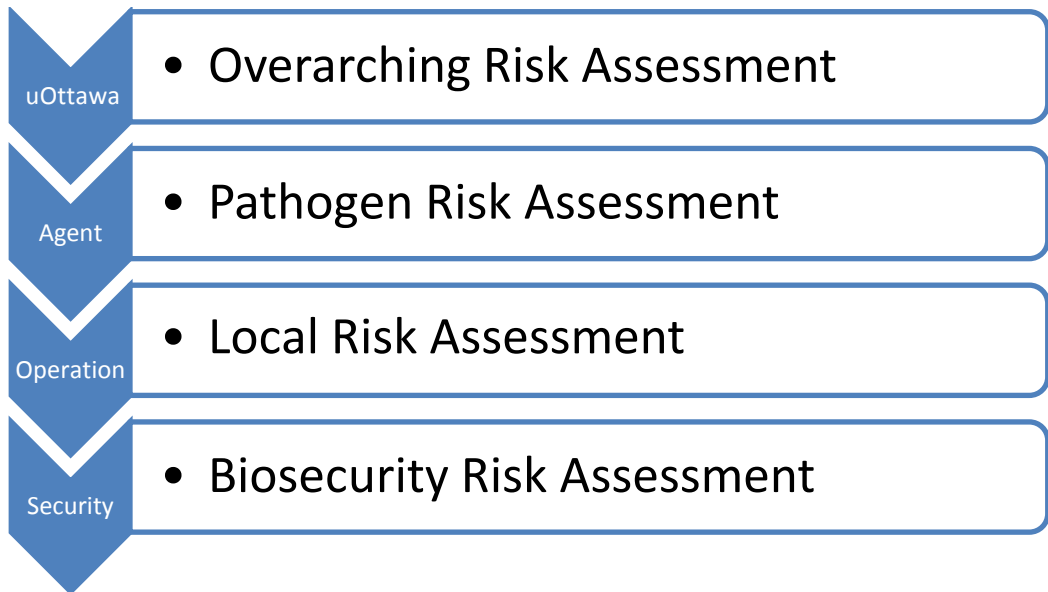


BIORISK ASSESSMENT PROCESS



uOttawa Biosafety Program

Protecting individuals, the environment and science is based on the risk inherent into the material used, the work undertaken, the design and execution of the experiment, and qualification of the personnel. This guide provides guidance on the risk assessment process.

**Office of the Chief Risk Officer
Current as of: 2023**

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1. INTRODUCTION

While this guide is designed to provide direction and to assist you in developing a biorisk assessment; it is by no means comprehensive, and the only way to address the risk assessment process. But regardless of the approach taken a documented risk assessment must exist and meet the standard set by the Regulatory Bodies (Public Health Agency of Canada (PHAC), and Canadian Food Inspection Agency (CFIA))and the University of Ottawa.

Note: A documented biorisk assessment is a legislated requirement.

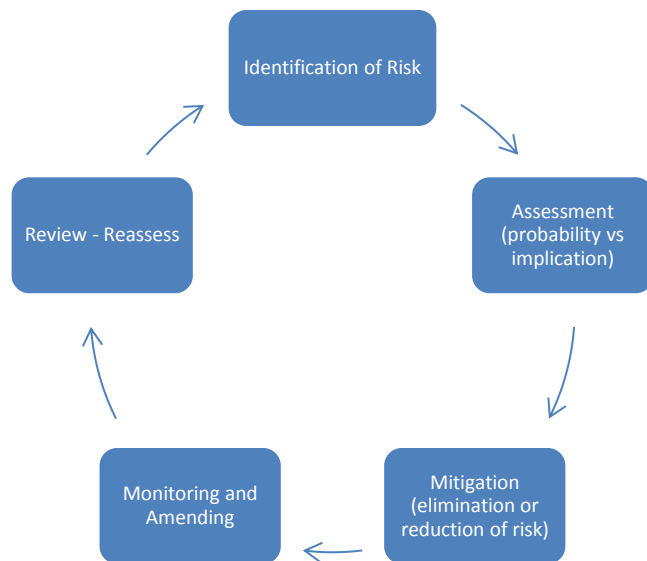
2. DEFINITIONS

The Public Health Agency of Canada defines biorisk assessment in four different ways depending upon the context.

