responsibilities, as well as with CLSI HSE or any other person exercising a duty imposed by a regulatory agency to promote safety.
- Ensure they have received work authorization which includes safety training and any other relevant safety information from their supervisor and/or CLSI HSE before commencing work in areas where hazardous agents are present.
- Notify their supervisor or the CLSI HSE when they become aware of any unsafe act or condition.

4.0 TRAINING

Anyone who will be working at the CLS must complete the required training courses specific to their work at the CLS. The training is valid for 2 years and refresher training may be required when significant changes are made in site operations or in safety and regulatory requirements. CLSI training includes the successful completion of online training modules and corresponding exams.

Training courses which may be assigned as required include:

- **Laboratory Safety Training:** Working in the laboratory facilities at the CLS. Provides information on general operational practices, sample and material transport, hazardous waste disposal and emergency response.
- **Biosafety Training:** For individuals working with unsealed biohazardous materials. Provides information on: biosafety regulations, CLSI policies, Laboratory Acquired Infections (LAI), Containment Level 2 operational practices and the transport and disposal of biohazardous materials. Individuals who have completed a biosafety training course at a Canadian institution and have supporting documentation may complete CLS site specific biosafety training.
- **Plan for Administrative Oversight:** For individuals maintaining the biosafety program. Provides communication and information in regards to the requirements of the HPTA Regulations.
- **Bloodborne Pathogen & Unconventional Pathogen Training:** For individuals using any human tissues/fluids that may contain bloodborne pathogens and/or unconventional pathogens. See section 6.1 and 6.2.

- **Biological Safety Cabinet Training:** For individuals who will require the use of a biological safety cabinet (BSC) while working at the CLS. Provides information on the proper use of the BSC, spill response and emergency response.

CLSI HSE will assign training modules as required based on the assessed hazards.

5.0 RISK ASSESSMENT

A risk assessment for any hazardous material that will be used at the CLS is mandatory [9]. A detailed local risk assessment shall be conducted to determine the containment and operational level required. The containment level required for work with a particular agent is based on the manipulations generally associated with laboratory scale research and clinical procedures. If a particular procedure poses a lower hazard than manipulation of a live culture, then a lower containment level may be appropriate. A researcher must be aware of the potential hazards of working with a particular organism.

In addition to the Risk Group Level classifications, the following factors associated with the laboratory operation should also be considered:

- Identifications of the biological material
- Potential for aerosol generation
- Quantity
- Concentration
- Agent stability in the environment (inherent biological decay rate)
- Type of work proposed
- Use of recombinant organisms (e.g., gene coding for virulence factors or toxins; host range alteration; oncogenicity; replication capacity; capability to revert to wild type).

5.1 APPROVAL PROCESS FOR PROPOSALS USING BIOLOGICAL MATERIALS

As described in CLSI *Health, Safety and Environment Manual* [9] all experiments at the CLS are reviewed and approved for HSE concerns. The *CLSI User Access Policy* [11] describes the process for the submission of an experiment proposal and the review process.

All research involving the use of live animals and/or animal tissues or fluids must comply with *CLSI Ethics Guideline: When Animals are Involved* [4].

All research involving human tissues and/or fluids must comply with *CLSI Ethics Guidelines: Involving Humans* [3].

Documentation to identify the sample, if available, should be attached to the proposal. This could include a technical sheet from the vendor or a Pathogen Safety Data Sheet (PSDS). A PSDS must be submitted for any biohazardous material. It is recommended that proposals using human or animal cell lines submit supporting documentation to identify the source as some cell lines may require ethics review.

CLSI will authorize an experiment to be conducted only after the activities associated with the experiment have been defined, hazards have been identified, adequate controls have been implemented and all required documents have been submitted. Users submit a proposal online through our e-USO system. Once approved, it is referenced as a Project. The Project page in the e-USO identifies specific controls and precautions required as part of the ECP. The ECP must be reviewed and confirmed by the user group in order to start their experiment. All processes for the Project are tracked through the e-USO system: sample sign-on, lab use and tracking of personnel on-site.

6.0 RISK GROUPS

Organisms have been categorized into 4 different Risk Group Levels (RGLs) based upon the particular characteristics of the organism, including the following:

- Pathogenicity
- Infectious dose
- Mode of transmission
- Host range
- Availability of effective preventive measures i.e. vaccines
- Availability of effective treatment

Risk Group Level 1 (RGL1) is designated as the lowest level of risk and Risk Group Level 4 (RGL4) as the highest risk level. The materials included in RGL2 to RGL4 are considered "biohazardous". Information on specific organisms is maintained by the corresponding federal agency (i.e., PHAC for human pathogens, CFIA for animal pathogens).

