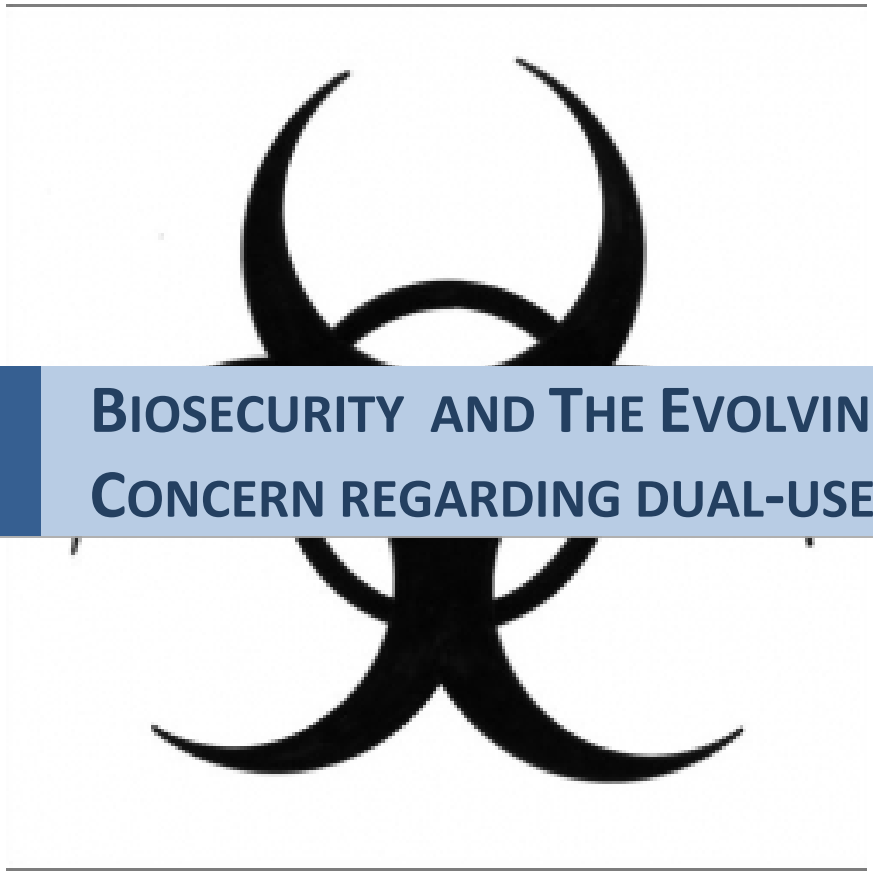
uOttawa



BIOSECURITY AND THE EVOLVING CONCERN REGARDING DUAL-USE

WHAT HAS CHANGED, AND WHAT MUST BE ADDRESSED

Office of the Chief Risk Officer

(OCRO)

INTRODUCTION

Biosecurity is a word that has been introduced into the regulatory framework with alarming regularly. Yet within the university community research direction is rarely directed to synthesis or modifying biological agents to make them more pathogenic, virulent, or to be candidates for malicious or dual use. For this reason the prospect of biosecurity concern is difficult to comprehend.

To understand the basis of the development of biosecurity oversight requirements, one must appreciate the issues driving the process in terms of the global perspective, technological advancements and accessibility to both information and materials which may pose new threats associated with the use of biological agents.

Strategic Initiatives, international partnerships, innovation and emerging technologies raise both the prospective of great beneficial discoveries, while at the same time represent a potential risk. This document will highlight some of the key issues.

HISTORICAL INCIDENTS and TRENDS

Founding events that lead to the development of biosecurity concerns can be traced back to the emergence of HIV, use of anthrax as an agent for terrorism, reconstruction of the influenza strain responsible for the Spanish flu, theft of *Yesinia pestis* from a laboratory among others.

Events such as those listed above ensure biosecurity fears remain in the forefront of legislative change.