- a) Overarching Risk Assessment** **Target: Biosafety Program**
- A broad risk assessment that supports the biosafety program as a whole and may encompass multiple containment zones within an organization. The overarching risk assessment identifies hazards, risks, and mitigation strategies for the proposed activities involving regulated materials. Mitigation and management strategies reflect the type of biosafety program needed to protect personnel from exposure and to prevent the release of regulated materials.
- b) Pathogen Risk Assessment** **Target: Pathogen**
- An evaluation of the inherent characteristics of a biological agent (i.e., microorganism, protein, nucleic acid, or biological material containing parts thereof), which determines its risk group classification. A pathogen risk assessment involves the analysis of four key risk factors including pathogenicity, pre- and post-exposure measures, communicability and impact on the animal population
- c) Local Risk Assessment (LRA)** **Target: Operations**
- A site-specific risk assessment used to identify hazards based on the regulated material in use and the activities being performed. This analysis informs risk mitigation and risk management strategies, which are to be incorporated into the physical containment design and operational practices of the facility.
- d) Biosecurity Risk Assessment** **Target: Security & Dual-Use**
- A risk assessment in which the regulated materials, and other related assets (e.g., equipment, animals, sensitive information, personnel, non-infectious material) are defined and prioritized, the likelihood of threats, vulnerabilities, and associated consequences are assessed, and appropriate mitigation strategies are recommended to protect these assets against potential biosecurity events.

The Canadian Food Inspection Agency risk assessment process targets the same types of concerns , but is applied to a much larger context; including live animals, semen, embryos, animal products and by-products, aquatic and avian species, plant pest and injurious organisms.

3. RISK ASSESSMENT PROCESS



While this may seem to be a lot of effort, support is embedded into the Biosafety Program and Institutional Approval

- Biohazardous Material Use Certificate (BMUC) and supporting document assist in documenting inventory, training and containment.
- It is recommended to discuss the risk assessment with a new user with a focus on the potential risk and mitigation strategies for their project. Hence if a copy is retained it assists in demonstrating due diligence. It is also a means of continuous review of the biorisk assessment for the lab.
- Biosafety Program will continue to identify means of supporting the research community by training, developing standard operating procedures where applicable or templates as needs arise.

SPECIFIC AREAS TO BE COVERED IN A BIOLOGICAL RISK ASSESSMENT ARE:

- Biological agent characteristics
- Research design – experimental protocols
- Lab operations: procedures, equipment, containment
- Personnel
- Security & Emergency Response

MITIGATION STRATEGIES:

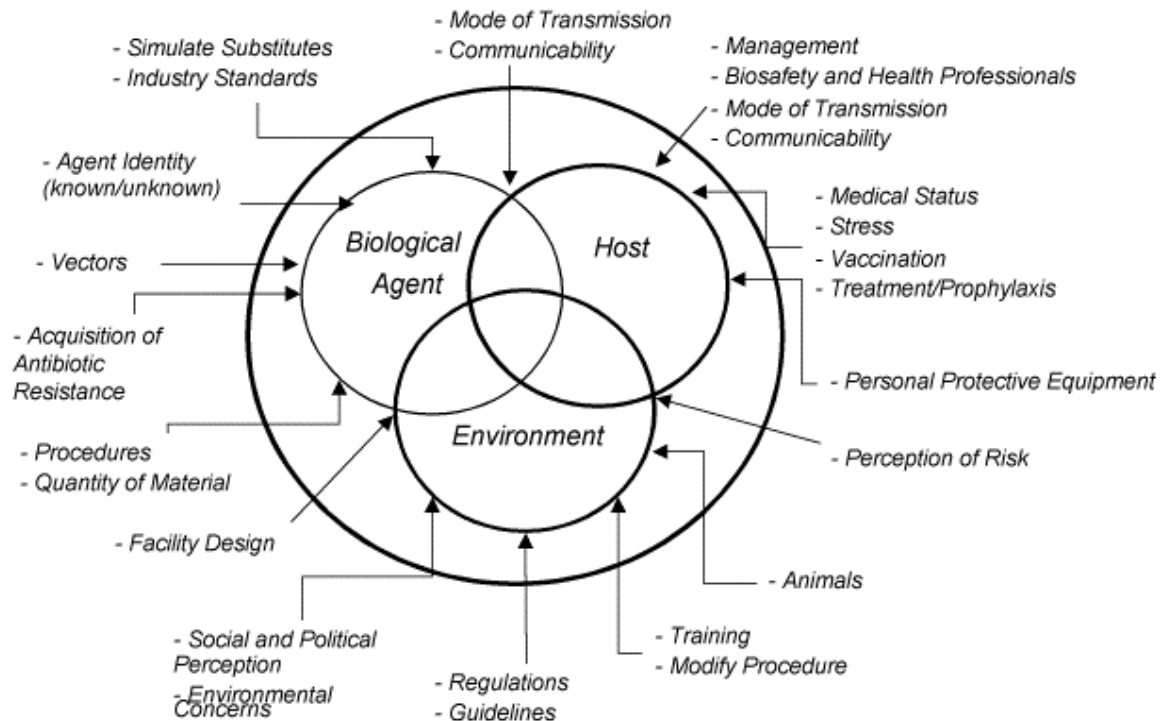
- Elimination, substitution, engineering control, administrative control, PPE
- Standardized processes
- Exposure Control & Medical Surveillance
- Training

SECURITY AND EMERGENCY RESPONSE:

- Regulatory concern over the potential for “Dual-Use”, engineered risk, or releases to the environment are driving the standards being set by Regulators
- Therefore these risks must be evaluated as part of the risk assessment process.
- In addition security of your own material and response of potential emergencies, such as equipment failure must be assessed and mitigated.

Figure 2. Expanded Risk Assessment Factors

Source: <https://www.absa.org/0100johnson.html>



UNDER PINNING THE RISK ASSESSMENT PROCESS is the growing concern of the potential risk of emerging infectious diseases (EID) and the relationship between human, domestic animal and wildlife EID. The scope being beyond the classical human and domestic animal, but to address the potential for cross-species infectivity, impacting agriculture and aquaculture, and the existing natural biomes, and the potential implications associated with emerging and invasive species. Thus international trade implications are impacting importation and exportation controls.

Recognition of this context is important as it helps in one's ability to identify, quantify and mitigate the risk that could result in the inadvertent exposure or release of biological agents with detrimental results.

THE BENEFITS OF UNDERTAKING A RISK ASSESSMENT ARE:

- Ensuring risks are identified and mitigated;
- preventing the accidental release or contamination of research samples;
- Demonstration of due diligence and compliance to regulatory requirements.
- Identification of training and supervision needs;
- Evaluation of procedural changes;
- Evaluating security controls; and

- Evaluation of emergency planning, including spill response.

FREQUENCY OF RISK ASSESSMENT:

The preferred timing of a risk assessment coincides with:

- planning the research project,
- a significant change in the project (a new infectious agent, or potentially infectious agent, new procedures or techniques, new equipment, a relocation of activities, or during/after renovations),
- Upon renewal of Biological Material Use Certificate (BMUC).

QUALIFICATIONS FOR A RISK ASSESSOR:

The qualifications required by these individuals and others mandated to undertake a risk assessment are:

- knowledge of the hazards associated with the material (pathogenicity, infectious dose, mode of transmission, environmental stability etc.);
- an understanding of the relationship between personnel, operational procedures, agent specific risk, work flow, and facility design;
- knowledge of the procedures and techniques which present risk ; and
- knowledge of containment requirements.

Communication is critical to ensure both junior and senior members of the laboratory are aware of the risk, implications and mitigation strategies employed.