6.1 RISK GROUP LEVEL 1

RGL1 (low individual and low community risk) – "Any biological agent that is unlikely to cause disease in healthy workers or animals" [19].

RGL1 also encompasses any live animals or animal materials (i.e., tissue, blood, body fluids, etc.) that are deemed healthy (showing no signs of disease and from a reputable source), and any animal, human or plant proteins (excluding prions and toxins).

6.2 RISK GROUP LEVEL 2

RGL2 (moderate individual risk, low community risk) – "Any pathogen that can cause human disease but, under normal circumstances, is unlikely to be a serious hazard to laboratory workers, the community, livestock, or the environment. Laboratory exposures rarely cause infection leading to serious disease; effective treatment and preventive measures are available, and the risk of spread is limited" [19].

RGL2 also encompasses any unfixed human materials (i.e., blood, body fluids, tissue, etc.), fixed human neurological tissues and any animals that have been challenged with a RGL2 organism or are diseased.

The CLS facility is currently designed to accommodate up to RGL2 organisms only.

6.3 RISK GROUP LEVELS 3 & 4

RGL 3 and 4 organisms are not permitted to enter, be used, or stored at the CLS facility. For more information see the *Canadian Biosafety Standard and the Canadian Biosafety Handbook*, as amended from time to time [19].

7.0 BIOLOGICAL MATERIAL HAZARDS

7.1.1 Pathogen Safety Data Sheets (PSDS) for Infections Substances

- a) Content for PSDS for infectious materials is slightly different than those for SDS for chemicals. Sections of a PSDS include:
 - i. Health hazards (pathogenicity, infectious dose and mode of transmission)
 - ii. Vectors
 - iii. Viability & susceptibility to disinfectants and physical inactivation
 - iv. Medical surveillance
 - v. Treatment and immunization options
 - vi. Laboratory hazards and containment requirements
- b) PSDS sheets are maintained by PHAC for human pathogens [25]

7.1.2 Personal Exposure

- a) When working with infectious material, events that can lead to an infection include:
 - i. Exposure to infectious aerosols
 - ii. Spills and splashes
 - iii. Accidental needlestick injuries
 - iv. Cuts from sharp objects and broken glass
 - v. Bites and scratches from animals or ectoparasites
 - vi. Oral pipetting (prohibited)
 - vii. Centrifuge accidents
 - viii. Secondary spread of infectious materials to non-laboratory areas [8].
- b) Infectious substances can enter the body and cause infection through:
 - i. Ingestion – transfer of microorganisms to the mouth via fingers, oral pipetting or contaminated objects such as pens, food or drink.
 - ii. Injection/inoculation – accidental inoculation with needles, sharps, cuts from sharp objects and broken glass, bites and scratches from animals or parasites.
 - iii. Inhalation – inhalation of airborne microorganisms in the form of aerosols.

- iv. Contact – splashes of infectious materials into the eyes, mucous membrane, broken skin and transfer of microorganism to eyes and mucous membranes by contaminated fingers.

7.1.3 Infectious (Biohazardous) Material

- a) WHMIS Health Hazard Group, Biohazardous Infectious Materials Class (Category 1)
- b) Infectious materials can cause illness in humans and/or animals
- c) Infectious organisms may also produce toxins that are harmful to humans and animals (see section 2.8.4)
- d) Infectious materials classified RGL2 are the highest level of infectious organisms allowed at the CLS (see section 2.2)



7.1.3.1 Handling Precautions

- a) Read the PSDS, ECP, SOPs and labels before work is initiated
- b) Follow appropriate containment level for the material
- c) Minimize contamination by following good laboratory practices. See Section 8
- d) Handle material while wearing the appropriate PPE
 - i. Handle the material in designated areas and where engineering controls are in place to prevent exposure
 - ii. Never dispose biohazardous materials in regular garbage, see the section on Waste Disposal (Section 11) for the proper disposal procedures
 - iii. Remove PPE and wash hands thoroughly before exiting the laboratory
 - iv. Biohazardous material must be in closed, sealed containers while on the experimental floor. The surfaces of the containers must be disinfected and free of any pathogenic material
 - v. Always decontaminate items and workspace(s) with the appropriate disinfectant paying special attention to the proper contact time and concentration (see Section 12)

7.1.4 Biological Toxins

- a) Biological toxins are non-replicating and are not communicable between individuals but are capable of pathologic effects associated with infectious disease
- b) Biological toxins are different from chemical toxins in that they are highly toxic in minute quantities, there are no short-term exposure limits, ceiling limits or time weighted averages and toxicological data are often limited
- c) Toxins usually represent a hazard via aerosolization, ingestion or percutaneous injection. Some mycotoxins are dermally active

