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Development of a Threat Assessment Framework Applicable to Dual Use Biotechnology

Results of a Study to Determine the Feasibility, Applicability and Potential Design of a Threat Assessment Framework Concept

Lyle Makosky
InterQuest Consulting, Ottawa

Eric R. Stephen
Directorate of Science & Technology, Human Performance
Defence R&D Canada

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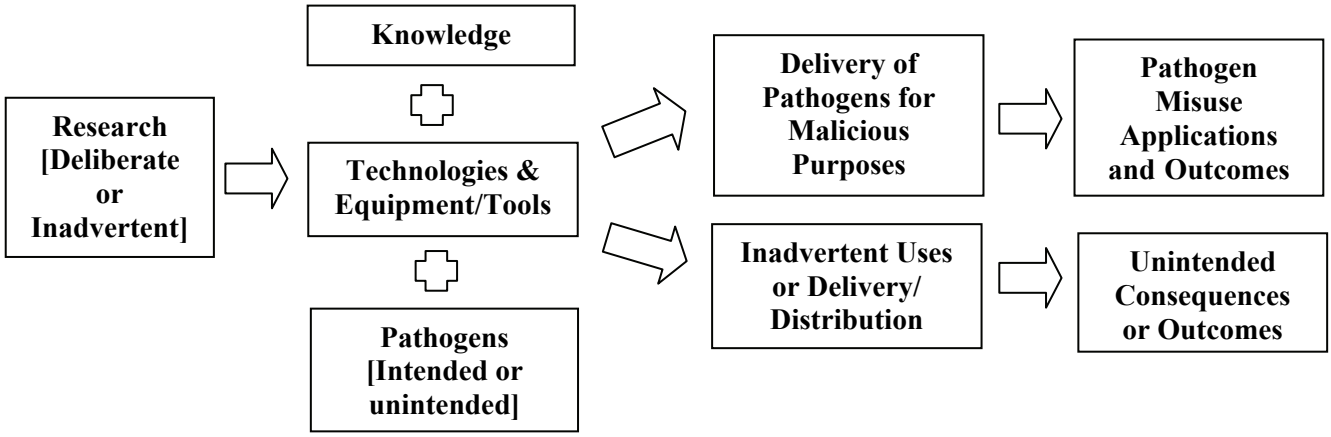
EXECUTIVE SUMMARY AND RECOMMENDATIONS

Canada needs a strategy and approach to deal with dual use biotechnology. The approach must be developed, shared and commonly applied by the key stakeholders implicated including scientists (private and public sector), R&D funding agencies, scientific publishers and their editors, security professionals and law enforcement (counter-terrorism), and government regulators. Following the first Canadian National Forum on Dual Use Biotechnology in March 2006, it was determined that a Canadian approach would need certain tools, analytical aids and guidance frameworks to inform the Canadian strategy. The concept of a Threat Assessment Framework (TAF) was projected to be one of those key aids and hence a study was commissioned to examine the feasibility, applicability and potential design of a Threat Assessment Framework Concept. A study was undertaken involving a preliminary literature review, scan of factors and drivers in the current context and an extensive set of interviews with subject matter experts (SME).

After preliminary conversations with experts and scanning initial literature in the field, it was evident that the dual use (DU) issue is very complex with different opinions on the scope and fundamental concerns and even the terminology to define and elaborate it. Therefore, to provide a conceptual starting point and terminology, we created a graphic portrayal of dual use as a process. This process view helps to deconstruct the complex idea into connected sequential and concurrent events/outputs and provides a topical reference point to examine the elements and issues involved in dual use biotechnology.



By using this conceptual process, we reasoned that we could design a threat analysis for each step/threat element which may enable a more discrete set of risk management strategies and policies to be applied to the different elements. As well, we should be able to create an overall assessment of a range of whole dual use threat processes (i.e., an identified research type yielding knowledge that is used to produce a bioterror pathogen applied in a defined set of societal conditions).

By arraying the process elements against a set of assessment components, as in the proposed concept for a Threat Assessment Framework table following, we can design a threat analysis for each process element (the table columns) and develop concepts, terminology and analysis tools for each assessment component (the table rows) and combine these into a threat assessment approach for whole DU processes (i.e., diagonal slices across the table).

Draft Concept for a Threat Assessment Framework

DU Process Elements / Assessment Components	Research (Deliberate or Inadvertent)	Knowledge (Creation and Dissemination)	Technologies & Equipment/ Tools	Pathogens (Intended or Unintended)	Delivery or distribution of Pathogens (Deliberate and Inadvertent)	Pathogen Misuse Applications (or Unintended Consequences or Outcomes)
1. Types						
2. Risk-Benefit Analysis						
3. Actors (inadvertent)						
4. Actors (deliberate)						
5. Potential will occur (inadvertent research)						
6. Probability will occur (deliberate research misuse)						
7. Impact if occurs (inadvertent or deliberate)						
8. Summary Analysis						
9. Threat Management						
10. Policy Position						

Through the interviews, the draft TAF concept was further elaborated and strengthened with added design thinking, concepts and reference examples to draw upon.

The results of the study indicated:

- Confirmation of the presence and seriousness of the DU challenge;
- Confirmation that Canada needs a strategy and policy to guide its approach to this challenge;
- The concept of a threat assessment tool or aid has great merit and would be very useful in supporting a Canadian approach;
- The concept of a threat assessment tool or aid is needed on a global level to: establish common terminology and models; set the agenda of concern; define common responses and enable a more common and collaborative approach;
- The preliminary concept for a TAF as outlined in the interviews (and in this report) was found to have great merit as an innovative approach with a very good starting focus and relevant elements, and it was urged that the concept be a starting point for further development of a TAF;
- The process of exploring and developing a TAF for Canada should be utilized to help create awareness, understanding and involvement among stakeholders of the DU challenge and the need for joint management responses, and to help socialize a sense of joint responsibility and the need for and approach to the concept of risk assessment and risk management in this area.

In the interview process, there were some concerns expressed about the concept of a TAF, in particular:

- Whether it could actually be developed and presented as a workable tool given the huge scope of misuse activities and issues involved, the complexity of the subject and the layered and detailed analysis implied. However, the draft concept was seen as a very promising and workable framework on which to proceed, accompanied by a strong urging to keep it understandable and workable.
- Whether it would dominate the Canadian strategy and drive policy rather than being seen as an aid or enabler to help inform strategy and policy. Nevertheless, the concept of a TAF was seen as an important, even critical, enabler to help inform strategy and policy development and hence the initiative should proceed with this caution in mind.
- Whether it would become the front edge of a move to adopt a severe, controlling approach that would unduly constrain bioscience research and the sharing of related knowledge or add another unwelcome and difficult administrative overburden to this science and knowledge sharing community. Participants were assured that the eventual use of the TAF as a tool is still to be determined and would be defined through multistakeholder involvement and that the stakeholders and sponsors involved in this initiative shared the intent to develop a Canadian approach (to dual use biotechnology) based on common awareness, self-governance and self-management, ethical principles/codes of conduct, shared responsibility and joint action, through as workable an approach as possible. Given this expressed intent, the TAF initiative was urged to proceed, especially given the benefits and enabling role perceived for such an aid.

The following are recommendations by the writer on the Threat Assessment Framework based on the literature review, the results of the SME interviews conducted and the experience in developing and reviewing the draft concept for a TAF as outlined in the report.

A Canadian approach to the dual use challenge needs and would be well supported by a Threat Assessment Framework. This framework would help to: scan for and scope the potential risks and threats involved and to determine which would merit attention and a joint approach and thereby to develop the 'Agenda of Concern;' define the necessary assessment terminology for common use and the reasoning and the basis of ratings and judgement to guide future assessments; allow the parties to assess typical and atypical/individual case threat events/activities to produce an assessment profile and summary rating that would enable threat prioritizing and a management emphasis to be developed; and determine joint strategies and policy positions to establish among the stakeholders in response to the agenda of concern and individual cases as they arise or are proactively projected to emerge.

Therefore, it is recommended that:

1. The concept of a Threat Assessment Framework (TAF) be pursued post haste and a model developed through the collaborative input of a cross section of stakeholders implicated in dual use biotechnology.
2. The TAF model should draw upon the draft concept outlined in this report and the feedback/lessons arising from its review in this study, accompanied by a strong urging to keep it understandable and workable.
3. There should be two TAF models for Canada. One TAF model would be focused on 'Legitimate research with inadvertent misuse' and the other on 'Illegitimate research with

deliberate misuse,' and would draw upon the concepts and learning in this study. Both would be designed with a global context and scope but would have subsections that consider the Canadian context and are tailored to specific conditions and the agenda of concern most relevant to Canada.

4. The TAF models be pilot tested with a selection of case examples that would fully explore the scope of the TAF and would be applied by a small expert stakeholder group.
5. The TAF model be utilized to:
   a. scan for and scope the potential risks and threats involved and to determine which would merit attention and a joint approach and thereby to develop the 'Agenda of Concern';
   b. define the necessary assessment terminology for common use and the reasoning and the basis of ratings and judgement to guide future assessments;
   c. allow the parties to assess typical and atypical/individual case threat events/activities to produce an assessment profile and summary rating that would enable threat prioritizing and a management emphasis to be developed.
6. The process of exploring and developing a TAF for Canada be utilized to help create awareness, understanding and involvement among stakeholders of the DU challenge and the need for joint management responses and to help socialize the concept of risk assessment and risk management in this area.
7. Through the development of the TAF, the stakeholders should determine joint Canadian strategies and policy positions in response to the 'agenda of concern' and for individual cases as they arise or are proactively projected to emerge. The Canadian approach (to dual use biotechnology) should be based on common awareness, self-governance and self-management, ethical principles/codes of conduct, shared responsibility and joint action, through as workable an approach as possible.
8. The TAF model, correlated strategies and policies be used to inform a Canadian international view and approach on dual use biotechnology and to advocate for an international Threat Assessment Framework, ideally based on the core concepts and learning of this TAF model when developed.

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1.0 INTRODUCTION

Advances in the biosciences over the past decade have been rapid and transformative. While these advances offer significant benefit to society, they also provide very significant challenges in terms of security. Concerns over misuse and/or accidental use/release (dual use) although not new, are now being viewed through a security lens. The increased degree of concern being voiced is reflective of the technological advances being achieved over ever decreasing time frames. The world stage has changed significantly, as have generation of and widespread access to scientific information that could easily, in many cases, be subverted to "terrorist" ends. This is illustrated through the breadth of knowledge growth and its dissemination in traditional fora, a growth in knowledgeable people able to comprehend this information base but also in technology advances that place the ability to act on the knowledge base at a very basic level. There is a wide-spread view that public or private sector-based scientists, supported through investments by pharmaceutical, environmental and agricultural interests working in the fields that comprise biotechnology, presents the opportunity and the ability to assess the implications of their own work and to work within a regime of self-control that is, for the most part, self-governing (if only loosely if at all defined). There are a growing number of unscrupulous state and non-state actors who would use their ability to access technology at multiple levels to influence a political agenda in a local or broader context. A variety of groups have been assembled in the relatively recent past to address this dual use (DU) issue and include but are not limited to the following:

1. 1997 UNESCO initiative "Possible Consequences of the Misuse of Biological Sciences"
2. 1999 Stockholm International Peace Research Institute report "Biological and Toxin Weapons: Research, Development and Use from the Middle Ages to 1945"
3. 2002 Carnegie International Non-proliferation Conference session on "Preventing the Misuse of Biotechnology"
4. 2003 New York Academy of Sciences symposium "National Security and Biological Research: What are the Boundaries?"
5. 2004 International Committee of the Red Cross fora "The Risks of Potential Misuse of the Life Sciences for Hostile Purposes" and "Responsibilities of Actors in the Life Sciences to Prevent Hostile Use"
6. 2004 US National Academies report "Biotechnology Research in an Age of Terrorism: Confronting the Dual Use Dilemma"
7. 2004 Health Canada issue paper "The Dual Use Dilemma for Biotechnology Research in Canada"
8. 2004 OECD Workshop "Promoting Responsible Stewardship in the BioSciences: Avoiding Potential Abuse of Research and Resources"
9. March 2006 National Forum on Dual Use Biotechnology
10. October 2006 Workshop on "Biosecurity of Microbial Biological Resources - Complementing Innovation"

Unfortunately there are far too many recent examples that would point to a need for action. The classic references that are made to the Australian mouse pox vaccine employing Interleukin-4 and a more recent, partially Canadian story, on the synthesis of an influenza strain in a Canadian government facility, that replicates the virus responsible for the deaths of 40 million people in the 1918 flu pandemic are only two examples. Defence R&D Canada and Health Canada

commissioned, using Canadian Biotechnology Strategy Emerging Issues Funds, an initial research survey, analysis, and consultation to develop a draft strategy paper: "Dual Use Biotechnology A Canadian Perspective" (McFadden Report) on how Canada should respond to the issue of stewardship of biotechnology to reduce the potential abuse of biotechnology. The results of this survey indicated:

- a low awareness of knowledge on the aspects of dual use technologies;
- better monitoring of dual use biotechnology was warranted with the recognition that a fine balance would need to be struck between advancing accountability and stifling the very activities that are the subject of any oversight measures; and
- self-protective measures that minimize the threat of misuse of Canadian resources or knowledge are desirable for reasons that extend beyond the national agenda.