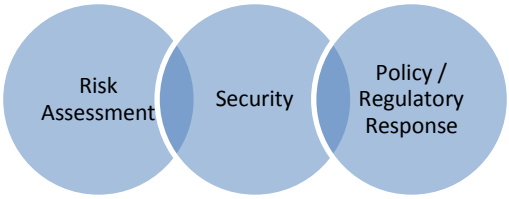
THREAT

Historically the threat assessment focused on international state conflict and limited to military security. It now encompasses:

- health, environmental degradation, climate change, organized crime, refuge migration, and terrorism,
- threat arising from transnational, international, and non-state actors, and
- focus on individual, group and community security versus solely state security.

The biosecurity debate revolves around:

- Are naturally occurring infectious disease a security threat?
- Do laboratory activities and advances in biotechnology pose a threat?
- What is the proper balance in biological life science between openness and security?
- What is an acceptable cost in terms of prevention of a biological threat and reacting to that threat?



The threat is also now being evaluated in terms of the social, economic and environmental impact on Canada being:

- able to fulfill its international obligations,
- avoid loss of revenue (health care, agriculture, aquaculture, forestry...), and
- prevent transfer of material, knowledge and individual.

BIOSECURITY

Biosecurity is defined as the security measures designed to prevent the loss, theft, misuse, diversion, or intentional release of regulated materials, and other related assets (e.g., personnel, equipment, non-infectious material, animals, sensitive information).

Biosecurity applies to:

- agriculture (crops and livestock),
- human and zoonotic agents and the environmental concerns,
- prevention or limiting the transmission of infectious pathogens or pest to animals or crops,
- to include risks to the economy associated with invasive non-indigenous species,
- also included genetically modified organism (GMO), and
- potentially restrict knowledge transfer.

In response to the biological terrorist threat the definition was expanded in the late 1990's to include the protection of microbial agents from loss, theft, diversion or intentional misuse.

Dual Use threat was added to the definition of biosecurity in 2004 by the US National Science Advisory Board in response to the 2001 Bioterrorism Anthrax Incident. The concept was extended beyond just the pathogenic agent to consider:

- techniques and technologies that can be used to create new pathogenic organisms or biologically active compounds,
- synthetic biology,
- systems biology,
- gene therapy,
- RNA interference, and
- genomics, neurobiology and immunology capacity to contribute to the development of biological weapons.

National Academies of Science has since expanded to be security against the inadvertent, inappropriate or intentional malicious or malevolent use of potentially dangerous biological agents or biotechnology including the: development, production, stockpiling or use of biological weapons as well as outbreaks of newly emergent and epidemic disease.

Regardless of the source of the definition,
it is the ever expanding definition that is important to note.

DUAL USE RESEARCH OF CONCERN (DURC)

PHAC defines dual use potential as “Qualities of a pathogen or toxin, scientific method, intellectual property, or other related asset that allow it to be either used for legitimate scientific applications (e.g., commercial, medical, or research purposes), or intentionally misused to cause harm or disease. Examples of assets with dual-use potential include pathogens or toxins that could be used as a biological weapon (i.e., for bioterrorism), a method that facilitates propagation of such pathogens in a non-traditional laboratory setting, or the discovery that a certain mutation results in resistance to all available treatments.

In assessing this risk, there are inherent bias embedded into life science research which must be recognized, these include principles such as:

- Research by its nature is to push beyond the known,
- The principle of “primum non-nocere” (above all, do no harm) is a founding principle, and
- the Canadian judicious system is based on the presumption of innocence.

Fundamentally the dual-use concern is based on:

- accessibility of information and materials,
- advancement of technology, and
- gain-of-function (GOF)

It is recognized that the benefit gained in undertaking DURC can justify proceeding in some cases. Hence there is a reliance on the process of the evaluation of the associated risk and the ability to eliminate the risk or to mitigate it if elimination is not achievable.