4. OVERARCHING RISK ASSESSMENT

The uOttawa Biosafety Program is designed not only to identify and prioritize biorisk and security concerns but also to implement measures to mitigate this and to assist the University Community in addressing their role within this program whether they are direct users or have a support role. It responds to both regulatory initiatives, existing risk and trends in use practices and knowledge needs. Inherently this can only be achieved by assessing these factors and undertaking an overarching risk assessment process. Key elements are:

Biosafety Program	Risk identification, assessment, mitigation and management process undertaken at the uOttawa. Based on an Institutional Biosafety Approval (IBA), regulatory compliance monitoring and report, and facilitates compliance through standardize procedures, training, and education.
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Identification and risk assessment	Institutional Biosafety Approval (IBA) – disclosure of biological agents in use. Assess inventory and location enabling risk prioritization and mapping Searchable database. Identifies and analyzes trends. Undertakes and reviews risk assessment findings and ensures risk mitigation.
Containment Zone	Defines containment zones within the University, by Building, Faculty, and Department. Applies the Canadian Biosafety Standard and other containment standards. Considers HEPA inventory, location, certification and history, which are recorded, and reviewed. Assess life cycle management for critical equipment.
Mitigation Strategies	Implementation of Standard Operating Procedures. Develops and implements guidelines, policies and procedures. Writes informational bulletins on specific issues and risks.
Communication	Biosafety Program keeps track of key activities and issues pertaining to risk, security and compliance. Communicates to the Biosafety Committee and Deans current standing. Recommends, advises and champions appropriate measures to ensure compliance to senior management. “Bio-Bulletin” email correspondence highlights key initiatives, risk and changes to User community. Biosafety Web page primary access point for biosafety and biosecurity related information.

5. PATHOGEN RISK ASSESSMENT

PHAC has a free Pathogen Risk Assessment Course which introduces the concepts of risk assessment and risk groups and goes on to discuss the factors and methodology involved in assessing the risk of a pathogen or toxin. At the end of this course, learners will be able to identify the factors considered when undertaking a pathogen risk assessment. The following section summarizes risk factors.

**strongly recommended*

The pathogen risk assessment takes into account whether the biological material is considered a:

- Human pathogen
- Animal pathogen
- Aquatic pathogen
- Plant pathogen

It is also taken into account whether the pathogen is subject to official control.

- National Notifiable Diseases
- Domestic Substances List

- Reportable Diseases
- Immediately Notifiable Diseases
- Annually Notifiable Diseases
- Plant Protection Regulations
- Quarantine Act
- Foreign Animal Disease
- OIE Listed Disease (World Organization for Animal Health)
- Security sensitive biological agents (SSBAs)
- Australia Group List of Human and Animal Pathogens and Toxins for Export Control (for SSBAs)
- Or other control not listed here

Factors (Pathogen Safety Data Sheets: <http://www.phac-aspc.gc.ca/lab-bio/res/psds-ftss/index-eng.php>)

- Pathogenicity and Virulence
- Availability of effective prophylactic and therapeutic treatments
- Communicability
- Impact of Release
- Host Range
- Natural Distribution
- Unknown/Emerging Pathogen

PRODUCTS OF BIOTECHNOLOGY (Bt)

Products of biotechnology may include **Genetically Modified Organisms (GMOs), viral vectors, and synthetic biological devices and systems**. Although the risk group and containment level may have been determined for a particular pathogen, modifications to a pathogen that increase risks posed by the pathogen may result in changes to specific physical containment or operational practice requirements. Modifications may be intentional (e.g., through the use of recombinant DNA [rDNA] technology) or incidental (e.g., resulting from pathogen evolution following passage through an in vivo model).

- Does the modification alter pathogenicity or virulence or decrease the effectiveness of anti-infective agents?
- Does the modification alter pharmacological activity (e.g. resistance to antibiotics)?
- Does the modification delete genetic material or introduce novel genetic material with potentially adverse effects (e.g., insertion of an oncogene)?
- Does the inserted gene encode a toxin or a relatively uncharacterized toxin??
- Can the modification alter the host range or cell tropism?
- Does the modification create novel mechanisms or undesirable traits in transgenic animals?
- Does the modification produce attenuated strains of recombinant pathogens that have lost virulence factors?
- Does the modification produce host bacterial or viral vectors with limited ability to survive outside the laboratory?