7.1.4.1 Handling Precautions:

- a) In addition to the operational practices for Containment level 2 described in the Canadian Biosafety Standards and Guidelines, and the Canadian Biosafety Standards Handbook, as amended from time to time [19], the following handling precautions must also be followed:
- i. Samples must be secured when not directly supervised and only accessible to authorized personnel associated with the CLSI Experimental Permit
 - ii. The CLSI Experimental Permit must accurately reflect the type and total quantity of toxin on-site at the CLS as the permit functions as the inventory
 - iii. Preparation and manipulation of the toxin must be conducted in a BSC
 - iv. Do not use fume hoods for dry powdered toxins as they can be aerosolized easily due to the high volume of exhaust air
 - v. Signs must be posted at laboratory entrances indicating that toxins are in use, restricting access to authorized personnel, and listing any special entry requirements
 - vi. Toxins are to be transported in spill and leak proof secondary containers (see section 6.7)
 - vii. Before removal from containment, primary containers are to be decontaminated and placed within clean secondary containers
 - viii. The interior of the BSC should be decontaminated immediately prior to use and must be decontaminated immediately upon completion of use; signs indicating that toxins are in use are to be placed on cabinets that have not been decontaminated
 - ix. Laboratory personnel must use long-sleeved labcoats and appropriate gloves
 - x. Personal protective clothing must be autoclaved prior to sending them to be cleaned if material is spilled on them
 - xi. Gloves are to be inspected and checked for punctures, holes etc. before use
 - xii. Care is to be taken when selecting glove material
 - a) When the work involves powdered toxins, glove material should be selected to minimize static electricity. Gloves and surfaces may be dampened to reduce static electricity
 - b) Glove material must also be impervious to the toxin being worked with and any diluents
 - xiii. Ensure there is a functioning emergency shower and emergency eyewash station accessible within 10 seconds
 - xiv. Decontamination procedures (e.g. autoclaving, chemical disinfectants) should be assessed for each toxin by consulting current literature, as the optimal procedures for each toxin vary widely

- xv. Decontamination solutions should be routinely tested to ensure that they are at the proper concentrations. Many commonly used agents can rapidly lose their activity
- xvi. When working with infectious organisms which may have toxins care must be taken to ensure that both the infectious agent and the toxin are neutralized
- xvii. For most protein toxins, a sodium hypochlorite, or sodium hypochlorite and sodium hydroxide mixture provides effective decontamination.
 - a) Surfaces may be decontaminated with a 0.5% solution of sodium hypochlorite
 - b) Solid and liquid waste may be decontaminated with a solution of 2.5% sodium hypochlorite and 0.25 N sodium hydroxide. Solid waste should be soaked in solution and allowed to stand for 5 hours. Liquid waste should be mixed in a 1:1 ratio with solution and allowed to stand for 8 hours.

Note: The preferred method is highly variable and should be determined for the specific toxin in question.

- b) Every effort is to be made to work with less than one human lethal dose of toxin
- c) Two knowledgeable individuals should be present in the laboratory during toxin operations whenever high-risk procedures are performed including, but not limited to:
 - i. Working with more than one human lethal dose
 - ii. Intentional creation of aerosols;
 - iii. Working with powdered/lyophilized toxins
 - iv. Creating primary containers
 - v. Work involving a fast-acting toxin
- d) Both individuals must be familiar with all the procedures being performed, the signs and symptoms of possible exposure, emergency response and first aid

7.2 LABORATORY ACQUIRED INFECTIONS

Individuals working in a laboratory that handles infectious substances may be at risk of exposure to the substances. There are a number of ways in which infectious substances can enter the body and cause infection, including ingestion, injection, inhalation, or contact. The types of events that lead to an exposure or infection include spills and splashes, needle stick injuries, cuts, bites or scratches, or other laboratory accidents.

Over 5000 cases of laboratory acquired infections (LAIs) and 190 deaths have been reported up to 1999 [18]. These numbers are believed to be underestimated due to underreporting. Approximately 80% of all reported LAIs were not linked to any notable event or laboratory accident. Proper operational practices and techniques must be used to minimize the risk of exposure. See CLSI *Laboratory Safety* [10] document for specific operational practices that are required at the CLS.