Resources and Procedures for determining dual use risk are found in:

Appendix A Decision Tree: Identification of Dual-Use Potential in Life Science Research.
Appendix B uOttawa Biosecurity and Dual Use Research of Concern: Identification, Evaluation, and Mitigation Guide.
Appendix C Security sensitive biological agents and toxins.
Appendix D Dual use research of concern reporting form.

There is a legal obligation in Canada and under the University's Human Pathogen and Toxins Licence to identify, evaluate, and mitigate any potential dual-use risk in research.

RISK ASSESSMENT

The risk assessment process is designed not necessarily to stop DURC, but to allow the risk and benefit to be assessed and to determine what mitigation and communication strategies need to be deployed to ensure the safe use and dissemination of information to be achieved.

Remember that risk is often expressed as an equation **(Risk=Impact X Probability / Cost),** so while there is a potential one must evaluate what the probability is, or the potential cost implications.

To delineate risk for DURC, and thereby minimize comprehensive review of all projects, a risk scale is being applied.

Category 1 Low risk exist as the material is either risk group 1 or 2 and the research has not been identified as having a potential DURC classification.

Category 2 Risk Group 2 material that has been modified such that there is a potential DURC risk.

Category 3 Security Sensitive Biological Agent or Toxin is being used, and/or associated technology, knowledge or product is deemed to meet the definition of DURC.

*Note: the following acronyms will be used to denote the categories: DURC-1, DURC-2 DURC-*3.

TRAINING AND EDUCATION

While it may be easy to disregard the risk; failure to do so will only justify regulators to increase the requirements for additional controls to be put in place which may not be required if diligence is applied throughout the life span of the research. A security culture will ensure your research property (material and intellectual) will be protected.

Developing the appropriate biosecurity culture requires continuous education, communication and enforcement. This document supports this goal.

Dual use activities require specific and more rigours training then the basic Principles of Biosafety, and will be tailored to the research at hand, with the involvement of the Office of the Cheif Risk Officer under the authority of the Biosafety Program.

IMPLICATIONS FOR RESEARCH

Biosecurity framework within the research laboratory is comprised of 7 key activities:

1. Physical requirements,
2. Personnel management,
3. Material control,
4. Accountability,
5. Information security,
6. Transportation security, and
7. Program management.

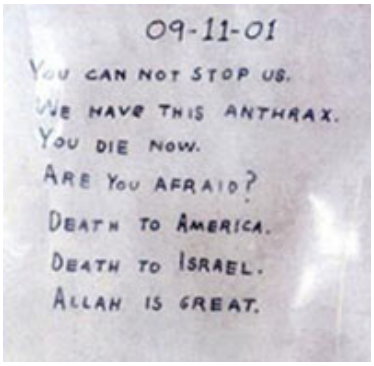
All parties in the laboratory are responsible for full filling these requirements, regardless if they are involved in the DURC project or not. Risk Assessments must be updated whenever experimental factors change, which would nullify the existing risk assessment: changes in experimental procedures, new experimental results, new sources of funding or collaborations, changes in personnel or inventory…

The University also adopts the following biosecurity framework, as good management practices for dual-use research management:

- guidelines,
- awareness,
- ongoing mandatory education,
- evaluation and review of research for dual-use potential,
- risk assessment and risk management,
- periodic evaluation and
- compliance

CLOSING REMARK

IT ONLY TAKES ONE PERSON TO CHANGE THE FACE OF REGULATIONS, RESEACH AND PUBLIC SECURIITY.