- Is the genetically modified organism (GMO) replication competent?
- Can there be novel hazards of the GMO that may not be well characterized?
- Are potentially pathogenic factors associated with the donor nucleic acid segment?
- What are the properties of the donor nucleic acid segment?
- If the modification has resulted in a form of attenuation, how extensively has this strain been utilized without incident and/or has the attenuation been proven in animal models?
- Does the modification have an effect of increasing or decreasing the efficacy of available treatment or prophylaxis?

Bt- Risk Group 1 Risk Group 1 The modified biological material is a risk group 1 organism; the modifications have not changed the risk.

Bt- Risk Group 1 Risk Group 2 The wild type is a risk group 2 organism; the modifications have not changed the risk. DNA from risk group 2 or 3 organisms is transferred into risk group 1 organisms; but not the whole genome.

Bt- Risk Group 1 Risk Group 3 The modified biological material is a risk group 3 organism; the modifications have not changed the risk. The modified biological material is based on a risk group 2 organism, however, the modifications have increased the risk.

Bt- Risk Group 1 Risk Group 4 The modified biological material is a risk group 4 organism; the modifications have not changed the risk. DNA from risk group 4 organisms is transferred into risk group 1 organism in absence of demonstration of lack of virulence or pathogenicity.

CELL LINES

Many cell lines do not inherently pose a risk to the individuals manipulating them in the laboratory. However, cell lines can harbour infectious materials. A pathogen risk assessment should be performed for every new cell line that is manipulated in a laboratory in order to determine the appropriate level of precautions to be taken.

Cell cultures can carry unsuspected infectious material originating from their source or acquired through laboratory manipulation (e.g. viral transformation, contamination). Given the thousands of characterized cell lines and the thousands of species of human and animal pathogens, it would not be feasible or possible to test cell lines for the presence of every possible infectious agent.

As an alternative, the pathogen risk assessment for non-recombinant cell lines can be evaluated by considering the following factors.

- Source of cell line Provides an indication of possible contaminants and latent viruses. For example, tumor cells may have oncoviruses; some pathogens are predominantly found in their target tissue.
- Source tissue Provides an indication of possible contaminants and latent viruses. For example, tumor cells may have oncoviruses; some pathogens are predominantly found in their target tissue.
- Type May provide indication of potential risks. For example, primary cultures are not well characterized and may harbour pathogens from an infected donor; continuous cell lines have undergone a transformation to become immortal; intensively characterized, established cell lines may be less likely to contain infectious material;
- Source population The particular breeding group or colony of the specimen from which the cell line was derived can provide some indication of the likelihood a given pathogen is present. For example, cells from a 'specific pathogen free' primate colony are much less likely to harbour simian B virus than cells from 'wild caught' primates.

The particular breeding group or colony of the specimen from which the cell line was derived can provide some indication of the likelihood a given pathogen is present. For example, cells from a 'specific pathogen free' primate colony are much less likely to harbour simian B virus than cells from 'wild caught' primates.

These factors do not take into account the possibility of contamination from other cell lines that may have been handled simultaneously in the past. This is noted because there have been infections acquired in the laboratory that originated from a cell line that, unknown to the worker, had been contaminated with a pathogen.

- Modified or recombinant cell lines, the criteria discussed in the Products of Biotechnology section should be considered, as well as the potential activation of endogenous viruses present in many mammals.

Primary specimens Are those derived directly from a human or animal. These materials are covered by the uOttawa Biosafety program although the HPTA and HPTR do not apply to human pathogens or toxins that are in an environment in which they naturally occur (i.e., in primary specimens). It should be noted, however, that specimens obtained from an animal that has been intentionally exposed to a human pathogen or toxin (e.g., experimental infection or inoculation) is subject to regulation. Additionally, the HAA and HAR apply to any imported primary specimen that contains an animal pathogen or part of one that retains its pathogenicity, regardless of whether its presence is naturally occurring or not.