7.3 BLOODBORNE PATHOGENS

Bloodborne Pathogens are pathogenic microorganisms that are present in human blood and can cause disease in humans. These pathogens include, but are not limited to, hepatitis B virus (HBV) and human immunodeficiency virus (HIV). All unfixed human tissues, blood and other body fluids may contain bloodborne pathogens and are considered biohazardous substances at the CLS. Body fluids, other than blood, which may contain bloodborne pathogens include:

- Semen
- Vaginal secretions
- Synovial fluid
- Cerebrospinal fluid
- Pleural fluid
- Peritoneal fluid
- Pericardial fluid
- Amniotic fluid

Universal precautions must be used when handling any materials that may contain or may be contaminated with bloodborne pathogens. Universal precautions describe a prevention strategy where all blood and potentially infectious materials are treated as if infectious regardless of the health status of the source individual. Universal precautions include the following:

- Always wear PPE when there is any risk of exposure
- Remove PPE that is torn or punctured or has otherwise lost its ability to function as a barrier to bloodborne pathogens
- Use goggles, aprons and/or face shields when there is a risk of splashing or aerosolization
- Practice proper hygiene and use good hand washing technique
- Use safety engineered sharps and practice safe sharps disposal

In general, manipulations should follow Containment Level 2 operational practices [10].

7.4 UNCONVENTIONAL PATHOGENS

Some progressive neurological diseases (transmissible spongiform encephalopathies (TSE)) are caused by "unconventional pathogens" such as prions (proteinaceous infectious particles). Examples include Creutzfeld-Jacob disease in humans, Bovine Spongiform Encephalopathy in cattle and Scrapie in sheep and goats. These agents are resistant to destruction by chemical (10% formalin, glutaraldehyde, 70% ethanol, iodine) and physical (UV light, ionizing radiation, boiling) treatments that normally inactivate other pathogens.

Tissues more likely to contain prions include brain, spinal cord, dura matter, pituitary, and eye (optic nerve and retina). Tissues less likely to contain prions include cerebrospinal fluid, kidney, liver, lung, lymph nodes, spleen and placenta.

The most likely route of transmission for prion disease agents to humans is through ingestion or inoculation. Procedures to avoid accidental cuts and punctures as well as proper hygiene are the best approaches to protect workers. PPE such as cut resistant gloves should be used and care must be taken to avoid punctures. The following precautions should be observed when handling neurological tissue from infected or potentially infected humans or animals:

- Handle tissue as RGL2 or higher
- Handle formalin-fixed tissues and paraffin-embedded blocks as if infectious
- Follow up-to-date disinfection protocols

Note: Prion work is not currently permitted at the CLS.

7.5 METHODS FOR MINIMIZING AEROSOL HAZARDS

- a) Aerosol formation is potentially the most significant source of contamination when working with biohazardous materials
- b) Aerosols remain airborne for long periods and can easily travel throughout the laboratory contaminating surfaces
- c) Certain laboratory methods are known to create aerosols and proper technique can minimize this hazard
- d) Using an Inoculating loop
 - i. Only use closed loops with a shank no longer than 6 cm in length (prevents vibrations)
 - ii. Ensure loop is cooled prior to inserting into the culture
 - iii. Do not heat loop in open flame
 - a. Use micro incinerator or disposable loops
- e) Plating cultures
 - i. Streak plate only where the surface is smooth
- f) Pipetting
 - i. Always use mechanical pipetting aids
 - ii. Do not force out last drop in pipette/ pipette tip
 - iii. Drain pipette gently with the tip against the inner wall of the vessel
 - iv. Work over absorbent material (e.g. plastic backed pad)
 - v. Do not mix material by alternate suction and expulsion through a pipette (use a vortex mixer)
- g) Centrifugation
 - i. Use sealed safety cups and sealed rotors
 - ii. Load and unload cups in BSC
- h) Blending and homogenizing
 - i. Only use laboratory blenders with tight fitting gasket lid and leak proof bearings

- ii. Wait for aerosols to settle before opening lid

i) Opening tubes

- i. Avoid using tubes with push-in or screw-in closures
- ii. Use vortex mixer instead of inverting tubes to mix
- iii. Wait 30 seconds after mixing to open tube
- iv. Open tubes of biohazardous materials in BSC only

j) Pouring infectious material

- i. Do not pour off supernatant, cell washes etc. Use pipettes or aspirators instead

k) Breakage of containers

- i. Use plastic containers when possible
 - a. Plastic minimizes risk of aerosols and accidental cuts due to container breakage

8.0 CONTAINMENT LEVELS

The classification of organisms to risk groups is not meant to establish the actual handling of biological materials in the laboratory. Containment levels provide users with a description of the minimum containment required for handling an organism safely in a laboratory setting. The containment level describes the engineering, operational, technical and physical requirements for manipulating a particular pathogen. The containment levels are applicable to diagnostic, research and clinical facilities. There are specific containment requirements for facilities that will house animals and are covered in the CLSI *Animal Care and Use* [2] document.