October 2001 U.S. Anthrax letter
Source: http://www.selectagents.gov

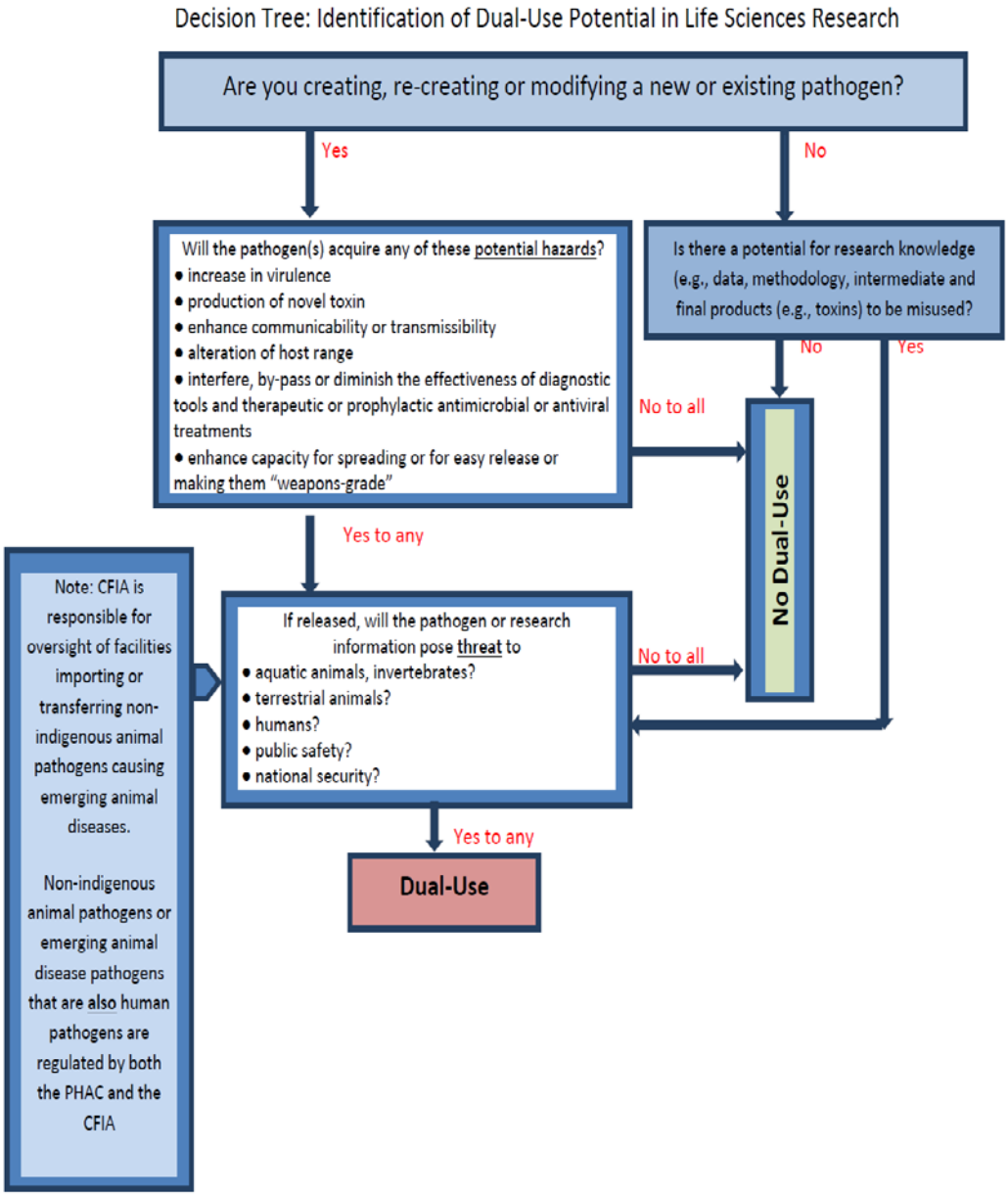
REFERENCES

International Security, Volume 34, Number 4, Spring 2010, pp. 96-132 **(Biosecurity Reconsidered – Calibrating Biological Threat and Responses**, G. Koblenz)

Science and Security in a Post 9/11 World: A Report Based on Regional Discussions Between the Science and Security Communities Committee on a New Government-University Partnership for Science and Security, National Research Council