TOXINS *(additional information on the PHAC training on Toxin)*

In the laboratory setting, the routes of exposure for microbial toxins are similar to those for infectious agents, including ingestion, inhalation, and absorption (dermal, percutaneous, ocular).

Toxins are very potent, biologically produced poisons, and many have specific host targets. The symptoms of exposure to toxins are usually similar to those of infection with the host organism.

Handling purified toxin may be much more hazardous than handling its parent organism. If you plan on working with toxins, you should complete a toxin risk assessment.

MICROBIAL TOXINS

Microbial toxins In general, toxins are not volatile or dermally active. In a laboratory or biomedical setting, aerosols and needlesticks are the primary routes of infection. The potential for aerosolization is increased when working with the dry form, so solutions should be used whenever possible.

Specific issues to consider Toxins of greatest concern in the laboratory differ from those commonly associated with foodborne outbreaks. Common food poisoning outbreaks can lead to vomiting and diarrhoea, whereas ingestion of microbial exotoxins (e.g. Clostridium botulinum toxin) in even minute amounts can result in death.

In addition to the items already discussed in this course, the following risk assessment factors are specific to toxins:

- Amount of toxin being handled
- Degree of toxicity (intoxication/lethality dose data)
- Health effects data for exposure
- Lethal dose for specific toxin

Given the potency of some microbial toxins, every effort should be made to work with less than one human lethal dose of toxin.

Combining features of chemical and biological safety with a zero exposure approach is an effective way to mitigate risk. Extra care must be taken when handling multiple toxins, as toxin-toxin interactions can potentially alter a toxin's potency. If other hazards, such as infectious agents, are also handled, physical and operational controls for both hazards should be implemented.

The following tables summarize in general terms, factors to be considered and provide a rating scale which helps in determining the potential risk. A risk level one represents a minimal risk category, where as a risk level four indicates a very high potential risk to health or the economy. By considering each factor and assigning a risk level to each; one can quickly determine the overall risk level for an agent. Should one factor be judged to present a greater risk than the other, engineering and procedural controls should be implemented where possible to reduce this risk.

Table 1: Risk Summary Table

Risk Factor	Risk Group	Risk Factor	Risk Group	Risk Factor	Risk Group
Pathogenicity /virulence		Infectious Dose		Mode of transmission	
Transmissibility		Environmental Stability		Host Range	
Endemicity		Economic Considerations		Vectors	
Recombinants		Availability of Prophylactic and therapeutic treatments		Overall Risk Group	

Table 2: Risk Factor Assessment Table

Risk Factor	Risk Level 1	Risk Level 2	Risk Level 3	Risk Level 4
Pathogenicity / Virulence	Unlikely to cause disease, low individual and community risk	Mild or moderate disease, moderate individual risk, low community risk, any pathogen that can cause disease but under normal circumstances, is unlikely to be a serious hazard to a healthy laboratory worker, the community, livestock or the environment	Serious livestock, poultry or wildlife disease; high individual risk, low community risk: any pathogen that usually causes serious disease or can result in serious economic consequences or does not ordinarily spread by casual contact form one individual to another	Severe livestock, poultry or wildlife disease / high individual risk, high community risk, also causes human disease, any pathogen that usually produces very serious and often fatal disease, often untreatable and may be readily transmitted form one individual to another, or from animal to human or vice-versa, directly or indirectly, or by casual contact.
Infectious Dose	Not applicable (not known to cause disease)	Variable or high (1,000-5,000 organisms or greater)	Medium (10 –1,000 organisms)	High (1-10 organisms)
Mode of Transmission / Route of Infection	Not applicable (not known to cause disease)	Primary exposure hazards are through ingestion, inoculation and mucous membrane route (not generally through the airborne route)	May be transmitted through airborne route; direct contact; vectors	Readily transmitted, potential for aerosol transmission
Ability to Spread / Transmission / Communicability	Not applicable (not known to cause disease)	Geographical risk of spread if released form the laboratory is limited, or very limited; transmission is relatively limited	Geographical risk of spread if released form the laboratory is moderate, direct animal to animal or human to human transmission occurs relatively easily – transmission between different animal species may readily occur	Geographical risk of spread if released form the laboratory is widespread
Environmental Stability	Not applicable	Short term survival (days); can survive under ideal conditions	Resistant (days to months)	Highly resistant (months to years) e.g. spores
Host Range	Not applicable (not known to cause disease)	Infects a limited number of species	Infects multiple species	Infects many species of animals/ plants