Subsequent to this effort, and expanding on the McFadden Report, a national forum was convened in March of 2006 entitled the "National Forum on Dual Use Biotechnology." This forum brought together experts in the field from the national (federal non-defence and defence, academia, scientific publishers, biotechnology industry) and international scientific and policy communities. Forum participants took part in a facilitated discussion, supported by expert presentations, designed to open and advance dialogue on the DU issue. The Forum developed a profile of the issues in dual use biotechnology that might affect Canadian policy and may need to be addressed in the development of a Canadian approach. A number of issues that should be considered in more detail over time as the dual use issue is explored were developed. The issue of security with respect to the dual use potential of biotechnology is relatively new and views vary widely among stakeholder groups. There is little if any guidance across borders; the guidance under consideration lies anywhere between non-binding codes of practice and legislation. Collaboration between policymakers and stakeholders will be necessary for the successful development of practices and procedures to deter and/or detect the inappropriate use of biotechnological resources. The challenge for policymakers and stakeholders resides in striking an appropriate balance between security measures for materials that could be used in an offensive state or non-state initiated action and an operational environment conducive to advanced biomedical research. The tension between publication of sensitive data that could, for instance, provide terrorists with a how-to manual and the increasing anxiety in the scientific community that curbing the dissemination of research may only impair our ability to counter biological threats needs to be explored.

Following the 2006 National Forum, it was clear that a Canadian strategy and policy would be needed to provide guidance and leadership on this issue within Canada and to support Canadian advocacy and positions in international fora. It was also suggested that certain advisory, analytical and decision making tools and reference frameworks would be needed to support such a Canadian approach and among them, the idea of a threat assessment aid was raised. With this context, DRDC decided to pursue the idea through a commissioned study that would consider the feasibility, applicability and potential design of a Threat Assessment Framework (TAF) concept. The study would scan current developments and trends in the governance and management of dual use biotechnology, identify the core issues that need to be addressed in such a threat assessment framework, explore core elements for the framework, and if deemed feasible, undertake a preliminary concept development for the framework.

2.0 STUDY APPROACH

The following steps were undertaken for the study:

1. Reviewed related background materials provided by DRDC, plus undertook a selective literature review to orient the study and to develop the concepts and ideas for further development and testing with subject matter experts.
2. Conducted an assessment of threat elements, both actual and potential drawing upon open source material and in particular, through interviews with subject matter experts.
3. Interviewed a range (20+) of selected domestic and international subject matter experts that included scientists (private and public sector), R&D funding agencies, scientific publishers and their editors, security professionals, and law enforcement (counter-terrorism) (see Appendix A for a list of those interviewed and the study leader). The interviews generally lasted 60-75 minutes (see Appendix B for the interview questions). Their input was obtained on:
    a. Foundation concepts and issues in dual use biotechnology that need to be addressed in any threat assessment framework (with examples);
    b. The identification of core concepts for a threat assessment framework for DU biotechnology;
    c. Testing the validity and usefulness of an emerging threat assessment framework (i.e., created, evolved and tested a model as the interviews progressed);
    d. Specific constructs and models and related terminology for the assessment components; and
    e. Advice on the scope and priority focus of applications of the threat assessment framework.
4. Conducted a limited literature review by scanning a select range of documents (articles, reports, studies, etc.) and institutions/websites/portals for analyses, trends and recommendations that explore aspects of dual use, dual use monitoring and management, and threat/risk assessment in order to extract useful context and contributions to this analytical project. Solicited further useful body of knowledge sources/recommendations in the interviews with the subject matter experts and engaged select follow up scans.
5. Prepared a summary report of the findings, including an overview of the TAF and its application. Provided a preliminary estimation of promising areas for threat management mitigating strategies and potential domains where a Canadian approach and policy position may be needed.

Note: There were three fundamental scope/definition questions that arose during the interviews; namely, whether the concept should be designed around/called Threat Assessment or Risk Assessment; whether the term “dual use” was still appropriate and served us well; for the purposes of the threat assessment too, whether the scope of DU biotechnology should be narrowed only to biotechnology research involving the creation or modification of dangerous pathogens in particular through genetic engineering or should be expanded to allow naturally occurring pathogens/agents and other emerging or hybrid technologies or technologies that increased the dangerous quality of the pathogens without necessarily using genetic engineering. These are addressed as follows:

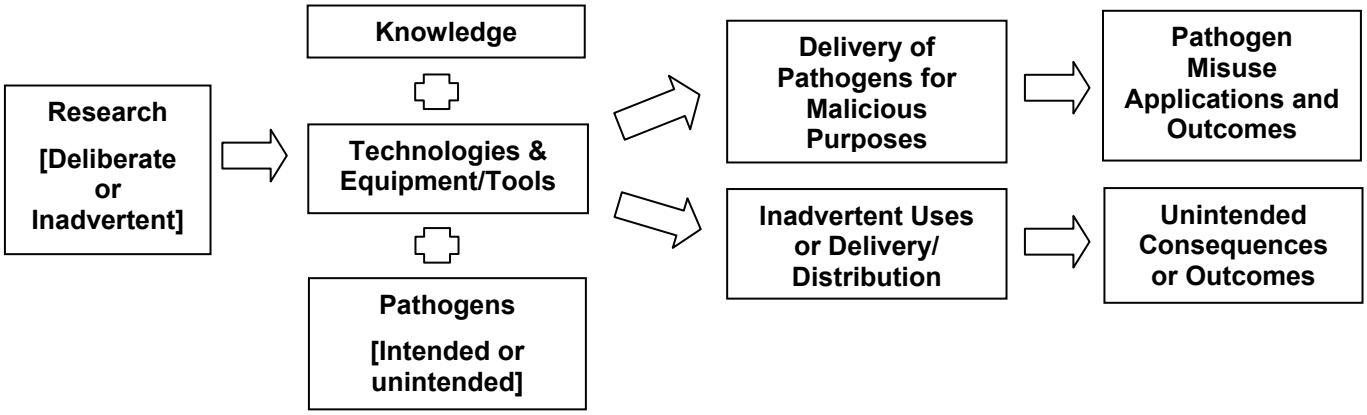
- Threat Assessment (TA) or Risk Assessment? Some participants offered that 'risk assessment' would be a preferred terminology/method as it is less value-laden, less provocative, implies something is 'at risk' without necessarily concluding a negative consequence and implies that the focus is on first determining the risks and then deciding how to mitigate them…..others agued that 'threat assessment' immediately connotes the nature of the problem (i.e., that the risk(s) involved translates into a 'threat') and appropriately suggests that there is potential for a negative and grave consequence and suggests that the focus is on determining the extent of the threat and then examines how to preempt or control them. We have adopted the approach of a 'threat assessment' terminology/methodology since the seriousness of the DU biotechnology challenge and the safety and security issues and consequences demand a heightened emphasis offered by a threat-based approach.
- Dual Use Terminology….is it still appropriate? Various concerns were raised with this title (e.g., it is confusing and misleading (is it implied that there are two uses of concern/benefit?); what is the issue it is trying to point to? etc.). Alternatives were suggested, most of which called for a descriptive phrase that identified the challenge that required attention in terms of the behaviour of those involved not on the threat event, viz: "Responsible, principled, and ethical management of vulnerable biosciences research and its results." These definitional questions which have been appropriately raised should be addressed in subsequent development. For the purposes of this study, we have used the current concept of 'dual use' which is the concern for the potential access to and misuse of biosciences research for malicious purposes.
- Scope of DU Biotechnology Threat Assessment…..engineered biotechnology or broader? At this stage of development, the sponsors suggest that the scope of the study emphasize mainly biosciences/biotechnology research involving the creation or modification of dangerous pathogens in particular through genetic engineering, while allowing consideration (for potential future evolution of the TAF tool) of naturally occurring pathogens/agents (especially where they are utilized with technological delivery mechanisms such as weaponization for terrorist purposes) and other emerging or hybrid technologies or technologies that increased the dangerous quality of the pathogens without necessarily using genetic engineering.

Note: the references, documents and sources accessed and considered in this study are listed in Appendix L.

3.0 CONCEPT OF A DUAL USE PROCESS

After preliminary conversations with experts and scanning initial literature in the field, it was evident that the dual use issue is very complex with different opinions on the scope and fundamental concerns and even the terminology to define and elaborate it. Therefore, to provide a conceptual starting point and terminology, we created a graphic portrayal of dual use as a process. This process view helps to deconstruct the complex idea into connected sequential and concurrent events/outputs and provides a topical reference point to examine the elements and issues involved in DU biotechnology.

In the graphic below, we portray DU biotechnology in process terms as per the following flow of steps with the potential of threat elements occurring at each step (i.e., Deliberate/inadvertent dual use research is conceived and undertaken…..producing knowledge (which may be accessible/distributed), and technologies and related equipment/tools, and pathogen(s) (intended or unintended).....which may then be employed in a delivery mechanism for malicious purposes (e.g., further configure or weaponize the pathogen for bioterror or biowarfare purposes) or which may have inadvertent uses or distribution….which can then be misused to inflict destruction, destabilization or terror or may have unintended consequences or outcomes arising from the inadvertent use. While 'deliberate' and 'inadvertent' research and associated results occur through similar means and steps in the process, we have distinguished them separately as the issues and threats involved can be quite different.



By using this conceptual process, we reasoned that we could design a threat analysis for each step/threat element which may enable a more discrete set of risk management strategies and policies to be applied to the different elements. As well, we should be able to create an overall assessment of a range of whole dual use threat processes (i.e., an identified research type yielding knowledge that is used to produce a bioterror pathogen applied in a defined set of societal conditions).

By arraying the process elements against a set of assessment components, as in the proposed concept for a Threat Assessment Framework (TAF) table following, we can design a threat analysis for each process element (the table columns) and develop concepts, terminology and analysis tools for each assessment component (the table rows) and combine these into a threat assessment approach for whole DU processes (i.e., diagonal slices across the table). In the next section, we explain the structure of this concept for the Threat Assessment Framework and subsequently expand on each part (see Appendix C for the full framework).

Draft Concept for a Threat Assessment Framework

DU Process Elements / Assessment Components	a) Research (Deliberate or Inadvertent)	b) Knowledge (Creation and Dissemination)	c) Technologies & Equipment/ Tools	d) Pathogens (intended or unintended)	e) and f) Delivery or distribution of Pathogens (deliberate and inadvertent)	g) and h) Pathogen Misuse Applications Or Unintended Consequences or outcomes
1. Types						
2. Risk-Benefit Analysis						
3. Actors (inadvertent)						
4. Actors (deliberate)						
5. Potential will occur (inadvertent research)						
6. Probability will occur (deliberate research misuse)						
7. Impact if occurs (inadvertent or deliberate)						
8. Summary Analysis						
9. Threat Management						
10. Policy Position						

4.0 STRUCTURE OF THE THREAT ASSESSMENT FRAMEWORK

The **columns** of the Threat Assessment Framework (TAF) consist of:

a) Research – includes all the types of research in the biosciences that combine molecular research with genetic engineering as well as other hybrid technologies and which are vulnerable to potential misuse, whether the research is deliberate or inadvertent;

b) Knowledge – the generation, storage, access and distribution of information on scientific research methods, practices and results from vulnerable research that is subject to potential misuse;

c) Technologies and equipment/tools – the scientific methodologies and technologies that are used to conduct the vulnerable research and/or the specific methodology that is learned from conducting the research in question; the equipment and/or tools/aids used to conduct the research in question;

d) Pathogens – the pathogenic microorganisms and biological agents (both plant and animal) that are employed and/or produced through such vulnerable research, whether intended or unintended;

e) Delivery or distribution of pathogens for malicious purposes – the delivery or distribution system used to expose the pathogens to broad or select areas of society and the environment;

f) Inadvertent uses or inadvertent delivery/distribution – the potential ways through which unintended research products with pathogenic qualities could be exposed in society or the environment;

g) Pathogen misuse applications and outcomes – the ways in which pathogens can be applied with malicious intentions and the potential impacts or outcomes; and

h) Unintended consequences or outcomes – the potential consequences or outcomes resulting from the exposure of untended research pathogenic products.

The **rows** of the TAF consist of:

1. Types – ways of listing, organizing or categorizing each of the dual use process elements (i.e., the columns in the TAF table);
2. Risk-Benefit Analysis – classic risk (potential for harm) and benefit (value added) analysis applied to each of the column elements; involves a summative assessment of the risks and benefits weighed together;
3. Actors (inadvertent misuse behaviours) – an analysis of the mainly legitimate scientists engaged in vulnerable research and the factors involved in their activities and intentions;
4. Actors (deliberate misuse behaviours) – a profile and analysis of those who could/would pursue the misuse of scientific research and its products for malicious purposes and the factors involved in their activities and intentions (motivation, intent, capability, opportunity);
5. Potential will occur (inadvertent research with unintended consequences) – to enable the assessment of the potential a risk event/activity will occur (Could it occur?) and is

focused on legitimate research science engaged in inadvertent research producing inadvertent results with unintended consequences;

6. Probability will occur (deliberate misuse research with intended consequences) – the first half of classic risk assessment (i.e., probability/likelihood versus impact/consequence) and enables projecting the probability or likelihood a risk event/activity will occur (would it occur?); considers certain factors that influence probability (availability, feasibility, cost etc); involves a summative assessment of probability;
7. Impact if occurs (inadvertent or deliberate) – the second half of risk assessment and enables projecting the impact or consequences if the activity/event occurs; considers the areas of vulnerability and the types of impact; involves a summative assessment of impact;
8. Summary Analysis – allows for a summative assessment using the framework by: summarizing a threat assessment for a case example in a column; or providing a summary of the policy picture for any column; or a summary assessment for a whole DU process (i.e., a diagonal slice across the table), etc.;
9. Threat Management – a supplement to the TAF table, it allows the identification of mitigating or risk management strategies for any column or overall DU process; and
10. Policy Position – a supplement to the TAF table, it allows the identification of policy positions to guide the approach for any column or overall DU process.

5.0 ELABORATING THE THREAT ASSESSMENT FRAMEWORK

The following elaborations of the TAF reflect the ideas arising from the literature review but mainly reflect the results of the extensive interviews with domestic and international subject matter experts.