SANDIA REPORT (SAND2010-6487)Printed October 2010, **Biosafety Risk Assessment Methodology** Susan Caskey*, Jennifer Gaudioso,Shigematsu++, George Risi+++Esmeralda Prat** Prepared by Sandia National Laboratories Albuquerque, New Mexico 87185 and Livermore, California 94550

APPENDIX A DECISION TREE: IDENTIFICATION OF DUAL-USE POTENTIAL



As per the Canadian Biosafety Guideline: Dual-Use in Life Science Research

Identification, Evaluation And Mitigation Guide

APPENDIX B uOttawa BIOSECURITY AND DUAL USE RESEARCH OF CONCERN: IDENTIFICATION, EVALUATION, AND MITIGATION GUIDE.

PURPOSE:

As required by the Canadian Government, it is important to determine if research activities may meet the classification of Dual User Research of Concern (DUCR). If the potential has been identified a risk assessment will determine if the potential benefits of the research out weight the risk, and if so can the risk be mitigated. This Guide will assist in undertaking this process.

TARGET AUDIENCE:

- Principal Investigators
- Biosafety Committee

DEFINITION OF DURC

PHAC defines dual use potential as “Qualities of a pathogen or toxin, scientific method, intellectual property, or other related asset that allow it to be either used for legitimate scientific applications (e.g., commercial, medical, or research purposes), or intentionally misused to cause harm or disease. Examples of assets with dual-use potential include pathogens or toxins that could be used as a biological weapon (i.e., for bioterrorism), a method that facilitates propagation of such pathogens in a non-traditional laboratory setting, or the discovery that a certain mutation results in resistance to all available treatments".

QUALIFICATION CRITIERIA FOR A DURC REVIEW

To delineate risk for DURC, and thereby minimize comprehensive review of all projects, a risk scale has been applied. To qualify the research must meet either a DURC Category 2 or 3, as described below.

Category 1 Low risk exist as the material is either risk group 1 or 2 and the research has not been identified as having a potential DURC classification.

Category 2 Risk Group 2 material that has been modified such that the following potential risks exist:

1. demonstrating how to render a vaccine ineffective,
2. conferring resistance to therapeutically useful antibiotics or antiviral agents,
3. enhancing the virulence of a pathogen or rendering a non-pathogen virulent,
4. increasing transmissibility of a pathogen,
5. altering the host range of a pathogen,
6. enabling the evasion of diagnostic/detection modalities, or
7. enabling the weaponization of a biological agent or toxin.

These are considered “experiments of concern”, or what are colloquially known as ‘the Seven Deadly Sins’

Category 3 Security Sensitive Biological Agent or Toxin (Appendix D) is being used, and/or associated technology, knowledge or product is deemed to meet the definition of DURC.

While the use of a SSBA will require additional security clearance by the Public Health Agency of Canada (PHAC), a comprehensive review may not be required if the “experiments of concern” are not planned. Note that annual reviews must be taken to ensure the research has not inadvertently incorporated the “experiments of concern”.

*Note: the following acronyms will be used to denote the categories: DURC-1, DURC-2 and DURC-*3 .

REVIEW PROCESS

1. **Verify if the research actually meets DURC criteria.**

2. **Review the Principal Investigators (PI) assessment of DURC potential and supporting rationale.**

   Review the PI assessment of the aims of the research products and see if it is anticipated to produce one or more of the applicable “experiments of concern”.

3. **Conduct a DURC risk assessment to determine what DURC criteria are involved, and the implications.**

   Research knowledge, information, technology and products could pose a risk of being misapplied and hence a threat to human, agriculture, environment, material and national security. The risk assessment is designed to identify:
   - in what ways this could occur; the ease by which this could occur by a third party and; the magnitude, nature and scope of potential misuse.

a) **The ways** in which knowledge, information, technologies or products from research could be used to harm: people, crops, animals, environment, economy or security.