8.1 CONTAINMENT LEVEL 1

8.1.1 Laboratory (CL1)

This level applies to the basic laboratory handling agents requiring containment level 1. CL1 requires no special design features beyond those suitable for a well-designed and functional laboratory. Biological Safety Cabinets (BSCs) are not required. Work may be done on an open bench top and containment is achieved through good microbiological laboratory techniques and practices [19].

8.2 CONTAINMENT LEVEL 2

8.2.1 Laboratory (CL2)

This level applies to the laboratory handling agents requiring containment level 2. The primary exposure hazards associated with organisms requiring CL2 are through the ingestion, inoculation, and mucous membrane route. Agents requiring CL2 facilities are not generally transmitted by the airborne route, but care must be taken to avoid the generation of aerosols (aerosols can settle on bench tops and become an ingestion hazard by contamination of the hands) or splashes. Primary containment devices such as BSCs and centrifuges with sealed rotors or safety cups are to be used, as well as personal protective equipment (gloves, laboratory coats, protective eyewear). BSCs must be used for procedures that may produce infectious aerosols. Environmental contamination must also be minimized by the use of hand washing sinks and decontamination facilities (autoclaves) [19]. Biohazard signs must be posted at the entrance to a CL2 area when work involving RGL2 organisms is occurring and entry into the lab is restricted.

Proper operation of a BSC can be found in the *Biological Safety Manual Operation and Maintenance Procedure* [23].

CL2 is the highest level of containment at the CLS.

8.3 CONTAINMENT LEVELS 3 & 4

The CLS does not have containment level 3 or 4 facilities. For additional details see the *Canadian Biosafety Standard and the Canadian Biosafety Handbook*, as amended from time to time [19].

8.4 OPERATIONAL PRACTICES

For operational practices for CLS laboratories please see CLSI *Laboratory Safety* [10].

9.0 EXPOSURE CONTROL PLAN

An Exposure Control Plan (ECP) is required for all work that involves unsealed biohazardous materials at the CLS. The spokesperson or designate must supply the CLSI HSE department with an ECP for review. The ECP should offer enough detail so that someone not familiar with the Project should be able to follow it. The ECP will be included with the permit and posted where the biohazardous materials are in use. The ECP should include, but is not limited to:

- Pathogen details
- List of workers who may be exposed during the course of the experiment
- Ways in which the material can enter the body and the risks associated with entry
- Signs and symptoms of any illness that may arise from exposure
- Proper handling of hazards (describe safety control measures: PPE, engineering controls, etc.)
- Emergency response procedures for spills and worker exposure

- Methods of cleaning, disinfection and disposal of any materials or equipment that may become contaminated with hazardous materials
- Immunization Program and/or Medical Surveillance, if required

The CLS has an Exposure Control Plan template available for use [7]. Contact the Biological, Chemical and OHS Lead for details.

10.0 DECONTAMINATION

A basic principle of biosafety is that all contaminated materials be decontaminated prior to disposal. Decontamination includes both *sterilization* (the complete destruction of all microorganisms including bacterial spores) and *disinfection* (the destruction and removal of specific types of microorganisms). Sterilization is most commonly done with the use of an autoclave and disinfection through the use of different chemicals.

Users must ensure that disinfection procedures specific to the particular organism to be used are forwarded to CLSI HSE for review prior to its use at the CLS.

10.1 AUTOCLAVING

The use of saturated steam under pressure (autoclaving) is the sterilization method most often used and is the most dependable procedure for ensuring the complete destruction of microorganisms. The autoclave is located in Room 1118.

10.2 CHEMICAL DISINFECTION

The following factors can influence the effectiveness of any disinfectant:

- Concentration of the chemical being used
- Presence of organic material
- Amount of time required for the chemical to be effective
- Temperature and pH at which the chemical is effective
- Level of contamination involved
- Type of contamination involved
- Physical characteristics of the contaminated surface/object

Microorganisms vary in their susceptibility to the action of chemical agents. Generally, lipid-containing viruses are the most susceptible. Then in order of increasing resistance are: vegetative bacteria, fungi, non-lipid viruses, *Mycobacterium tuberculosis*, *Coccidia*, bacterial spores and prions. The latter are the most difficult to inactivate / destroy. It is important to know both the characteristics of the chemical agent and the biological agent involved to ensure an effective decontamination procedure.

10.2.1 Disinfectants Include:

Chlorine: Effective against vegetative bacteria, mycobacteria, viruses, fungal spores and some sporicidal activity. Working solutions should be prepared fresh and kept in light-protected containers. Minimum contact time of 15 minutes. For prion materials, 2% free chlorine solution with a minimum of 1-hour contact time is recommended.

Alcohols: 70% alcohol is most effective against enveloped viruses and vegetative bacteria. Longer exposure is required against fungi and mycobacteria, and there is no activity against bacterial spores.