5.1 Row 1: Types

DU Process Elements / Assessment Components	a) Research (Deliberate or Inadvertent)	b) Knowledge (Creation and Dissemination)	c) Technologies & Equipment/ Tools	d) Pathogens (Intended or Unintended)	e) and f) Delivery or Distribution of Pathogens (Deliberate and Inadvertent)	g) and h) Pathogen Misuse Applications or Unintended Consequences or Outcomes
1. **Types**						

The purpose of this row is to list and categorize the dual use process elements of concern (e.g., research, knowledge, pathogens, etc.).

General descriptors – known, suspected, unknown types

Note: It is suggested that the TAF needs a Canadian perspective to guide the Canadian strategy. This implies that the whole TAF could be tailored to fit the conditions present in Canada and hence there would be a subset or selection of DU types that are most relevant to Canada. At this point we have maintained a global perspective in the design but recommend the development of a Canadian tailored TAF as a distinct model, perhaps within a globally viewed TAF.

a) Research (Column a)

It is proposed that the TAF present a pro forma list of types of research of concern or that might be vulnerable to misuse. However, the list should be indicative or representative rather than exhaustive as there are so many possibilities and emerging areas of crossover science development, it would be impossible to have a complete list. Most favoured for the start list include:

- The seven classes of Experiments of Concern from the 2004 report, "Biotechnology Research in an Age of Terrorism: Confronting the Dual Use Dilemma," by the US National Research Council (Fink Committee) (see Appendix D);
- The seven Criteria for Identifying Dual Use Research of Concern in the report of the National Science Advisory Board for Biosecurity, July 2006 (see Appendix E);
- The three tiered approach of the Center for International and Security Studies at Maryland (CISSM) USA organizing experiments of concern into potentially dangerous, moderately dangerous, and extremely dangerous activities (see Appendix F).

b) Knowledge (Column b)

It is proposed that the TAF incorporate a generic set of knowledge descriptors that are indicative of sensitive knowledge arising from research of concern and that are candidates for monitoring. The preliminary generic set consists of accessible information that could assist those with malicious purposes. In general, descriptions of the process and methodology used in any of the seven experiments of concern (USNRC list) or the most dangerous types from

the CISSM list, that would enable the process to be reproduced, especially if with reasonable means. In particular, examples are:

- how to conduct the process to produce a dangerous pathogen;
- how to produce the pathogen;
- how to control related DNA synthesizers;
- how to isolate and purify a pathogenic microbe;
- how to modify a pathogen to increase its destructive qualities;
- how to use the pathogen.

c) Technologies and Equipment/Tools (Column c)

It is proposed that the TAF incorporate an outline of those technologies that define the scope of molecular biological research of concern. This would include:

- the core life science technologies that are used to produce pathogens of concern;
- synthetic genomics and synthetic chemistry;
- genetic manipulation, DNA synthesizers and recombinant DNA;
- novel applications of converging technologies;
- generation of biological or molecular entities through directed design (genetic engineering);
- manipulation of biological systems (bioregulators – immune, neurological, endocrine systems e.g. neurobiology);
- methods that enhance production, delivery or packaging of biologically active materials.

It is proposed that the TAF incorporate a representative cross section of the main equipment types and support tools necessary to enable research and production of dangerous pathogens. The purpose is to provide an early warning indication of significant acquisition of such equipment, especially by those designated as a security threat (e.g., dual use biological equipment items that can be used for both peaceful research and biological weapons production such as fermenters, containment facilities, freeze-drying equipment and aerosol testing chambers [see Appendix G for Australia Group list]).

d) Pathogens (Column d)

It is proposed that the TAF present a pro forma list of pathogens of concern or that might be vulnerable to misuse. However, the list should be indicative or representative rather than exhaustive as there are so many possibilities and new emerging microbes, it would be impossible to have a complete and current list. The purpose would be to raise awareness of the types of pathogens that warrant responsible and ethical management and could be candidates for some level of review under the TAF. In general the list would include plant pathogens and anti-crop agents, animal pathogens, biological agents and toxins.

In general, the construct chosen would be shaped by the set of criteria to be used to select the types of pathogens/agents. Initial criteria are suggested to be: infective dose (the smallest quantity of the agent needed to infect); pathogenicity (the disease-causing ability of the organism); virulence (the strength of the agent); lethality (the ability of the organism to cause death); transmissibility (the ability of the organism to transfer among or across species). It was also noted that there is a future science focus which is shifting from the design of the pathogen virulence/lethality to focus on the vulnerability of the target (e.g., ways to affect the immune system, which would require a proactive scan for and inclusion of such agents).

Most favoured for the start list included:

- In *Nature Biotechnology* (February 2007), the US Center for Disease Control (CDC) classifies agents that could be used in bioterrorism into three categories: Category A, B or C (see Appendix H):

  > **Category A agents**
  > The CDC defines Category A agents as organisms that pose a risk to national security because they are easily disseminated or transmitted from person to person, result in high mortality rates and have the potential for a major public health impact, might cause public panic and social disruption, and require special action for public health preparedness.
  >
  > **Category B agents**
  > The CDC defines Category B agents as organisms that are moderately easy to disseminate, result in moderate morbidity rates and low mortality rates, and require specific enhancements of CDC's diagnostic capacity and enhanced disease surveillance.
  >
  > **Category C agents**
  > These include emerging pathogens that could be engineered for mass dissemination in the future because of availability, ease of production and dissemination, and potential for high morbidity and mortality rates and major health impact.

- The Australia Group of signatory countries list of biological agents, plant pathogens and animal pathogens (see Appendix I).

However, there was strong urging to adopt a more flexible and expansive view of the pathogen list as expressed in the US National Academies of Science report on "Globalization, BioSecurity and the Future of the Life Sciences" (2006), viz:

> **2. The committee recommends adopting a broader perspective on the "threat spectrum."2**a. Recognize the limitations inherent in any agent-specific threat list and consider instead the intrinsic properties of pathogens and toxins that render them a threat and how such properties have been or could be manipulated by evolving technologies. 2b. Adopt a broadened awareness of threats beyond the classical "select agents" and other pathogenic organisms and toxins, so as to include, for example, approaches for disrupting host homeostatic and defense systems and for creating synthetic organisms.

This suggests the need for an adaptive and continuously evolving scope for the pathogen/agent threat spectrum that would include naturally occurring pathogens/agents (especially where they are utilized with technological delivery mechanisms such as weaponization for terrorist purposes) and other emerging or hybrid technologies or technologies that increased the dangerous quality of the pathogens without necessarily using genetic engineering.

e) Deliberate delivery or distribution of pathogens (Column e/f)

It is proposed that the TAF present an outline of potential delivery systems that could be used for deliberate distribution of dangerous pathogens in society and the environment by those with malicious intent. This would include:

- ways to increase the deliverability such as through weaponization and the associated dispersal factor (ease and effectiveness with which the organism or toxin can be dispersed, characteristics of the organism or toxin that allow it to be dispersed through means such as aerosols or inhalation);
- how deliverability is affected by pathogen scale, stability and viability/survival over time, especially if it has been engineered;
- indicators of potential delivery design/activity such as the acquisition and use of 'stabilizers.'

f) Inadvertent delivery or distribution of pathogens (Column e/f)

It is proposed that the TAF present an outline of potential ways in which inadvertent accessibility, release or distribution of dangerous pathogens could occur within the chain of custody in legitimate research environments (this would also assist in enhancing awareness and good management and control practices in the research community). It is expected that this outline would mainly consist of known research areas / processes / environments requiring safety controls and augmented by targeted practices and controls that would respond to biosecurity concerns such as an emphasis on:

- dangerous pathogen release possibilities from legitimate research affecting the health and safety of research practitioners;
- dangerous pathogen release possibilities from legitimate research affecting the safety and security of society and the environment;
- dangerous pathogen accessibility issues and possibilities (e.g., weaknesses in the chain of custody) that could allow the safety and security of society to be compromised by allowing access by those with malicious intent.

g) Intentional pathogen misuse applications/outcomes (Column g/h)

It is proposed that the TAF present an outline of the range and types of misuse applications of bioscience research and resulting dangerous pathogens undertaken by those with malicious intentions. Again, the goal is not to be complete but to offer an indicative profile of the possibilities to enable this element to be incorporated in the threat assessment characterization. Misuse applications will obviously vary according to:

- the actors (e.g., biocrimes by lone actors; biological warfare by well developed states; biological warfare by rogue states; bioterrorism by non-state actors);
- their targets (humans, agriculture, animals);
- their intentions (mass destruction, disruption/destabilization, psychological terror, etc.); and
- the impacts or outcomes.

h) Unintentional pathogen misuse applications/outcomes (Column g/h)

The unintentional application of bioscience research with dangerous pathogens will largely be covered in the previous section on 'Inadvertent Distribution' but a few additional possibilities would be added. As well, this section would profile a representative range of possible consequences or outcomes of such unintended applications.

5.2 Row 2: Risk-Benefit Analysis

DU Process Elements / Assessment Components	a) Research (Deliberate or Inadvertent)	b) Knowledge (Creation and Dissemination)	c) Technologies & Equipment/ Tools	d) Pathogens (Intended or Unintended)	e) and f) Delivery or Distribution of Pathogens (Deliberate and Inadvertent)	g) and h) Pathogen Misuse Applications or Unintended Consequences or Outcomes
2. Risk-Benefit Analysis						

The purpose of this row is to apply a risk-benefit analysis to each of the column elements where risk is generally defined as the potential for harm and benefit is characterized as the value added if the event/activity occurs. The analysis typically involves comparing and weighing the risks and benefits together to produce a summary rating and net view on whether the risks outweigh the benefits or vice-versa.

Note: There were strong suggestions for a rigorous and balanced risk-benefit analysis dimension in the TAF, in particular to provide an appropriate way for the legitimate scientists to engage the threat assessment. In other words, encouraging the research community to apply a risk-benefit review of any contemplated research that might be an 'experiment of concern' would encourage awareness of the potential threat, enable a balanced view that properly represented the research case, allow for a self-managed response, and enable this dimension to enrich the overall threat assessment framework. A useful outline for "Assessing the Risks and Benefits of Communicating Research with Dual Use Potential" is provided in the report of the National Science Advisory Board for Biosecurity Draft Guidance documents on Dual Use Research in the Life Sciences, July 2006 (see Appendix J).

a) Research (column a)

It is proposed that the TAF present a risk-benefit template to apply to selected biosciences research of concern for their misuse potential. The template would include:

- risk factors such as: potential for harm; identifiable bioterrorism applications; incorporates techniques to create more dangerous pathogens; and
- benefits factors such as: value added; whether it addresses an important health or humanitarian problem; whether there are existing alternatives; the implications of not doing the research.

b) Knowledge(Creation and Dissemination) (column b)

It is proposed that the TAF present a risk-benefit template to apply to knowledge arising from selected biosciences research of concern for their misuse potential.

Note: This DU element is largely about the storing, access and dissemination of knowledge arising typically through publishing of scientific journals, etc. Hence this dimension will be aided by the progressive approaches being pursued by publication editors / editorial boards / publication peer review committees, etc. (and to a similar degree the screening being contemplated by research granting agencies) to create a disciplined self-managed approach to screening knowledge dissemination for research knowledge of concern. The challenge of acting on a concern for the safety and security of society while maintaining scientific

openness and creativity represents the most difficult challenge in the DU area and any insightful strategies that arise from this community will be helpful and should inform the design of this knowledge scan template. In addition, this dimension also includes potential unwarranted or undesirable access to such vulnerable knowledge through research collaborations, apprenticeships, and international academic graduate programs and hence these equally sensitive avenues will need careful risk factor definition. The template would include:

- risk factors such as: potential access to knowledge of concern through publications, websites, open database storage; potential access to knowledge through research collaborations, apprenticeships and academic graduate programs, etc.; and
- benefit factors such as: publication necessary to advance understanding of fundamental results; results necessary to inform global advances in related areas; collaborations bring synergistic and complementary expertise to bear; international academic programs central to open education and early adoption of ethical principles, etc.

The risk analysis in the National Science Advisory Board for Biosecurity Draft Guidance documents on Dual Use Research in the Life Sciences, July 2006 on "Assessing the Risks and Benefits of Communicating Research with Dual Use Potential" (see Appendix J) provides a useful construct for knowledge dissemination risk-benefit analysis.

c) Technologies and Equipment/Tools (column c)

It is proposed that TAF present a risk-benefit template to apply to those technologies and equipment/tools which are used in biosciences research of concern for their misuse potential. The risk application to technologies will largely have been implicitly raised in the row one review of Types of Technologies (i.e., the identification of the technologies of concern will automatically imply the similar risk factors for all of them [e.g., risk the technique will be used for malicious purposes etc.]). The benefits will be self-evident and particular to the technology.