- What type of knowledge, information, technology, or product is anticipated?
- How will results be shared, who will have access, closed or open distribution?
- What is the novelty, has it been reported before, what venues, the level of detail?
- Are products of research transferable to other pathogens, applications
- Does the research highlight vulnerability to existing practices, knowledge, counter measures?

b) **The ease** with which the knowledge, technologies, or products might be misused and the associated feasibility.
    - Consider the technical expertise and physical resources required.
    - Could the research products be directly misused and how?
    - Does other requirements/information already exist that could make this research vulnerable for misuse?
    - What time frame implications exist to make this an immediate, or near future threat?

c) **The magnitude**, nature and scope of potential consequences of misuse.
    - Consider what will be impacted: public health, agriculture, environment, economy, or terrorism.
    - Degree of negative impact: minor, moderate or major.
    - Are there counter measures available to mitigate potential, and readily available.

4. Assess the benefits.

Note: Source of funding should be considered: scientific merit determined by funding agency input could be consulted. Material transfer agreements, contracts, and start –up funding may or may not consider this in terms of DURC implications.

- What is the benefit to public health and safety?
- What are the contributions of this project to agriculture, economy, security...?
- How will this research be beneficial to science, health and safety of our communities?
- What is the time frame associated with the gain of benefits?
- Who will gain the benefit (large or small impact), who will accept the risk?

5. Assist the PI in drafting a mitigation strategy

- Determine if existing biosafety and biosecurity measures are adequate.
- Evaluate applicability of existing countermeasures.
- Modify the experimental design or methodology to remove, reduce or mitigate the risk.

- Evaluate the efficacy of medical countermeasures against SSBA.
- Consider experimentation timelines to reduce viability in external environment.
- Develop a communication plan, defining what may/may not be distributed beyond the lab, published or posted on line.
- Determine the monitoring and report requirements to ensure the integrity and diligence of the application of the measures implemented.
- Determine if regulatory approval is required or recommended.
- If appropriate measures cannot be found the research is denied.

6. **Review (at least annually,) active DURC risk mitigation strategies**.
    - Determine what experimental results would require a reassessment prior to the annual review.
    - Assess if research still aims to/or does incorporate the “experiments of concern”.
    - Evaluate the effectiveness of the mitigation strategy based on experimental results.
    - If the definition and the experimental outcomes no longer apply, withdraw the DURC mitigation strategies.

REFERENCES:

Tools for the Identification, Assessment, Management and Responsible Communication of Dual Use Research of Concern, A Companion Guide to the United States Government Policies for Oversight of Life

Governing'dual-use"research in Canada: A Policy Review. Bryn Williams-Jones, Catherine Olivier and Elise Smith, Sicence and Public Policy (2013) pp1-18

Sciences Dual Use Research of Concern, Prepare by National Institute of Health, September 2014

Public Health Emergency - Science, Safety, Security Emergency
https://www.phe.gov/s3/dualuse/Pages/default.aspx

U.S. Government Gain-of-Function Deliberative Process and Research Funding Pause on Selected Gain-of-Function Research Involving Influenza, MERS, and SARS Viruses

APPENDIX C SECURITY SENSITIVE BIOLOGICAL AGENTS AND TOXINS

http://www.phac-aspc.gc.ca/lab-bio/regul/ssba-abcse-eng.php

Security Sensitive Biological Agents List – Viruses

- Andes virus
- Chapare virus
- Chikungunya virus
- Choclo virus
- Congo-Crimean haemorrhagic fever virus
- Dobrava-Belgrade virus
- Eastern equine encephalitis virus
- Ebola virus
- Guanarito virus
- Hantaan virus
- Hendra virus (Equine morbillivirus)
- Highly pathogenic avian influenza virus
- Japanese encephalitis virus
- Junin virus
- Kyasanur Forest virus
- Laguna Negra virus
- Lassa fever virus
- Louping ill virus
- Lujo virus
- Machupo virus
- Marburg virus
- Monkey pox virus
- Murray Valley encephalitis virus
- Nipah virus
- Omsk haemorrhagic fever virus
- Oropouche virus
- Powassan virus
- Reconstructed 1918 influenza virus
- Rift Valley fever virus
- Rocio virus
- Sabia virus
- Seoul virus
- Severe acute respiratory syndrome-related coronavirus (SARS-CoV)
- Sin nombre virus