Phenolics: Generally used with detergents. Effective against enveloped viruses and vegetative bacteria. They are not as effective against fungi and mycobacteria and no activity against bacterial spores.

Quaternary Compounds: Colourless, odourless and non-irritating. Their effectiveness is reduced by organic material. They are effective against Gram-positive bacteria and they have limited effectiveness against enveloped viruses, fungi, and Gram-negative bacteria.

Glutaraldehydes: Broad spectrum of antimicrobial activity including non-enveloped viruses and mycobacteria. Limited shelf life and could cause adverse health effects including mucus membrane irritation and contact dermatitis.

Hydrogen Peroxide: Effective against vegetative bacteria, mycobacterium, fungi, viruses, and spores. It is incompatible with aluminum, copper, zinc, and some plastics.

Table 10.2.1 Relative Susceptibility of Microorganisms to Chemical Disinfectants

Susceptibility	Infectious Agent	Disinfectants reported to be effective
Extremely Resistant	Prions	Unusually resistant to chemical disinfectants. High concentrations of sodium hypochlorite or heated strong solutions of sodium hydroxide are reported to be effective
Highly Resistant	Protozoal oocysts	Ammonium hydroxide, halogens (high concentrations), halogenated phenols
	Bacterial Endospores	Some acids, aldehydes, halogens (high concentrations), peroxygen compounds
Resistant	Mycobacteria	Alcohols, aldehydes, some alkalis, halogens, some peroxygen compounds, some phenols
	Non-enveloped viruses	Aldehydes, halogens, peroxygen compounds
Susceptible	Fungal spores	Some alcohols, aldehydes, biguanides, halogens, peroxygen compounds, some phenols
	Gram-negative bacteria	Alcohols, aldehydes, alkalis, biguanides, halogens, peroxygen compounds, some phenols, some Quaternary Ammonium Compounds
	Enveloped viruses	
	Gram-positive bacteria	
Highly Susceptible	Mycoplasmas	Acids, alcohols, aldehydes, alkalis, biguanides, halogens, peroxygen compounds, phenols, Quaternary Ammonium Compounds

Quinn P, Merkey BK, Disinfection and Disease Prevention in Veterinary Medicine, *Disinfection, Sterilization and Preservation*, 5th edition. Lippincott Williams and Wilkins, 2001:1069-1103

11.0 HAZARDOUS WASTE DISPOSAL

Hazardous waste material must be segregated, collected and disposed in accordance with the *Hazardous Material Management Plan* [8], as well as the *Laboratory Waste Disposal* procedure [22].

The following general principles must be followed with respect to the generation and disposal of hazardous waste:

- Minimize the generation of hazardous wastes
- Segregate biohazardous and non-biohazardous waste at the point of generation
- All biohazardous waste must be collected in appropriate containers and rendered harmless by either chemical decontamination or heat sterilization before internally disposed.
 - The majority of biological waste at the CLS is collected, sealed and sent for disposal through a third-party vendor, in association with the University of Saskatchewan.

12.0 EMERGENCY PROCEDURES

Laboratories working with biological material must be prepared to deal with a spill. Laboratories are equipped with spill kits and workers must be familiar with the *CLSI Emergency Response Plan* [5] and associated biological spill procedures.

The *CLSI Emergency Response Plan* [5] outlines the steps to be taken if there is a failure of the safety equipment (e.g. fume hood, BSC) along with other emergencies such as fire and bad weather.

13.0 TRANSPORTATION

Transport of biohazardous materials to, from and within the CLS facility must follow the *CLSI Sample and Material Transport Procedures* [12]. All biohazardous substances must remain contained in sealed, leak-proof sample holders or primary containers when outside the designated laboratory. The sample holder or container must have its surfaces disinfected to ensure external sterility and be transported within a secondary container in case the primary container breaks or leaks.

Transportation of infectious substances within Canada is regulated by Transport Canada's *Transportation of Dangerous Goods Regulations* [21]. Transport Canada defines the labeling, packaging and documentation requirements for shipping infectious substances within Canada. Shipping regulations for infectious materials by air are defined by the International Civil Aviation Organization (ICAO) and the International Air Transport Association (IATA) [17].

13.1 IMPORT AND EXPORT OF PATHOGENS

Importation and transfer of human pathogens is controlled by the *Human Pathogens and Toxins Act* [14]. A Pathogen and Toxin license is maintained by the Biosafety Officer. This information is supplied to customs in the event that a human pathogen requires importation into Canada.