The risk application to equipment and tools can draw from the issues and risks identified in international conventions and controls on the export of equipment and tools that may enable research of concern (see Australia Group list in Appendix F).

d) Pathogens (intended or unintended) (column d)

It is proposed that the TAF present a risk-benefit template to apply to the list of pathogen types of concern. It would be logical to derive the risk factors (and the benefit factors) from the associated characteristics of the pathogens and risk qualities of the pathogen classes that are already defined. The risk factors are likely to group under generic factors such as pathogenicity, lethality, virulence, etc.

e) Deliberate delivery or distribution of pathogens (column e/f)

It is proposed that the TAF present a risk-benefit template to apply to potential delivery systems that could be used for deliberate distribution of dangerous pathogens in society and the environment by those with malicious intent. Risk factors would be drawn in part from the analysis of Row 1 Delivery Types and would include:

- increased deliverability such as through weaponization and the associated dispersal factor (e.g., ease and effectiveness with which the organism or toxin can be dispersed;

characteristics of the organism or toxin that allow it to be dispersed through means such as aerosols or inhalation);
- deliverability risk associated with pathogen scale, stability and viability/survival over time;
- availability including the number of facilities that stock such organisms or toxins and their geographic distribution;
- amplification (e.g., the ease with which the organism can be grown in culture and its growth rate); and
- available skills and knowledge (e.g., the ubiquity of the skills and knowledge necessary to amplify the organism).

f) Inadvertent delivery or distribution of pathogens (column e/f)

It is proposed that the TAF present a risk-benefit template to apply to the potential ways in which inadvertent accessibility, release or distribution of dangerous pathogens could occur within the chain of custody in legitimate research environments (incorporating both safety and security risk factors), with an emphasis on risks associated with:

- dangerous pathogen release possibilities from legitimate research affecting the health and safety of research practitioners;
- dangerous pathogen release possibilities from legitimate research affecting the safety and security of society and the environment;
- dangerous pathogen accessibility issues and possibilities (e.g., weaknesses in the chain of custody) that could allow the safety and security of society to be compromised by allowing access by those with malicious intent.

g) and h)Pathogen misuse applications/outcomes (intentional or unintentional)(column g/h)

Note: there is no risk-benefit analysis or template suggested for this element (column in the TAF) as it represents the end application or misuse of a dangerous pathogen and the associated impacts/outcomes, and hence a risk-benefit analysis would not be a useful approach at this point (and in part the outcomes are a manifestation of the risks). In addition, the risks that such events will occur, in the sense of the potential or probability, will be addressed in Row 4 dealing with probability analysis.

5.3 Row 3: Actors Analysis (Inadvertent Misuse Behaviours)

DU Process Elements / Assessment Components	a) Research (Deliberate or Inadvertent)	b) Knowledge (Creation and Dissemination)	c) Technologies & Equipment/ Tools	d) Pathogens (Intended or Unintended)	e) and f) Delivery or Distribution of Pathogens (Deliberate and Inadvertent)	g) and h) Pathogen Misuse Applications or Unintended Consequences or Outcomes
3. **Actors (inadvertent)**						

The purpose of the next two rows is to identify the main potential actors involved in intended or unintended misuse applications of bioscience research and to provide a selection of descriptors that can be used to provide a profile of those actors involved with such threat events or activities. This Actors analysis has been split into separate rows to address *inadvertent* (Row 3) and *deliberate* (Row 4) misuse motivations and behaviours.

Note: The actor assessment is only applied within certain relevant columns (DU Process Elements) and not across the whole row using the following.

Note: Since the scope of the TAF is still to be determined (as a start point it is presumed to start with biosciences / life sciences research involving genetic engineering (e.g., biotechnology), it is not determined whether the TAF would include pandemic flus and other naturally occurring viruses/pathogens etc. and if so then, natural sources would need to be added to the actors list.

Actors

- Legitimate scientists engaged in bioscience research that involves research types of concern and/or produces *intended* dangerous pathogens and/or intentional knowledge that is susceptible to safety and security concerns (may exist in institutional/academic, private sector or independent lab environments);
- Legitimate scientists engaged in bioscience research that involves research types of concern and/or produces *unintended* dangerous pathogens and/or unintentional knowledge that is susceptible to safety and security concerns (may exist in institutional/academic, private sector or independent lab environments);
- Owners, custodians and distributors of vulnerable knowledge on research types of concern, such as editors and publishers of scientific journals and managers of institutional knowledge databases;
- Manufacturers and distributors of scientific equipment that would be needed to support research of concern;
- States (well-developed) engaged in biological warfare preparations using bioscience research types and products/pathogens of concern.

Motivations

- Generally for legitimate scientists the motivation is to pursue answers to appropriate scientific questions;
- Generally for owners, custodians and distributors of knowledge of concern, the motivation is the sharing of knowledge to advance common understanding and to provide the basis for more advanced research;
- Generally for well-developed states, biowarfare preparations are no longer present, countries have signed onto nonproliferation conventions prohibiting such development and the remaining issues relate to control and destruction of stockpiled pathogens, control of sensitive knowledge on how to produce such pathogens, and current ethical practices of personnel formerly engaged in such preparations.

Behaviours

- Failure to follow ethical principles and practices in research of concern, allowing potential access to knowledge or products or leading to the release of dangerous pathogens;
- Failure to understand the vulnerability and danger involved in certain research of concern, and not being prepared to manage the results and consequences of the research, especially when the products are unintended dangerous pathogens;
- Failure to consider the vulnerability and security issues/implications in the storage, access and distribution of knowledge related to research of concern;

- Failure to manage the control and destruction of stockpiled pathogens for previous biowarfare purposes, as well as the control of sensitive knowledge on how to produce such pathogens, and to ensure the current ethical practices of personnel formerly engaged in such preparations.

5.4 Row 4: Actors Analysis (Deliberate Misuse Behaviours)

DU Process Elements / Assessment Components	a) Research (Deliberate or Inadvertent)	b) Knowledge (Creation and Dissemination)	c) Technologies & Equipment/ Tools	d) Pathogens (Intended or Unintended)	e) and f) Delivery or Distribution of Pathogens (Deliberate and Inadvertent)	g) and h) Pathogen Misuse Applications or Unintended Consequences or Outcomes
4. **Actors (deliberate)**						

The purpose of this row is to identify the main potential actors involved in intended misuse applications of bioscience research of concern and to provide a selection of descriptors that can be used to provide a profile of those actors involved with such threat events or activities and which incorporates both motivations and behaviours.

Note: The actor assessment is only applied within certain relevant columns (DU Process Elements) and not across the whole row using the following.

Actors

- Illegitimate scientists engaged in bioscience research that involves research types of concern and/or produces *intended* dangerous pathogens and/or intentional knowledge that is susceptible to safety and security concerns;
- States (well-developed) engaged in biological warfare preparations using bioscience research types and products/pathogens of concern;
- Rogue states engaged in: biological warfare preparations using bioscience research types and products/pathogens of concern; or state supported bioterrorism research with pathogens of concern; or providing support to terrorist initiatives intending to conduct research of concern and/or produce and misuse dangerous pathogens with the intention to cause selective or mass destruction, disruption/destabilization, psychological terror, etc.;
- Non-state actors engaged in: bioterrorism research with pathogens of concern; accessing pathogens of concern through legitimate or illegitimate sources; developing delivery systems to distribute such pathogens; developing and executing plans to misuse dangerous pathogens with the intention to cause selective or mass destruction, disruption/destabilization, psychological terror, etc.

Motivations

- Generally for illegitimate scientists (engaged in bioscience research that involves research types of concern and/or produces *intended* dangerous pathogens and/or intentional knowledge that is susceptible to safety and security concerns) the motivation is to provide results that support biowarfare or bioterrorism activities or criminal activities;

- Generally for well-developed states, biowarfare preparations are no longer present, countries have signed onto nonproliferation conventions prohibiting such development and the remaining issues relate to control and destruction of stockpiled pathogens, control of sensitive knowledge on 'how to' produce such pathogens, and current ethical practices of personnel formerly engaged in such preparations;
- For rogue states engaged in biological warfare preparations or state supported bioterrorism research with pathogens of concern or providing support to terrorist initiatives, the motivation is political and ideological with the intention to cause selective or mass destruction, disruption/destabilization, psychological terror, etc.;
- For non-state actors engaged in bioterrorism research with pathogens of concern, accessing pathogens of concern, developing delivery systems to distribute such pathogens and developing and executing plans to misuse dangerous pathogens, the motivation may be political and ideological, with the intention to cause selective or mass destruction, disruption/destabilization, psychological terror, etc. or it may be to support criminal activities.

Behaviours

- Failure to follow ethical principles and practices in research of concern, allowing potential access to knowledge or products or leading to the release of dangerous pathogens;
- Failure to manage the control and destruction of stockpiled pathogens for previous biowarfare purposes, as well as the control of sensitive knowledge on how to produce such pathogens, and to ensure the current ethical practices of personnel formerly engaged in such preparations;
- Providing results on research of concern to those with malicious intent; providing access to pathogens of concern; developing delivery systems to distribute such pathogens and developing and executing plans that misuse dangerous pathogens, with the intention to cause selective or mass destruction, disruption/destabilization, psychological terror, etc. or it may be to support criminal activities.

Profile Descriptors

In the area of deliberate misuse of biotechnology, the set of descriptors recommended to present the profile of actors involved are proposed to consist of:

- *Motivation* - as outlined above;
- *Intent* - the objective of the actor;
- *Capability* - the capability of the actor to conduct the research and/or produce the pathogen, or develop the delivery system or execute the plan to achieve the intention;
- *Opportunity* - the opportunity that the actor has to undertake the misuse.

Note: During the interviews, it was noted that the four descriptors are the same as the factors that police forces use in investigating a crime and hence the science and methods of police investigation may be a useful resource to draw upon to design this section.

5.5 Row 5: Potential will occur (inadvertent research with unintended consequences)

DU Process Elements / Assessment Components	a) Research (Deliberate or Inadvertent)	b) Knowledge (Creation and Dissemination)	c) Technologies & Equipment/ Tools	d) Pathogens (Intended or Unintended)	e) and f) Delivery or Distribution of Pathogens (Deliberate and Inadvertent)	g) and h) Pathogen Misuse Applications or Unintended Consequences or Outcomes
5. Potential will occur (inadvertent research)						

The purpose of this row is to enable the assessment of the potential a risk event/activity will occur (Could it occur?) and is focused on legitimate research science engaged in inadvertent research producing inadvertent results with unintended consequences.

Note: Interview feedback suggested that for legitimate research scientists, institutions and knowledge managers/distributors, this row should be focused on the *potential* that an activity/event will occur rather than the *probability*. Hence we propose that there be two separate rows (5 and 6) to focus first on legitimate but inadvertent biotechnology research misuse using the concept of potential (i.e., *Could* it occur?) and then in row 6 a focus on deliberate research misuse using the concept of probability (i.e., *Would* it occur?).

The risk potential template for 'legitimate research with inadvertent misuse' would outline the potential risk events/activities drawn largely from the legitimate actors analysis in Row 3, augmented by the development of risk factors in Row 2, and would provide a 'potential' rating scale for assessing generic and individual cases, based on the conditions associated with the event/activity (e.g., high, moderate, low, negligible potential). Following is an example:

> Risk event/activity - legitimate research scientist conducting biotechnology research with dangerous pathogens produces inadvertent results of concern accompanied by the creation of a more dangerous pathogen with unknown pathogenicity and with relatively open access to the knowledge of the research methodology. Hence this represents a failure to follow ethical principles and practices in research of concern, allowing potential access to security sensitive knowledge or products. Case conditions - lack of institutional awareness of consequences of research, plus variable history of ethical principles/practices being applied plus lack of controls on the management and distribution of knowledge about the research. Risk potential rating (Could it occur?) [high, moderate, low, negligible] – for this example above rating assessed as *high* given the conditions present.

5.6 Row 6: Probability will occur

DU Process Elements / Assessment Components	a) Research (Deliberate or Inadvertent)	b) Knowledge (Creation and Dissemination)	c) Technologies & Equipment/ Tools	d) Pathogens (Intended or Unintended)	e) and f) Delivery or Distribution of Pathogens (Deliberate and Inadvertent)	g) and h) Pathogen Misuse Applications or Unintended Consequences or Outcomes
6. Probability will occur (deliberate research misuse)						

The purpose of this row is to provide the first half of classic risk assessment (i.e., probability/likelihood versus impact/consequence) and enables projecting the probability or likelihood a risk event/activity will occur (Would it occur?) and considers certain factors that influence probability (availability, feasibility, cost, etc.) and involves a summative assessment of probability (e.g., high, moderate, low, negligible).

The risk probability template for 'illegitimate research with deliberate misuse' intentions would outline the potential risk events/activities drawn largely from the Row 1 Types, augmented by the development of risks/risk factors in Row 2, and combined with the Row 4 Actors analysis (deliberate misuse behaviours), and would provide a 'potential' rating scale for assessing generic and individual cases.

Probability factors include:

- *Availability/accessibility* - the availability and ease of access to vulnerable research methodology, knowledge, enabling technologies, pathogen stock, and agent delivery systems;
- *Feasibility/complexity* - the feasibility of conducting the research and producing the pathogen, then creating the delivery system for destructive use and executing the plan to distribute the agent. Depends upon the complexity of the methodology, enabling equipment requirements, predictability of the results etc.;
- *Cost/efficiency* - the financial cost of conducting the research and the cost base over time;
- *Prevalence and endemic nature* for the country/region concerned - the degree the research and associated pathogens are prevalent / occur frequently in the country/region and whether the agents are endemic or common to that country/region, such as certain naturally occurring dangerous viruses;
- *Historical experience* with same or similar events/activities/products - a comparison of past misuse/non-use of such events/products to identify the limiting factors that prevented or enabled it to proceed and in particular, the reasons why it was not successful / did not progress when it has been stopped/failed (and hence whether those factors are present in the new case) *Note*: A useful source of past events/incidents is the Monterey Institute's Center for Non-proliferation Studies which maintains an open source database of all known CBRN incidents.

Note: This risk probability analysis could be applied to each of the TAF columns (research, knowledge, etc.) with the risk events/activities selected from each column, combined with selected actors and associated intentions and the above probability factors tailored to fit the focus of each column (e.g., What is the probability a non-state actor can access knowledge on certain research methodology of concern, sufficient to reproduce the research?). In addition, whole DU processes can be defined from risk activities across several columns (e.g., What is the probability a rogue state can conduct a certain type of research of concern, by accessing research knowledge from public sources, purchasing enabling equipment in western markets, and developing a delivery system to distribute the dangerous agent to a target country?).

Note: There are a variety of useful constructs and references on risk assessment that could be useful methodology sources including the International Risk Governance Council, see the report "White Paper on Risk Governance" 2005 (Appendix K outline of methods for calculating probabilities).

