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 must be undertaken to identify to 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
- Dual Use Research of Concern Biosafety Sub-Committee

DEFINITION OF DURC

While PHAC defines dual use as "Qualities of a pathogen or toxin that allow it to be either used for legitimate scientific applications (e.g., commercial, medical, or research purposes), or intentionally misused as a biological weapon to cause disease (e.g., bioterrorism)", which also includes: data, methodology, intermediate and final products.

The National Institute of Health in the United States has expanded the definition to: "Life science research that, based on current understanding, can be reasonably anticipated to provide knowledge, information, products or technologies that could be directly misapplied to pose a significant thereat with broad potential consequence to public health and safety, agricultural crops and other plants, animals, material or national security." This is of importance for US funded research or collaborations.

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 category 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 there is a potential DURC risk. Risk Group 2 material that has been modified such that the following potential risk exists:

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 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 DURC-3 .

REVIEW PROCESS

(DURC-1, DURC-2, & DURC-3)

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

   Note: To be confirmed with PHAC is the ability to excluded are attenuated SSBA genes of SSBA, in-silico experiments such as bioinformatics approaches , modeling experiments, health impact modeling of toxins, vaccine delivery methods, surveillance mechanisms), as this would align with US funding requirements.*

   *** Verify the proof of non-attenuation of material.

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 can reasonably anticipated to produce one or more the applicable "experiments of concern".

(DURC-2, & DURC-3)

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

   a) **The ways** in which knowledge, information, technologies or products form 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 of the DURC.**

   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

(Note not the complete listing off all documents reviewed)

APPENDIX A 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 B
DUAL USE RESEARCH OF CONCERN REPORTING FORM

PART ONE RESEARCH REPORTING

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 they contain SSBA or have experimental protocols that involve specific experimental protocols which increase the risk associated with the outcome. If at least one above criteria are 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.

PART TWO DURC RISK ASSESSMENT

Research knowledge, information, technology and products (KITP) 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.

1. **The ways** in which knowledge, information, technologies or products form 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
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    d) **The ease** with which the knowledge, technologies, or products might be misused and the associated feasibility.
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