Importation of animal and plant pathogens is regulated by CFIA. Permits are required for importation of all animal and plant pathogens into Canada. The CLS must submit a Facility Certification for the Importation of Animal Pathogens form along with the Application for Permit to Import form in order to obtain an import permit. If animal pathogens are brought into Canada under a permit that restricts its distribution within Canada further approval from CFIA is required before the pathogen can be transferred.

13.2 NEW SUBSTANCES NOTIFICATION

Regulation of substances new to Canada falls under the Canadian Environmental Protection Act (CEPA). New substances include chemicals, polymers, inanimate and animate products of biotechnology ("biotechnology" is not limited to genetic engineering; animate products may be naturally occurring or genetically modified) [15]. CEPA requires a pre-import or pre-manufacture assessment process for new substances. Environment Canada must receive notification from the company or individual that will be importing or manufacturing the new substance. This notification will then be assessed by the departments of Environment and Health to determine if there is any risk to human health, the environment or its biological diversity.

The Domestic Substances List [14] is used to determine if a substance is "new". Any substance that is not on this list or is a domestic substance used for a significant new activity is subject to notification. Micro-organisms or other organisms which are used for research and development and are used below the maximum quantities within proper containment facilities are exempt from notification. The maximum quantity to be imported must be under 50mL or 50g (includes micro-organism and media).

14.0 BIOSECURITY

The Public Health Agency of Canada requires facilities handling infectious agents to have a biosecurity plan in place. Biosecurity is implemented to prevent the theft, misuse, or intentional release of pathogens. A primary component to a biosecurity plan must be a detailed risk assessment and should review and list the relevant assets, define the threats, outline the vulnerabilities, and determine the countermeasures or mitigation strategies specific for each facility. The biosecurity plan should then address the following factors: physical protection, personnel suitability/reliability, pathogen accountability, and related incident and emergency response [19]. At the CLS, the highest level of infectious agent in use will be RGL2; therefore, the biosecurity risk is low. Even so, the CLSI has systems in place to prevent the misuse, theft, and intentional release of pathogens that may be used.

14.1 CLSI BIOSECURITY PLAN

14.1.1 Risk Assessment

Each experiment conducted at the CLS is reviewed by the CLSI HSE department for health, safety and environmental concerns. This review identifies all hazards, precautions and controls required for the experiment, and created an ECP. Once approved, the user group can sign onto the Project during their scheduled beamtime. They are also able to use lab space, by reserving workstations within the e-USO portal.

14.1.2 Physical Protection

The CLSI has policies in place to restrict the access of individuals to the facility. These policies are outlined in the *CLSI Health, Safety and Environment Manual* [9]. The CLS facility has a card access security system in place which restricts entry into the building and to specific areas within the building to authorized personnel. When biohazardous materials are in use biohazard signs are posted at the beamline and the lab where the materials are being used or stored. When the signs are posted, access to these areas is restricted to authorized personnel. The CL2 laboratory used for biohazardous work is equipped with a card reader that allows the CLS to physically restrict entry into this area when biohazardous materials are in use.

14.1.3 Personnel Suitability/Reliability

Access to the facility and to specific areas within the CLS facility is limited to registered users and CLSI employees and contractors who have completed specific training or who are escorted by trained personnel. All visitors to the CLS are required to be escorted by trained personnel. Any non-compliance will be corrected and reported to the individual's manager. During the use of RGL2 organisms, access to the lab where the materials are being used or stored will be restricted to those individuals on the permit and those on official business with appropriate training or supervision.

14.1.4 Information Management

All information regarding experimental design is kept secure using an internal database, which is segregated from other internal systems. Access to this system is controlled with username and password as well as permissions based on employee role within the CLS. Access to the CLS intranet and other internal databases (training, etc.) is managed through username and passwords as well as based on the role assigned within the CLS.

14.1.5 Accountability

When an experiment is being performed at the CLS, the Project must be handed over by beamline staff and signed on by Users prior to commencing the experiment. Lab workstations must be booked using the active Project within the e-USO system. These Projects list all materials and controls to be used. The samples must be secured when not directly supervised.

If RGL2 materials are used at the facility, they must be signed in and out by the CLS Lab Coordinator, Biological, Chemical and OHS Lead, or designate. Materials not being used must be stored in CL2 containment within the Life Science Lab. The Biological, Chemical and OHS Lead maintains an inventory of biohazardous materials based on the experimental schedule. Biohazardous materials arrive at the start of the scheduled experiment and are removed at the end of the experiment. Regular inspections of the storage locations within the lab ensure no biological materials remain at the facility. If any biological materials are discovered, the spokesperson will be contacted. If the materials are not claimed, they will be properly disposed of at a cost to the spokesperson.