5.7 Row 7: Impact if occurs

DU Process Elements / Assessment Components	a) Research (Deliberate or Inadvertent)	b) Knowledge (Creation and Dissemination)	c) Technologies & Equipment/ Tools	d) Pathogens (Intended or Unintended)	e) and f) Delivery or Distribution of Pathogens (Deliberate and Inadvertent)	g) and h) Pathogen Misuse Applications or Unintended Consequences or Outcomes
7. **Impact if occurs (inadvertent or deliberate)**						

The purpose of this row is to provide the second half of risk assessment and enables projecting the impact or consequences if the risk activity/event occurs. It also considers the areas of vulnerability and the types of impact, and involves a summative assessment of the impact.

Areas of vulnerability - addresses the societal domains which could be vulnerable to misuse applications, in particular the delivery (or threat of delivery) of dangerous pathogen agents or toxins. It includes:

- Public health - health and well being of the population
- Environment - the vitality and integrity of the natural and man-made environment
- Agriculture - the crops, grains and food chain supporting human or animal viability
- Animals - the health and well being of animals, both domesticated and naturally wild
- Infrastructure - both life supporting such as water supply, and for support of community and economic life such as the power grid, etc
- Economy - both domestic economic vitality, and international economic dimensions such as international trade
- Social and political stability - the societal culture, values and belief system and social stability plus the political and governance dimension of the society

Types of impact - addresses the range of intended impacts potentially contemplated by misuse actors and/or other outcomes arising from such misuse. It includes:

- Mass or selected destruction, i.e., lethal destruction of human or animal life, plant and crop life, vital food chain destruction; could include destruction of infrastructure
- Mass or selected disruption or destabilization (i.e., significant impact on the effective functions of society, including social and economic stability)
- Impact on mass psyche (i.e., disproportionate fear and lack of belief in self preservation, safety and security among society)
- Loss of confidence or credibility in key institutional fabric (i.e., lost confidence in political, institutional, academic/science dimensions or leadership in society)

Impact ratings - an example summative impact assessment rating scale could incorporate the following impacts:

- Catastrophic - severely compromises human, animal, or agricultural health on a scale that results in significant and wide spread destruction or loss, potentially resulting in loss of societal capacity to carry out key functions
- Major – severely compromises human, animal, or agricultural health on a limited scale that results in significant but limited destruction or loss but without limiting societal capacity to carry out key functions
- Moderate – compromises human, animal or agricultural health but on a small, selective scale that is contained
- Minor/negligible – affects human, animal or agricultural health but on a selective basis, and for which coping aids/methods exist that contain and limit the impact to temporary levels of discomfort

Note: Participants noted the need to add a time dimension to the impact assessment, so that impact ratings would be situated in a time period such as short (e.g., days to weeks), medium (e.g., months to few years) and long term (e.g., several years to decades).

5.8 Row 8: Summary Analysis

DU Process Elements / Assessment Components	a) Research (Deliberate or Inadvertent)	b) Knowledge (Creation and Dissemination)	c) Technologies & Equipment/ Tools	d) Pathogens (Intended or Unintended)	e) and f) Delivery or Distribution of Pathogens (Deliberate and Inadvertent)	g) and h) Pathogen Misuse Applications or Unintended Consequences or Outcomes
8. Summary Analysis						

The purpose of this row is to enable the summarizing of the threat assessment analysis that has been elaborated throughout the TAF table. The following options for summary threat assessments are proposed:

a) Threat assessment for each column of the TAF (i.e., for Research, Knowledge, Technologies, etc.) divided into two versions:
   - Legitimate research with inadvertent misuse - for each column, any identified event/activity that could pose a threat could be reviewed with a summary assessment

consisting of: a listing of the potential risks (drawn from Row 2 analysis) with the associated actors analysis (inadvertent misuse behaviours drawn from Row 3); the risk assessment rating of those risks (i.e., the Risk Potential rating = Could it occur? in Row 5) plus the Risk-Benefit Analysis (Row 2) to produce a summary rating and net view on whether the risks outweigh the benefits or vice-versa.

- Illegitimate research with deliberate misuse - for each column, any identified event/activity that could pose a threat could be reviewed with a summary assessment consisting of: a listing of the potential risks (drawn from Row 2 analysis) with the associated actors analysis (deliberate misuse behaviours drawn from Row 4); plus the Probability-Impact analysis (drawn from Rows 6 & 7) [i.e., probability or likelihood a risk event/activity will occur (Would it occur?) and the impact if it does occur].

b) A summary threat assessment for a whole DU process (i.e., a diagonal slice across the table). In this option, a whole set of linked potential events/activities selected from several or all the columns across the TAF table are connected and assessed using the tools/templates in each row (i.e., a research type activity is assessed using a selection of the tools in each row tailored to the research focus, and so on for the remaining linked activities), resulting in an overall assessment for:
   - a case of legitimate research with inadvertent misuse - a risk potential rating and risk-benefit analysis net view; or
   - a case of illegitimate research with deliberate misuse - an overall risk rating and probability-impact rating (e.g., to summarize and rate the probability that the results of a particular research on an immune system modification, with a risk-benefit profile of *x*, can be accessed and used by non-state actors, who will have the access to the knowledge and pathogen inputs, to produce a bioterror agent that attacks the immune system that would have a major impact on public health (disease susceptibility) of seniors and young children).

c) A set of archetype Threat Scenarios with full threat analysis and summary for each. It is proposed that a manageable number of scenarios be developed (e.g., 6-10) that would map over a wide range of threat situations incorporating a range of risk events/activities (from each of the TAF columns) involving different actors of interest. The scenario set with the associated Threat Assessment would then become a reference point/model for future threat assessments in that they would provide: the lines of inquiry and examination; the necessary assessment terminology for common use; the reasoning and the basis of ratings and judgement to guide future assessments; starting comfort and fluency with conducting threat assessments; and potentially a constituency of stakeholders who were familiar with the methodology and could be called upon in special situations to bring their experience and guidance to bear.

5.9 Row 9: Threat Management

DU Process Elements / Assessment Components	a) Research (Deliberate or Inadvertent)	b) Knowledge (Creation and Dissemination)	c) Technologies & Equipment/ Tools	d) Pathogens (Intended or Unintended)	e) and f) Delivery or Distribution of Pathogens (Deliberate and Inadvertent)	g) and h) Pathogen Misuse Applications or Unintended Consequences or Outcomes
9. **Threat Management**						

As noted earlier, the next two rows are not formally part of the proposed TAF but are supplemental sections to allow users to identify the associated management strategies and policies to address both general and specific case dual use biotechnology threats as revealed in the TAF table.

Row 9 allows the identification of risk mitigating actions or risk management strategies for any column in general, or selected events/activities from a column or an overall DU process case. It also allows concerned stakeholders to adopt a set of common strategies or actions to address agreed threats.

5.10 Row 10: Policy Position

DU Process Elements / Assessment Components	a) Research (Deliberate or Inadvertent)	b) Knowledge (Creation and Dissemination)	c) Technologies & Equipment/ Tools	d) Pathogens (Intended or Unintended)	e) and f) Delivery or Distribution of Pathogens (Deliberate and Inadvertent)	g) and h) Pathogen Misuse Applications or Unintended Consequences or Outcomes
10. **Policy Position**						

This row allows the identification of policies / policy positions to guide the approach for any column in the TAF (i.e., for the whole column or for any typical events/activities occurring in the column) or an overall DU process (a set of events/activities) and would be useful for state agencies (research granting or regulatory) or private sector associations or academic institutions.

6.0 USING THE THREAT ASSESSMENT FRAMEWORK

In the interview process, there were some concerns expressed about the concept of a TAF, in particular:

- Whether it could actually be developed and presented as a workable tool given the huge scope of misuse activities and issues involved, the complexity of the subject and the layered and detailed analysis implied. However, the draft concept was seen as a very promising and workable framework on which to proceed, accompanied by a strong urging to keep it understandable and workable.
- Whether it would dominate the Canadian strategy and drive policy rather than being seen as an aid or enabler to help inform strategy and policy. Nevertheless, the concept of a TAF was seen as an important, even critical, enabler to help inform strategy and policy development and hence the initiative should proceed with this caution in mind.
- Whether it would become the front edge of a move to adopt a severe, controlling approach that would unduly constrain bioscience research and the sharing of related knowledge or add another unwelcome and difficult administrative overburden to this science and knowledge sharing community. Participants were assured that the eventual use of the TAF as a tool is still to be determined and would be defined through multi stakeholder involvement and that the stakeholders and sponsors involved in this initiative shared the intent to develop a Canadian approach (to dual use biotechnology) based on common awareness, self-governance and self-management, ethical principles/codes of conduct, shared responsibility and joint action, through as workable an approach as possible. Given this expressed intent, the TAF initiative was urged to proceed, especially given the benefits and enabling role perceived for such an aid.

Following are the several ways that the TAF could be used to conduct threat assessments and inform management strategy and policy regarding dual use biotechnology:

1. Develop a threat assessment model for any column of the TAF (i.e., for DU research, knowledge, technologies, pathogens, etc.) that would provide general guidance to that column and a basis for conducting individual case assessments for events/activities occurring in that column. This could be differentiated into separate models for the two types of 'legitimate research with inadvertent misuse' and 'illegitimate research with deliberate misuse.'

2. Apply assessment to individual threat cases within a column (e.g. review the creation and dissemination of a certain type of knowledge of concern). This could be applied separately to the two types of 'legitimate research with inadvertent misuse' and 'illegitimate research with deliberate misuse.'

3. Develop a summary threat assessment for a whole DU process (i.e., a diagonal slice across the table). In this option, a whole set of linked potential events/ activities selected from several or all the columns across the TAF table are connected and assessed using the tools/templates in each row (whether for a case of legitimate research with inadvertent or a case of illegitimate research with deliberate misuse).

4. Develop a set of archetype threat scenarios with full threat analysis and summary for each. These would map over a wide range of threat situations incorporating a range of risk events/activities (from each of the TAF columns) involving different actors of

interest. The scenario set with the associated threat assessment would then become a reference point/model for future threat assessments.

5. Use the threat assessment models for each column to develop agreed, shared multi-stakeholder strategies to mitigate and manage the threat, ideally before it occurs.
6. Use the threat assessment models and mitigating strategies for each column to develop agreed, shared multi-stakeholder policies to guide principled action and practices by stakeholders.

7.0 RECOMMENDATIONS

Following are recommendations by the writer on the Threat Assessment Framework based on the literature review, the results of the subject matter expert interviews conducted and the experience in developing and reviewing the draft concept for a TAF as outlined in this report.

Canada needs a strategy and approach to deal with dual use biotechnology. One that is developed, shared and commonly applied by the key stakeholders implicated including scientists (private and public sector), R&D funding agencies, scientific publishers and their editors, security professionals and law enforcement (counter-terrorism), and government regulators. Such a Canadian approach needs and would be well supported by a TAF. This framework would help to:

- scan for and scope the potential risks and threats involved and to determine which would merit attention and a joint approach and thereby to develop the 'Agenda of Concern;'
- define the necessary assessment terminology for common use and the reasoning and the basis of ratings and judgement to guide future assessments;
- allow the parties to assess typical and atypical/individual case threat events/activities to produce an assessment profile and summary rating that would enable threat prioritizing and a management emphasis to be developed; and
- determine joint strategies and policy positions to establish among the stakeholders in response to the agenda of concern and individual cases as they arise or are proactively projected to emerge.

Therefore, it is recommended that:

1. The concept of a TAF be pursued post haste and a model developed through the collaborative input of a cross section of stakeholders implicated in dual use biotechnology.
2. The TAF model should draw upon the draft concept outlined in this report and the feedback/lessons arising from its review in this study, accompanied by a strong urging to keep it understandable and workable.
3. Two TAF models for Canada be developed. One TAF model would be focused on 'legitimate research with inadvertent misuse' and the other on 'illegitimate research with deliberate misuse,' and would draw upon the concepts and learning in this study. Both would be designed with a global context and scope but would have subsections that consider the Canadian context and are tailored to specific conditions and the agenda of concern most relevant to Canada.
4. The TAF models be pilot tested with a selection of case examples that would fully explore the scope of the TAF and would be applied by a small expert stakeholder group.
5. The TAF model be utilized to:
    a. scan for and scope the potential risks and threats involved and to determine which would merit attention and a joint approach and thereby to develop the 'Agenda of Concern;'
    b. define the necessary assessment terminology for common use and the reasoning and the basis of ratings and judgement to guide future assessments;

   c. allow the parties to assess typical and atypical/individual case threat events/activities to produce an assessment profile and summary rating that would enable threat prioritizing and a management emphasis to be developed.

6. The process of exploring and developing a TAF for Canada be utilized to help create awareness, understanding and involvement among stakeholders of the DU challenge and the need for joint management responses and to help socialize the concept of risk assessment and risk management in this area.
7. Through the development of the TAF, the stakeholders should determine joint Canadian strategies and policy positions in response to the 'Agenda of Concern' and for individual cases as they arise or are proactively projected to emerge. The Canadian approach (to dual use biotechnology) should be based on common awareness, self-governance and self-management, ethical principles / codes of conduct, shared responsibility and joint action, through as workable an approach as possible.
8. The TAF model, correlated strategies and policies be used to inform a Canadian international view and approach on dual use biotechnology and to advocate for an international TAF, ideally based on the core concepts and learning of this TAF model when developed.