- St Louis encephalitis virus
- Tick-borne encephalitis virus (Russian Spring-Summer encephalitis virus)
- Variola virus
- Venezuelan equine encephalitis virus
- Western equine encephalitis virus
- Yellow fever virus

Security Sensitive Biological Agents List – Bacteria

- Bacillus anthracis
- Brucella abortus
- Brucella melitensis
- Brucella suis
- Chlamydophila psittaci (formerly known as Chlamydia psittaci)
- Francisella tularensis
- Burkholderia mallei (Pseudomonas mallei)
- Burkholderia pseudomallei (Pseudomonas pseudomallei)
- Yersinia pestis
- Coxiella burnetii
- Rickettsia prowazekii

Security Sensitive Biological Agents List – Toxins (and trigger quantity)

- Alpha toxin (5 mg)
- Botulinum neurotoxin (0.5 mg)
- Cholera toxin (20 mg)
- Clostridium botulinum C2 and C3 toxins (5 mg)
- Clostridium perfringens Epsilon toxin (5 mg)
- Hemolysin (10 mg)
- Shiga-like toxin (verotoxin) (1 mg)
- Shigatoxin (1mg)
- Staphylococcus enterotoxins, Type B (1 mg)
- Staphylococcus enterotoxins, types other than Type B (10 mg)
- Staphylococcus aureus Toxic shock syndrome toxin (5 mg)

Security Sensitive Biological Agents List – Fungi

- Coccidioides immitis
- Coccidioides posadasii

Laboratories that work with strains of bacteria that produce SSBA toxins are not captured by the SSBA designation as long as the SSBA toxin is not produced to levels above the trigger quantity [i]. If work with strains of bacteria that produce SSBA toxins results in the production of quantities of SSBA toxins that exceed the SSBA toxin trigger quantities, the work would be subject to the SSBA designation.

APPENDIX D
DUAL USE RESEARCH OF CONCERN REPORTING FORM

Section A Principle Investigator

Name:	Biomaterial Use Certificate #:
Department:	Phone #:
Position:	Email :
	Laboratory Room #.

Section B Person preparing this Document (if not PI)

Name:	Phone#:
Email:	Position:

Section C Research Project

Title:	
Source of Funding:	
RE#, Contract #	
Start Date:	End Date:

Attach Protocol to be used:

Specific agent in use _____

SSBA: http://www.phac-aspc.gc.ca/lab-bio/regul/ssba-abcse-eng.php

Source of Material:

Company:
Individual:
Address:
Quantity:

Personnel:

Name	Position	DURC training	Security Clearance

Section D "Experiments of Concern"

PI's are required to assess their research project to determine if it involves specific experimental protocols which increase the risk associated with the outcome. If at least one criteria is met, a full DURC assessment must be undertaken.

1. Enhances the harmful consequences of the agent or toxin Yes No

   If yes, please explain how.

2. Disrupts immunity or the effectiveness of an immunization against the agent or toxin without clinical or agricultural justification. Yes No

   If yes, please explain how.

3. Confers to the agent or toxin resistance to clinically or agriculturally useful prophylactic ot therapeutic interventions against the agent or toxin or facilitates tits ability to evade detection methodology. Yes No

   If yes, please explain how.

4. Alters properties of the agent or toxin in a manner that would enhance its stability, transmissibility or ability to be disseminated. Yes No

   If yes, please explain how.

5. Alters the host range or tropism of the agent or toxin. Yes No

   If yes, please explain how.

6. Enhances the Susceptibility of a host population to the agent or toxin. Yes No

   If yes, please explain how.

7. Generates or reconstitutes an eradicated or extinct agent or toxin. Yes No

   If yes, please explain how.