14.1.6 Biosecurity Incident and Emergency Response

At the CLS facility “all accidents, occupational diseases and other hazardous occurrences affecting anyone at the CLS facility or the environment must be investigated by a qualified person appointed by the CLSI HSE Manager or designate” [9]. The loss or theft of any quantity of biohazardous materials, or an attempted or actual breach of security or sabotage is considered a hazardous occurrence and the CLSI HSE department must be immediately notified. The CLSI document *Event Evaluation, Investigation and Reporting* [6] document outlines the procedures for event evaluation, event investigation and requirements for reporting to outside agencies. Since only RGL1 and RGL2 materials are allowed at the CLS, the risk presented by these materials if lost or stolen is low.

The *CLSI Emergency Response Plan* [5] outlines the responses to multiple types of emergencies. In the event that an unauthorized person is in an area of restricted access, they will be immediately escorted out of the area, and the CLSI HSE department contacted. If the unauthorized person is a potential danger to the CLS staff, the University of Saskatchewan Campus Security will be contacted.

15.0 REFERENCES

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- [2] *Animal Care and Use* (11.1.55.3)
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- [4] *CLSI Ethics Procedure: When Animals are Involved* (22.1.1.4)
- [5] *CLSI Emergency Response Plan* (11.12.57.1)
- [6] *Event Evaluation, Investigation and Reporting Guideline* (11.1.52.5)
- [7] *Exposure Control Plan Form* (11.11.55.3)
- [8] *Hazardous Material Management Plan* (11.12.56.1)
- [9] *Health Safety and Environment Manual* (11.9.1.1)
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- [22] *Laboratory Waste Disposal Procedures* (11.7.56.7)
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REVISION HISTORY

<i>Rev.</i>	<i>Date</i>	<i>Description</i>	<i>Author</i>
A	2005-Oct-05	Original Draft	Allen Hodges
B	2007-Feb-05	Comments incorporated	Allen Hodges
0	2007-Dec-20	Issued for use (11.12.55.3). Renumbered as document changed from a plan to a guideline. Reviewed and revised by incorporating the Canadian Nuclear Safety Commission (CNSC) review comments	Corrine Harris
1	2008-Feb-07	Revised Sections 4.1, 4.2, 5.2, 8.0 and 12.0.	Corrine Harris
1A	2009-May-07	Corrected title from Biosafety Coordinator to Biological Safety Coordinator on title page. Moved section 3.0 to section 5.0. Added responsibilities in section 5.1 to 5.5. Removed details on RGL 3& 4 and CL3 & 4 as we limit work to RGL & CL 2. Added sections 7.0 (7.1 to 7.3), 9.0 (9.1 to 9.2). Added details on CLSI biosecurity Plan (sections 13.1.1.1 to 13.1.1.5). Added section on safety compliance, experiment audits and non compliance (section 14.0). removed reference not in text and added additional reference in Bibliography that are cited in text. Moved sections on animal containment to Animal Care and Use Guidelines (11.1.55.3). Alphabetized bibliography and changed corresponding references in text. Minor revisions to most other sections.	Jamie Van Cleemput
2	2009-Aug-10	Incorporated comments & Issued for use	Jamie Van Cleemput
2A	2014-Sep-23	Changed document name to CLSI Biosafety	Allen Hodges
3	2015-Jan-21	Issued for use.	Allen Hodges
3A	2015-Oct-19	Added information on aerosolized hazards, included reference for BSC use and maintenance, added Table 10.2.1 Relative Susceptibility of Microorganisms to Chemical Disinfectants	Meghan Allen
4	2016-Jan-07	Added information on the HPTR license, training for the Plan For Administrative Oversight, prion sensitive tissues. Added budgetary information to roles and responsibilities. Incorporated comments, issued for use.	Meghan Allen
4A	2016-Nov-02	Updated information as requested by Public Health Agency of Canada PAO review. Updated importation regulations.	Meghan Allen
5	2016-Nov-16	Issued for Use	Meghan Allen

5A	2017-Nov-01	Updated WHMIS information.	Stacie Rose
6	2017-Nov-18	Issued for use.	Stacie Rose
6A	2018-Jul-24	Updated permit and biosecurity information, Updated Biosafety Lead title.	Meghan Allen
7	2018-Dec-10	Incorporated comments, issued for use.	Meghan Allen
7A	2020-Apr-09	Annual review: updated titles, removed WHMIS 1988 referencing, included information that Prion work is not permitted at the CLS under the current licensing.	Meghan Allen
8	2020-Sep-11	Incorporated comments, issued for use.	Meghan Allen
8A	2025-Apr-08	Updated information on proposal review process, grammar and sentence structure, etc., removed reference to specific version of CBS and handbook, and replaced with "as amended from time to time"	Meghan Allen
9	2025-Apr-17	Issued for use.	Meghan Allen