APPENDIX A: PARTICIPANTS INTERVIEWED FOR THIS STUDY

Dr. Kent Harding
Chief Scientist
Defence Research & Development Canada
DRDC – Suffield

Ms. Marianne Heisz
Acting Director, Office of Laboratory Security, Centre for Emergency Preparedness and Response
Public Health Agency of Canada (PHAC)

Ms. Sandra Fry
Director, Ontario Laboratories Network,
Director, Ottawa Laboratory (Fallowfield)
Canadian Food Inspection Agency/CFIA

Professor Elisa Harris
Social Scientist
University of Maryland
Center for International & Security Studies at Maryland

Dr. Sam Kaplan
Professor and Chair, Department of Microbiology & Molecular Genetics
University of Texas Medical School
Houston, Texas
USA

Dr. Donald Low
Medical Microbiology
Department of Microbiology
Mount Sinai Hospital
Toronto

Dr. Frank Plummer
Scientific Director
National Microbiology Laboratory
Public Health Agency of Canada (PHAC)

Dr. David Evans
Professor and Chair
Medical Microbiology & Immunology
University of Alberta

Mr. Dan Dragon
Biosafety Officer
Office of Environmental Health and Safety
University of Alberta

Dr. Malcolm Dando
Social Scientist
University of Bradford,
United Kingdom

Dr. Peter A. Singer, MD, MPH, FRCPC
Senior Scientist and Co-Director, Program on Life Sciences, Ethics and Policy
McLaughlin-Rotman Centre for Global Health
Professor of Medicine
University of Toronto

Mr. Timothy Patraboy
Senior Scientist
Canadian Security Intelligence Service (CSIS)

Dr. Harry Deneer
Department of Microbiology
University of Saskatchewan

Dr. Shane K. Green
Lead, Social Impact Programs
Ontario Genomics Institute

Mr. Bart Pietrusiewicz
Policy Research Associate
BIOTECanada

Mr. David Brener
Director Research Translation
Canadian Institutes of Health Research

Dr. Tony Willis
Executive Officer, Counter-terrorism
Chemical, Biological, Radiological and
Nuclear Section, International Security
Division, Department of Foreign Affairs
Australia

Mr. Guy Collyer
Detective Sergeant
National Counter Terrorism Security Office
Foreign and Commonwealth Office
United Kingdom

Dr. Richard Villemur
Biochemistry / Molecular Biology
INRS – Institut Armand-Frappier, Laval

Ms. Wendy Johnson
Former Vice President R&D
Cangene Corporation

APPENDIX B: INTERVIEW QUESTIONS

1. What are the foundation concepts and issues in Dual Use Biotechnology that need to be addressed in any threat assessment framework (with examples)? Expand on each.
2. What does threat assessment mean in the field of Dual Use Biotechnology?
3. What are the possible core concepts for a threat assessment framework for DU biotech?
4. Does the DU process portrayed in the previous graphic seem promising as a starting point for the threat assessment framework portrayed in the draft framework table (following)?
5. Examine each column (questions a-f) and row (questions g-k) of the framework table:
   a. What are the categories or types of DU research that should be subject to assessment?
   b. What are the categories or types of DU research knowledge/information output that would be of potential concern?
   c. What are the categories of types of technologies and equipment/tools used in or arising from DU research that would be of potential concern?
   d. What are the categories or types of pathogens/biological agents that the threat assessment would be concerned with?
   e. How would we list the ways that pathogens can be altered or readied or weaponized so they become potential bioterror/biowarfare weapons?
   f. What are the more compelling ways that such pathogens can be employed for malicious, terrorist intent? What would be the objective(s) of such applications?

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   g. Can we organize the types of DU threats into 'Known, Suspected, Unknown'? How would we define each type?
   h. If we incorporate a 'risk-benefit' analysis, can we define risk = potential for harm; and benefit = a judgment of the value add, whether there are existing alternative, and the impact of not advancing the DU element? How would we assess each of these qualities? How would we render a summary judgment?
   i. Can we identify the well intentioned and potential malevolent actors in DU as State or Non-State/Rogue? Can we further profile those of concern by parameters such as: motivation (intentional, unintentional); intent; capability; and opportunity?
   j. As we move into classic risk analysis (probability versus impact) and build the 'probability it will occur' picture, can we employ probability parameters such as: availability/ accessibility; feasibility/complexity; and cost/efficiency? How would we assess each of these qualities? How would we render a summary judgment of likelihood?
   k. When we develop the impact profile, is it appropriate to first consider the vulnerability of domains such as public health, environment (both natural and man made), animals, social stability, the economy and the research system (which is engaged in DU research)? How would we characterize vulnerability for each of these domains? Can we then consider what the intentions are of the threat agent against each of the vulnerable domains using

an impact spectrum ranging from: mass or selected destruction; to mass or selected disruption/destabilization; to impact on mass psyche/terror; to loss of confidence/credibility? How would we render a summary judgment of impact?

6. When we undertake a summary application using the assessment framework, we could:
   a. Summarize the policy picture for any column (i.e., each step/threat element in the DU process), allowing us to outline the policy scope, how the assessment components are applied and where the greatest focus will be, plus monitoring guidelines, for that threat element (e.g., for knowledge generated by a DU research
   b. Provide a summary threat assessment for a case example in a column (e.g. the probability that a selected pathogen can be altered or readied or weaponized so it becomes a potential bioterror/biowarfare weapon and the impact if this occurs).
   c. Provide a summary threat assessment a threat assessment approach for a whole DU process (i.e., a diagonal slice across the table), e.g. to summarize and rate the probability that the results of a particular research on an immune system modification, with a risk-benefit profile of *x*, can be accessed and used by non-state actors, who will have the access to the knowledge and pathogen inputs, to produce a bioterror/biowarfare weapon that would produce an impact with consequences of *y* in the areas of *z*.

      Please comment on each of these summary application approaches……in terms of validity, usefulness, improvements.
7. Where and how would you see the threat assessment framework being of greatest value? What advice do you have on the scope and priority focus of applications of the threat assessment framework?

APPENDIX C: CONCEPT FOR A THREAT ASSESSMENT FRAMEWORK (TAF)

DU Process Elements / Assessment components	Research (Deliberate or Inadvertent)	Knowledge (Creation and Dissemination)	Technologies & Equipment/ Tools	Pathogens (Intended or Unintended)	Delivery or distribution of Pathogens (Deliberate and Inadvertent)	Pathogen Misuse Applications or Unintended Consequences or Outcomes
1. Dual Use Types - **known** - **suspected** - **unknown** ***Identify types of concern***	Seven classes of Experiments of Concern (USNRC) Three tiers of dangerous activities (Center for International Security Studies at Maryland) Seven criteria for identifying DU Research of Concern (NSABB)	How to conduct the process How to produce the pathogen How to control related DNA synthesizers How to isolate and purify a pathogenic microbe How to use the pathogen How to modify a pathogen increase destructive qualities Knowledge access and dissemination means and mechanisms (data bases, publishing, etc)	Core life science technologies to produce pathogens Products of convergent technologies Genetic modification techniques Synthetic genomics & synthetic chemistry Novel applications of converging technologies Enabling equipment types and support tools – export control list: Australia Group	Biological agents and toxins including plant pathogens and anti-crop agents & animal pathogens Selection/priority criteria: infective dose, pathogenicity, virulence, lethality, transmissibility CDC List of potential bioterrorism diseases and agents (Category A, B, C) Australia Group list of biological agents, plant, animal pathogens Broad view of threat spectrum (pathogen properties, evolving technologies)	Deliberate: - ways to increase deliverability e.g. weaponization (dispersal factor) - deliverability factors (pathogen scale, stability and stability/ survival over time) - indicators of delivery design such as acquisition of stabilizers Inadvertent: - dangerous pathogen release possibilities - access issues (chain of custody)	Intentional misuse: Combinations of - actors (biocrimes thru lone actors, biological warfare thru well developed states, biological warfare through rogue states, bioterrorism through non-state actors), and - their targets (humans, animals, agriculture), and - their intentions (destruction, disruption/ destabilization, psychological terror), and - the impacts Unintentional: see inadvertent distribution column

DU Process Elements / Assessment components	Research (Deliberate or Inadvertent)	Knowledge (Creation and Dissemination)	Technologies & Equipment/ Tools	Pathogens (Intended or Unintended)	Delivery or distribution of Pathogens (Deliberate and Inadvertent)	Pathogen Misuse Applications or Unintended Consequences or Outcomes
2. Risk – Benefit Analysis - **Risk = potential for harm** - **Benefit = value, whether existing alternatives, impact of not doing** ***Identify highest potential risk threat element (i.e., where the potential risks exceed potential benefits)***	*Risks* – potential for harm, identifiable bioterrorism applications, techniques to increase pathogenicity *Benefits* – value add, addresses important health or humanitarian issue, existing alternatives, impact of not doing	*Risks*: Storing, access and dissemination of knowledge arising from research of concern (publications, websites, open databases Unwarranted or undesirable access to sensitive knowledge through research collaboration, apprenticeships, graduate programs *Benefits*: Advance understanding Inform global advances Synergistic collaborations	*Risks*: See issues and risks identified in international conventions re technologies of concern and convention controls on export of equipment of and tools that may enable research of concern	*Risks*: See characteristics and risk qualities of the lists/classes of dangerous pathogens [group and rate under factors of pathogenicity, lethality, virulence, etc See US Risk Assessment of 28 bio-threat agents (threat, vulnerability and consequences)	*Risk*s: Deliberate Del Deliverability factors, e.g. weaponization, amplification, pathogen scale, stability, viability over time Availability of pathogens, skills and knowledge to deliver *Risks*:Inadvertent Del Release possibilities (chain of custody) Access issues and possibilities	*Risk analysis not applicable here, i.e. represents the whole event and outcomes*
3. Actors (Inadvertent Behaviours) ***Identify highest threats posed by certain actors with risk behaviours***	Actors - Legitimate scientists - Owners, custodians and distributors of knowledge - Manufacturers and distributors of scientific equipment - states engaged in biological warfare prep/control Motivations - scientists: pursue scientific answers - knowledge owners/distributors: Sharing knowledge and Provide basis for more advanced research - states; Control and destruction of stockpiles, control sensitive knowledge, ethical practices of personnel				Behaviours - failure to follow ethical principles & practices - failure to understand vulnerability and danger, not manage results - failure to consider vulnerability and security issues in access and distribution of knowledge - failure to manage control and destruction of stockpiled pathogens and related sensitive knowledge and related personnel	

DU Process Elements / Assessment components	Research (Deliberate or Inadvertent)	Knowledge (Creation and Dissemination)	Technologies & Equipment/ Tools	Pathogens (Intended or Unintended)	Delivery or distribution of Pathogens (Deliberate and Inadvertent)	Pathogen Misuse Applications or Unintended Consequences or Outcomes
4. Actors (Deliberate Misuse Behaviours) ***Identify highest threat actors***	Actors - Illegitimate scientists engaged in research of concern, producing intended pathogens - States engaged in biological warfare preparations - Rogue states engaged in biological warfare prep, state approved terrorist initiatives, support to terrorist initiatives, - Non-state engaged in bioterrorism research, accessing pathogens, developing delivery systems to distribute pathogens, developing and executing plans to misuse dangerous pathogens with intent Motivations - Illegitimate scientists: provide results that support biowarfare or bioterrorism - States: use of stockpiled pathogens or related knowledge - Rogue states: political and ideological, malevolent intent to harm or destabilize, exert influence - Non-state: political and ideological, malevolent intent to cause destruction and terror				Behaviours - Intentional disregard of ethical principles & practices - Intentional disregard for control and destruction of stockpiled pathogens and related sensitive knowledge and related personnel - Providing results on research of concern to those with malevolent intent; providing access to pathogens of concern; developing delivery systems; developing and executing plans to misuse dangerous pathogens with intent to cause selective or mass destruction, destabilization and psychological terror Profile descriptors - Motivation - Intent - Capability - opportunity	
5. Potential will occur [Could it occur?] **(inadvertent research with unintended consequences)** ***Identify potential that threat element could occur***	Risk Behaviours – drawn from Row 3 inadvertent behaviours - failure to follow ethical principles & practices - failure to understand vulnerability and danger, not manage results - failure to consider vulnerability and security issues in access and distribution of knowledge - failure to manage control and destruction of stockpiled pathogens and related sensitive knowledge and related personnel Risk factors – drawn from Row 2 risk analysis Case conditions – according to each situation			Risk potential rating (Could it occur?) - high - moderate - low - negligible		
6. Probability will occur [Would it occur?] (illegitimate research with deliberate misuse) ***Identify likelihood threat element will occur***	Risk events drawn from Row 1 types, augmented by risks/risk factors in Row 2 and combined with Row 4 Actors analysis (deliberate misuse) Probability factors - availability/accessibility; feasibility/complexity; cost/efficiency - prevalence and endemic nature - historical experience -			Risk probability analysis can be applied to each column or to whole DU processes of linked risk activities across several columns Probability rating (Would it occur?) - high/ moderate/low/negligible		

DU Process Elements / Assessment components	Research (Deliberate or Inadvertent)	Knowledge (Creation and Dissemination)	Technologies & Equipment/ Tools	Pathogens (Intended or Unintended)	Delivery or distribution of Pathogens (Deliberate and Inadvertent)	Pathogen Misuse Applications or Unintended Consequences or Outcomes
7. Impact if occurs ***Identify consequences of threat element occurrence in qualitative and quantitative terms***	Areas of vulnerability - Public health - Environment - Agriculture - Animals - Infrastructure - Economy - Social and political stability Types of impact - Mass or selected destruction - Mass or selected disruption/ destabilization - Impact on mass psyche/terror - Loss of confidence/ credibility			Impact ratings - Catastrophic - Major - Moderate - Minor/negligible		
8. Summary analysis ***Threat element probability of occurring and impact if occurs or,*** ***Potentiality for inadvertent occurrence and impact if occurs***	Summary options: ▪ Threat assessment for each column of TAF (i.e., Research, Knowledge, etc) with two versions: legitimate research with inadvertent misuse and illegitimate research with deliberate misuse ▪ Threat assessment for a whole DU process (i.e., diagonal slice across the whole table) with linked potential events/activities from several/all columns with two versions: legitimate research with inadvertent misuse and illegitimate research with deliberate misuse			▪ Set of archetype Threat Scenarios with full threat analysis for each (become reference models for further iterations and cases)		