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Endemicity	Enzootic	Generally enzootic (some low-risk exotics, zoonotics or reportable diseases)	Exotic, zoonotics or enzootic but subject to official control	Exotic
Economic aspects of introduction and/or release into the environment of the Canadian public	No economic and /or clinical significance	Limited economic and/or clinical significance	Severe economic and/or clinical significance	Extremely severe economic and/or clinical significance
Availability of prophylactic and therapeutic treatments	Not applicable (not known to cause disease)	Effective treatment and preventive measures are available	Prophylactic and /or treatments may or may not be readily available (or of limited benefit)	Prophylactic and/or treatments are not usually available
Vectors	Not applicable (not known to cause disease)	Do not depend on vectors or intermediate hosts for transmission May depend on vectors or intermediate host for transmission	May depend on vectors or intermediate host for transmission	May depend on vectors or intermediate host for transmission
Recombinants	The recombinant is a risk group 1 organism; modifications have not changed the risk	<p>The recombinant is a risk group 2 organism; modifications have not changed the risk</p> <ul style="list-style-type: none"> - DNA from risk group 2 or 3 organism is transferred into risk group 1 organism: but not the whole genome. - DNA from risk group 4 organism is transferred into risk group 1 organism (only after demonstration of a totally and irreversible defective fraction of the organism genome is present in the recombinant. - The recombinant is a risk group 3 or 4 organism, however, the modification has resulted in proven attenuation. 	<p>The recombinant is a risk group 3 organism; modifications have not changed the risk</p> <ul style="list-style-type: none"> - the recombinant is based on a risk group 2 organism, however, the modifications have increased the risk group to a 3. 	<p>The recombinant is a risk group 4 organism; modifications have not changed the risk</p> <ul style="list-style-type: none"> - DNA form risk group 4 organism is transferred into risk group 1 organism, without being able to demonstrate alack of virulence or pathogenicity.

7. BIOSECURITY RISK ASSESSMENT

The culmination of the risk assessment process is the determination that should the findings be that a risk exist that may or may be only partially mitigated, there still remains the need to ensure that the security measures are appropriate to the risk

While a supporting document has been drafted to address the security issues related to the material, and research activity; it is important that the completion of the risk assessment process provides the opportunity to assess the risk and what security measures are required.

PHAC Training module available at no cost:

<https://training-formation.phac-aspc.gc.ca/course/index.php?categoryid=7>

- Introducing Biosecurity
- Biosecurity Plan

The uOttawa Biosecurity Risk Document has been completed to meet the requirements.

8. RESOURCES

PHAC Training Modules <https://training-formation.phac-aspc.gc.ca/course/index.php?categoryid=7&browse=courses&perpage=20&page=0>

PubMed: <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi>

ProMed Mail: <https://promedmail.org>

<https://www.canada.ca/en/public-health/services/canadian-biosafety-standards-guidelines/third-edition>.

ABSA Risk Group Classifications: <https://my.absa.org/riskgroups>

OIE Technical Disease Cards: <https://www.woah.org/en/new-technical-disease-cards-on-line>

Merck Veterinary Manual: <https://www.merckvetmanual.com>

Biosafety in Microbiological and Biomedical Research Laboratories:

<https://www.cdc.gov/labs/pdf/CDC-BiosafetyMicrobiologicalBiomedicalLaboratories-2009-P.PDF>

Foreign Animal Diseases “The Gray Book”:

http://www.vet.uga.edu/vpp/gray_book/FAD/index.htm

Animal Health Australia - General Information about Animal

Diseases: <http://www.aahc.com.au>

<https://biosafety.wsu.edu>

CDC - Disease Information: <http://www.cdc.gov>

Diseases Database: <http://www.diseasesdatabase.com/index.asp>

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