DU Process Elements / Assessment components	Research (Deliberate or Inadvertent)	Knowledge (Creation and Dissemination)	Technologies & Equipment/ Tools	Pathogens (Intended or Unintended)	Delivery or distribution of Pathogens (Deliberate and Inadvertent)	Pathogen Misuse Applications or Unintended Consequences or Outcomes
9. Threat Management - Mitigating Strategies	Strategies to mitigate risk in research of concern	Strategies to mitigate risk in vulnerable/ sensitive knowledge creation and dissemination	Strategies to mitigate risk in access to vulnerable technologies of concern, and to mitigate risk in control of enabling equipment and tools	Strategies to mitigate risk in management of dangerous pathogens and agents of concern	Strategies to mitigate risk in access to and development of delivery and distribution systems for dangerous pathogen dissemination Strategies to mitigate risk in inadvertent release and access to dangerous pathogens	
10. Policy Position	Policies governing principles, positions and practices related to research of concern	Policies governing principles, positions and practices related to vulnerable/ sensitive knowledge creation and dissemination	Policies governing principles, positions and practices related to access to vulnerable technologies of concern, and to control of enabling equipment and tools	Policies governing principles, positions and practices related to the management of dangerous pathogens and agents of concern	Policies governing principles, positions and practices related to access to and development of delivery and distribution systems for dangerous pathogen dissemination Policies governing principles, positions and practices related to inadvertent release and access to dangerous pathogens	

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APPENDIX D: EXPERIMENTS OF CONCERN

Extracted from the publication "Biotechnology Research in an Age of Terrorism: Confronting the Dual Use Dilemma" United States National Research Council of the National Academies. The National Academies Press, 2004

Recommendation 2: Review of Plans for Experiments
We recommend that the Department of Health and Human Services (DHHS) augment the already established system for review of experiments involving recombinant DNA conducted by the National Institutes of Health to create a review system for seven classes of experiments (the Experiments of Concern) involving microbial agents that raise concerns about their potential for misuse.

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Experiments of Concern would be those that:

1. **Would demonstrate how to render a vaccine ineffective**. This would apply to both human and animal vaccines. Creation of vaccine- resistant smallpox virus would fall into this class of experiments.

2. **Would confer resistance to therapeutically useful antibiotics or antiviral agents**. This would apply to therapeutic agents that are used to control disease agents in humans, animals or crops. Introduction of ciprofloxacin resistance in *Bacillus anthracis* would fall into this class.

3. **Would enhance the virulence of a pathogen or render a nonpathogen virulent**. This would apply to plant, animal, and human pathogens. Introduction of cereolysin toxin gene into *Bacillus anthracis* would fall into this class.

4. **Would increase transmissibility of a pathogen**. This would include enhancing transmission within or between species. Altering vector competence to enhance disease transmission would also fall into this class.

5. **Would alter the host range of a pathogen.** This would include making nonzoonotics into zoonotic agents. Altering the tropism of viruses would fit into this class.

6. **Would enable the evasion of diagnostic/detection modalities**. This could include microencapsulation to avoid antibody-based detection and/or the alteration of gene sequences to avoid detection by established molecular methods.

7. **Would enable the weaponization of a biological agent or toxin**. This would include the environmental stabilization of pathogens. Synthesis of smallpox virus would fall into this class of experiments.

APPENDIX E: CRITERIA FOR IDENTIFYING DUAL USE RESEARCH OF CONCERN

From the report of the National Science Advisory Board for Biosecurity Draft Guidance documents on Dual Use Research in the Life Sciences, July 2006

Criteria for Identifying Dual Use Research of Concern

Research that, based on current understanding, can be reasonably anticipated to provide knowledge, products, or technologies that could be directly misapplied by others to pose a threat to public health, agriculture, plants, animals, the environment, or materiel.

Careful consideration should be given to knowledge, products, or technologies that:

a) Enhance the harmful consequences of a biological agent or toxin

b) Disrupt immunity or the effectiveness of an immunization without clinical and/or agricultural justification

c) Confer to a biological agent or toxin, resistance to clinically and/or agriculturally useful prophylactic or therapeutic interventions against that agent or toxin, or facilitate their ability to evade detection methodologies

d) Increase the stability, transmissibility, or the ability to disseminate a biological agent or toxin

e) Alter the host range or tropism of a biological agent or toxin

f) Enhance the susceptibility of a host population

g) Generate a novel pathogenic agent or toxin, or reconstitute an eradicated or extinct biological agent

APPENDIX F: DANGEROUS RESEARCH ACTIVITIES

As proposed by the Center for International and Security Studies at Maryland (CISSM) USA

Proposed a three tier approach with different monitoring and management mechanisms at each level.

Potentially dangerous activities: research that increases the potential for otherwise benign pathogens to be used as weapons or that demonstrates techniques that could have destructive applications. This could include research that increases the virulence of a pathogen or that involves the de novo synthesis of a pathogen, as was done in the poliovirus experiment. Oversight at this level would be exercised through a combination of personnel and facility licensing, project review, and where appropriate, project approval. Under our approach, the vast majority of microbiological research would either fall into this category or not be covered at all.

Moderately dangerous activities (i.e., involves pathogens already identified as public health threats): research involving controlled agents or related agents, especially experiments that increase the weaponization potential of such agents. This could include research that increases the transmissibility or environmental stability of a controlled agent, or that involves the production of such an agent in powder or aerosol form, which are the most common means of disseminating biological warfare agents. All projects that fall into this category would have to be approved at the national level and could be carried out only by licensed researchers at licensed facilities.

- Increasing virulence of listed/related agent
- Insertion host genes into listed/related agent
- Increasing transmissibility/environmental stability listed/related agent
- Powder or aerosol production of listed/related agent
- Powder or aerosol dispersal of listed/related agent
- De novo synthesis of listed/related agent
- Construction of antibiotic/vaccine-resistant related agent
- Genome transfer genome replacement or cellular reconstitution of listed/related agent

Extremely dangerous activities: research largely involving the most dangerous controlled agents, including research that could make such agents even more dangerous. This could include work with an eradicated agent such as smallpox or the construction of an antibiotic- or vaccine-resistant controlled agent, as was done during the Soviet offensive program. All projects in this category would have to be approved internationally, as would the researchers and facilities involved.

- Work with eradicated agent;
- Work with agent assigned BSL4/ABSL4
- *De novo* synthesis of above
- Expanding host or tissue range of listed agent
- Construction of antibiotic/vaccine resistant listed agent

APPENDIX G: LIST OF DUAL-USE BIOLOGICAL EQUIPMENT FOR EXPORT CONTROL

Reference: The Australia Group

1. Complete containment facilities at P3, P4 containment level

Complete containment facilities that meet the criteria for P3 or P4 (BL3, BL4, L3, L4) containment as specified in the WHO Laboratory Biosafety manual (Geneva, 1983) are subject to export control.

2. Fermenters*

Fermenters capable of cultivation of pathogenic micro-organisms, viruses or for toxin production, without the propagation of aerosols, and having all the following characteristics:

a. capacity equal to or greater than 100 litres;

*Sub-groups of fermenters include bioreactors, chemostats and continuous-flow systems.

3. Centrifugal Separators*

Centrifugal separators capable of the contiuous separation of pathogenic micro-organisms, without the propagation of aerosols, and having all the following characteristics:

a. flow rate greater than 100 litres per hour;
b. components of polished stainless steel or titanium;
c. double or multiple sealing joints within the steam containment area;
d. capable of in-situ steam sterilization in a closed state.

*Centrifugal separators include decanters.

4. Cross-flow Filtration Equipment

Cross-flow filtration equipment capable of continuous separation of pathogenic microorganisms, viruses, toxins and cell cultures without the propagation of aerosols, having all the following characteristics:

a. equal to or greater than 5 square metres;
b. capable of in-situ sterilization.

5. Freeze-drying Equipment

Steam sterilizable freeze-drying equipment with a condensor capacity greater than 50 kgs of ice in 24 hours and less than 1000 kgs of ice in 24 hours.

6. Equipment that incorporates or is contained in P3 or P4 (BL3, BL4, L3, L4) containment housing, as follows:

a. Independently ventilated protective full or half suits;
b. Class III biological safety cabinets or isolators with similar performance standards.

7. Aerosol inhalation chambers

Chambers designed for aerosol challenge testing with microorganisms, viruses or toxins and having a capacity of 1 cubic metre or greater.

The experts propose that the following item be included in awareness raising guidelines to industry:

1. Equipment for the micro-encapsulation of live micro-organisms and toxins in the range of 1-10 um particle size, specifically:

a. Interfacial polycondensors;
b. Phase separators.

2. Fermenters of less than 100 litre capacity with special emphasis on aggregate orders or designs for use in combined systems.

3. Conventional or turbulent air-flow clean-air rooms and self-contained fan-HEPA filter units that may be used for P3 or P4 (BL3, BL4, L3, L4) containment facilities.

APPENDIX H: CDC LIST OF POTENTIAL BIOTERRORISM DISEASES AND AGENTS

The US Center for Disease Control (CDC) classifies agents that could be used in bioterrorism into three categories: category A, B or C.

Category A agents.

The CDC defines Category A agents as organisms that pose a risk to national security because they are easily disseminated or transmitted from person to person, result in high mortality rates and have the potential for a major public health impact, might cause public panic and social disruption, and require special action for public health preparedness.

• Anthrax (*Bacillus anthracis*)
• Botulism (*Clostridium botulinum* toxin)
• Plague (*Yersinia pestis*)
• Smallpox (*Variola major*)
• Tularemia (*Francisella tularensis*)
• Viral hemorrhagic fevers
• Arenaviruses. Lymphocytic choriomeningitis virus, Junin
virus, Machupo virus, Guanarito virus, Lassa fever
• Bunyaviruses. Hantaviruses, Rift Valley fever
• Flaviviruses. Dengue
• Filoviruses. Ebola, Marburg

Category B agents.

The CDC defines Category B agents as organisms that are moderately easy to disseminate, result in moderate morbidity rates and low mortality rates, and require

specific enhancements of CDC's diagnostic capacity and enhanced disease surveillance.

• *Burkholderia pseudomallei*
• *Coxiella burnetii* (Q fever)
• *Brucella* spp. (brucellosis)
• *Burkholderia mallei* (glanders)
• Ricin toxin (from *Ricinus communis*)
• Epsilon toxin of *Clostridium perfringens*
• *Staphylococcus* enterotoxin B
• Typhus fever (*Rickettsia prowazekii*)
Food and waterborne pathogens
• Bacteria. Diarrheagenic *Escherichia coli*, pathogenic *Vibrio* spp., *Shigella* spp., *Salmonella* spp., *Listeria monocytogenes*, *Campylobacter jejuni* and *Yersinia enterocolitica*
• Viruses. Caliciviruses, hepatitis A
• Protozoa. *Cryptosporidium parvum*, *Cyclospora cayatanensis*, *Giardia lamblia*, *Entamoeba histolytica*, Toxoplasma and microsporidia
Additional encephalitide viruses
• West Nile, La Crosse, California encephalitis, Venezuelan equine encephalitis, Eastern equine encephalitis, Western equine encephalitis, Japanese encephalitis and Kyasanur Forest

Category C agents.

These include emerging pathogens that could be engineered for mass dissemination in the future because of availability, ease of production and dissemination, and potential for high morbidity and mortality rates and major health impact.

- Tick-borne hemorrhagic fever viruses
- Crimean-Congo hemorrhagic fever virus
- Tick-borne encephalitis viruses
- Yellow fever
- Multidrug-resistant tuberculosis
- Influenza
- Other Rickettsias
- Rabies
- Severe acute respiratory syndrome-associated coronavirus (SARS-CoV)

APPENDIX I: AUSTRALIA GROUP LIST OF BIOLOGICAL AGENTS

LIST OF BIOLOGICAL AGENTS FOR EXPORT CONTROL – July 2006

CORE LIST

**** New additions to the list are included in italics***

Viruses

V1. Chikungunya virus
V2. Congo-Crimean haemorrhagic fever virus
V3. Dengue fever virus
V4. Eastern equine encephalitis virus
V5. Ebola virus
V6. Hantaan virus
V7. Junin virus
V8. Lassa fever virus
V9. Lymphocytic choriomeningitis virus
V10. Machupo virus
V11. Marburg virus
V12. Monkey pox virus
V13. Rift Valley fever virus
V14. Tick-borne encephalitis virus (Russian Spring-Summer encephalitis virus)
V15. Variola virus
V16. Venezuelan equine encephalitis virus
V17. Western equine encephalitis virus
V18. White pox
V19. Yellow fever virus
V20. Japanese encephalitis virus
V21. Kyasanur Forest virus
V22. Louping ill virus
V23. Murray Valley encephalitis virus
V24. Omsk haemorrhagic fever virus
V25. Oropouche virus
V26. Powassan virus
V27. Rocio virus
V28. St Louis encephalitis virus
V29. Hendra virus (Equine morbillivirus)
V30. South American haemorrhagic fever (Sabia, Flexal, Guanarito)
V31. Pulmonary & renal syndrome-haemorrhagic fever viruses (Seoul, Dobrava, Puumala, Sin Nombre)
V32. Nipah virus

Rickettsiae

R1. Coxiella burnetii
R2. Bartonella quintana (Rochalimea quintana, Rickettsia quintana)
R3. Rickettsia prowazeki
R4. Rickettsia rickettsii

Bacteria

B1. Bacillus anthracis
B2. Brucella abortus
B3. Brucella melitensis
B4. Brucella suis
B5. Chlamydia psittaci
B6. Clostridium botulinum
B7. Francisella tularensis
B8. Burkholderia mallei (Pseudomonas mallei)
B9. Burkholderia pseudomallei (Pseudomonas pseudomallei)
B10. Salmonella typhi
B11. Shigella dysenteriae
B12. Vibrio cholerae
B13. Yersinia pestis
B14. Clostridium perfringens, epsilon toxin producing types2
B15. Enterohaemorrhagic Escherichia coli, serotype O157 and other verotoxin producing serotypes

Toxins as follow and subunits thereof:3

T1. Botulinum toxins4
T2. Clostridium perfringens toxins
T3. Conotoxin
T4. Ricin
T5. Saxitoxin
T6. Shiga toxin
T7. Staphylococcus aureus toxins
T8. Tetrodotoxin
T9. Verotoxin and shiga-like ribosome inactivating proteins
T10. Microcystin (Cyanginosin)
T11. Aflatoxins
T12. Abrin
T13. Cholera toxin
T14. Diacetoxyscirpenol toxin
T15. T-2 toxin
T16. HT-2 toxin
T17. Modeccin toxin
T18. Volkensin toxin
T19. Viscum Album Lectin 1 (Viscumin)

Fungi

F1. Coccidioides immitis
F2. Coccidioides posadasii

1. Biological agents are controlled when they are an isolated live culture of a pathogen agent, or a preparation of a toxin agent which has been isolated or extracted from any source, or material including living material which has been deliberately inoculated or contaminated with the agent. Isolated live cultures of a pathogen agent include live cultures in dormant form or in dried preparations, whether the agent is natural, enhanced or modified.

An agent is covered by this list except when it is in the form of a vaccine. A vaccine is a medicinal product in a pharmaceutical formulation licensed by, or having marketing or clinical trial authorisation from, the regulatory authorities of either the country of manufacture or of use, which is intended to stimulate a protective immunological response in humans or animals in order to prevent disease in those to whom or to which it is administered.

2. It is understood that limiting this control to epsilon toxin-producing strains of Clostridium perfringens therefore exempts from control the transfer of other Clostridium perfringens strains to be used as positive control cultures for food testing and quality control.

3. Excluding immunotoxins.

4. Excluding botulinum toxins and conotoxins in product form meeting all of the following criteria:

- are pharmaceutical formulations designed for testing and human dministration in the treatment of medical conditions;
- are pre-packaged for distribution as clinical or medical products; and
- are authorised by a state authority to be marketed as clinical or medical products.

Genetic Elements and Genetically-modified Organisms:

G1 Genetic elements that contain nucleic acid sequences associated with the pathogenicity of any of the microorganisms in the list.

G2 Genetic elements that contain nucleic acid sequences coding for any of the toxins in the list, or for their sub-units.

G3 Genetically-modified organisms that contain nucleic acid sequences associated with the pathogenicity of any of the microorganisms in the list.

G4 Genetically-modified organisms that contain nucleic acid sequences coding for any of the toxins in the list or for their sub-units.

***Technical note**:*

Genetic elements include inter alia chromosomes, genomes, plasmids, transposons, and vectors whether genetically modified or unmodified.

Nucleic acid sequences associated with the pathogenicity of any of the micro-organisms in the list means any sequence specific to the relevant listed micro-organism:

- that in itself or through its transcribed or translated products represents a significant hazard to human, animal or plant health; or
- that is known to enhance the ability of a listed micro-organism, or any other organism into which it may be inserted or otherwise integrated, to cause serious harm to human, animal or plant health.

These controls do not apply to nucleic acid sequences associated with the pathogenicity of enterohaemorrhagic Escherichia coli, serotype O157 and other verotoxin producing strains, other than those coding for the verotoxin, or for its sub-units***.***

WARNING LIST1

Bacteria

WB1. Clostridium tetani*
WB2. Legionella pneumophila
WB3. Yersinia pseudotuberculosis

* Australia Group recognises that this organism is ubiquitous, but, as it hasbeen acquired in the past as part of biological warfare programs, it isworthy of special caution.

1. Biological agents are controlled when they are an isolated live culture of a pathogen agent, or a preparation of a toxin agent which has been isolated or extracted from any source, or material including living material which has been deliberately inoculated or contaminated with the agent. Isolated live cultures of a pathogen agent include live cultures in dormant form or in dried preparations, whether the agent is natural, enhanced or modified.

An agent is covered by this list except when it is in the form of a vaccine. A vaccine is a medicinal product in a pharmaceutical formulation licensed by, or having marketing or clinical trial authorisation from, the regulatory authorities of either the country of manufacture or of use, which is intended to stimulate a protective immunological response in humans or animals in order to prevent disease in those to whom or to which it is administered.

Genetic Elements and Genetically-modified Organisms:

WG1 Genetic elements that contain nucleic acid sequences associated with the pathogenicity of any of the microorganisms in the list.

WG2 Genetic elements that contain nucleic acid sequences coding for any of the toxins in the list, or for their sub-units.

WG3 Genetically-modified organisms that contain nucleic acid sequences associated with the pathogenicity of any of the microorganisms in the list.

WG4 Genetically-modified organisms that contain nucleic acid sequences coding for any of the toxins in the list or for their sub-units.

***Technical note**:*

Genetic elements include inter alia chromosomes, genomes, plasmids, transposons, and vectors whether genetically modified or unmodified.

Nucleic acid sequences associated with the pathogenicity of any of the micro-organisms in the list means any sequence specific to the relevant listed micro-organism:

- that in itself or through its transcribed or translated products represents a significant hazard to human, animal or plant health; or
- that is known to enhance the ability of a listed micro-organism, or any other organism into which it may be inserted or otherwise integrated, to cause serious harm to human, animal or plant health.

LIST OF PLANT PATHOGENS FOR EXPORT CONTROL – April 2005

CORE LIST

Bacteria

PB1. Xanthomonas albilineans

PB2. Xanthomonas campestris pv. citri

PB3. Xanthomonas oryzae pv. oryzae (Pseudomonas campestris pv. oryzae)

PB4. Clavibacter michiganensis subsp. sepedonicus (Corynebacterium michiganensis subsp. sepedonicum or Corynebacterium sepedonicum)

PB5. Ralstonia solanacearum races 2 and 3 (Pseudomonas solanacearum races 2 and 3 or Burkholderia solanacearum races 2 and 3)

Fungi

PF1. Colletotrichum coffeanum var. virulans (Colletotrichum kahawae)

PF2. Cochliobolus miyabeanus (Helminthosporium oryzae)

PF3. Microcyclus ulei (syn. Dothidella ulei)

PF4. Puccinia graminis (syn. Puccinia graminis f. sp. tritici)

PF5. Puccinia striiformis (syn. Puccinia glumarum)

PF6. Pyricularia grisea / Pyricularia oryzae

Viruses

PV1. Potato Andean latent tymovirus

PV2. Potato spindle tuber viroid

Genetic Elements and Genetically-modified Organisms:

PG1 Genetic elements that contain nucleic acid sequences associated with the pathogenicity of any of the microorganisms in the Core List.

PG2 Genetically-modified organisms that contain nucleic acid sequences associated with the pathogenicity of any of the microorganisms in the Core List.

Technical note : Genetic elements include inter alia chromosomes, genomes, plasmids, transposons, and vectors whether genetically modified or unmodified.

Nucleic acid sequences associated with the pathogenicity of any of the micro-organisms in the list means any sequence specific to the relevant listed micro-organism:

- that in itself or through its transcribed or translated products represents a significant hazard to human, animal or plant health; or

- that is known to enhance the ability of a listed micro-organism, or any other organism into which it may be inserted or otherwise integrated, to cause serious harm to human, animal or plant health.

Items for Inclusion in Awareness-raising Guidelines

Bacteria

PWB1. Xylella fastidiosa

Fungi

PWF1. Deuterophoma tracheiphila (syn. Phoma tracheiphila)

PWF2. Monilia rorei (syn. Moniliophthora rorei)

Viruses

PWV1. Banana bunchy top virus

Genetic Elements and Genetically-modified Organisms:

PWG1 Genetic elements that contain nucleic acid sequences associated with the pathogenicity of any of the microorganisms in the Awareness-raising Guidelines.

PWG2 Genetically-modified organisms that contain nucleic acid sequences associated with the pathogenicity of any of the microorganisms in the Awareness-raising Guidelines.

Technical note : Genetic elements include inter alia chromosomes, genomes, plasmids, transposons, and vectors whether genetically modified or unmodified.

Nucleic acid sequences associated with the pathogenicity of any of the micro-organisms in the list means any sequence specific to the relevant listed micro-organism:

- that in itself or through its transcribed or translated products represents a significant hazard to human, animal or plant health; or

- that is known to enhance the ability of a listed micro-organism, or any other organism into which it may be inserted or otherwise integrated, to cause serious harm to human, animal or plant health

List of Animal Pathogens for Export Control – April 2005

Viruses

AV1. African swine fever virus

AV2. Avian influenza virus [2]

AV3. Bluetongue virus

AV4. Foot and mouth disease virus
AV5. Goat pox virus
AV6. Herpes virus (Aujeszky's disease)
AV7. Hog cholera virus (synonym: swine fever virus)
AV8. Lyssa virus
AV9. Newcastle disease virus
AV10. Peste des petits ruminants virus
AV11. Porcine enterovirus type 9 (synonym: swine vesicular disease virus)
AV12. Rinderpest virus
AV13. Sheep pox virus

AV14. Teschen disease virus
AV15. Vesicular stomatitis virus
AV16. Lumpy skin disease virus
AV17. African horse sickness virus

1. Except where the agent is in the form of a vaccine.
2. This includes only those Avian influenza viruses of high pathogenicity as defined in EC Directive 92/40/EC:

   "Type A viruses with an IVPI (intravenous pathogenicity index) in 6 week old chickens of greater than 1.2: or

   Type A viruses H5 or H7 subtype for which nucleotide sequencing has demonstrated multiple basic amino acids at the cleavage site of haemagglutinin"

Bacteria

AB3. Mycoplasma mycoides

Genetic Elements and Genetically-modified Organisms

AG1 Genetic elements that contain nucleic acid sequences associated with the pathogenicity of any of the microorganisms in the list.

AG2 Genetically-modified organisms that contain nucleic acid sequences associated with the pathogenicity of any of the microorganisms in the list.

Technical note : Genetic elements include inter alia chromosomes, genomes, plasmids, transposons, and vectors whether genetically modified or unmodified.

Nucleic acid sequences associated with the pathogenicity of any of the micro-organisms in the list means any sequence specific to the relevant listed micro-organism:

- that in itself or through its transcribed or translated products represents a significant hazard to human, animal or plant health; or

- that is known to enhance the ability of a listed micro-organism, or any other organism into which it may be inserted or otherwise integrated, to cause serious harm to human, animal or plant health.

APPENDIX J: ASSESSING RISKS AND BENEFITS OF COMMUNICATING RESEARCH WITH DUAL USE POTENTIAL

From the report of the National Science Advisory Board for Biosecurity Draft Guidance documents on Dual Use Research in the Life Sciences, July 2006

POINTS TO CONSIDER: A FRAMEWORK FOR ASSESSING THE RISKS AND BENEFITS OF COMMUNICATING RESEARCH WITH DUAL USE POTENTIAL

1) General Overview of the Research Information with Dual Use Potential

a) What information is provided?

b) To what extent is it novel?

2) Risk Analysis

a) Are there reasonably anticipated risks to public health from direct misapplication of this information?

i) e.g., is novel scientific information provided that could be intentionally misused to threaten public health?

ii) e.g., does the information point out a vulnerability in public health preparedness?

b) Is it reasonably anticipated that this information could be directly misused to pose a threat to agriculture, plants, animals, the environment, or materiel?

i) e.g., does the information point out a vulnerability with respect to agriculture, plants, animals, the environment, or materiel?

c) If a risk has been identified, in what time frame (e.g., immediate, near future, years from now) might this information be used to pose a threat to public health, agriculture, plants, animals, the environment, or materiel?

d) If the information were to be broadly communicated "as is," what is the potential for:

i) Public misunderstanding

(1) What might be the implications of such misunderstandings, e.g., psychological, social, health/dietary decisions, economic, commercial etc.?

ii) Sensationalism

(1) In what way might it result in widespread concern or even panic about public health or other safety/security issues?

If no risk has been identified, no further dual use communication considerations are necessary. If a risk has been identified, continue on.

3) Benefit Analysis

a) Are there potential benefits to public health and safety from application or utilization of this information?

b) Are there potential benefits of the information for agriculture, plants, animals, the environment, or materiel?

i) e.g., what potential solution does it offer to an identified problem or vulnerability?

c) Will this information be useful to the scientific community? If so, how?

d) If a benefit has been identified, in what time frame (e.g., immediate, near future, years from now) might this information be used to benefit science, public health and safety, agriculture, plants, animals, the environment, or materiel?

4) Risk vs. Benefit Assessment

a) Based on the risks and benefits identified, and considering the time frame in which these might be realized:

i) Do the benefits of communicating the information outweigh the risks?

ii) Do the risks outweigh the benefits?

5) Formulation of Recommendation Regarding Communication

Decisions about how to responsibly communicate research with dual use potential should address content, timing, and possibly extent of distribution of the information.

a) Content

i) Communicate as is.

ii) Communicate with addition of appropriate contextual information. For example, it may be important to address:

(1) The significance of the research findings for public health and safety, agriculture, the environment, or materiel

(2) How the new information or technology will be useful to the scientific community

(3) The biosafety measures in place as the research was carried out

(4) The dual use potential of the information

(5) The careful consideration that was given to the dual use concerns in the decision to publish

iii) Recommend communicating a modified version of the product.

(1) For example, is it possible to "de-couple" the material that poses security concerns from some or all of the potentially useful scientific information, or should specific information be removed (e.g., technical details about an enabling technology)?

b) Timing

i) Communicate immediately.

ii) Recommend that communication be deferred until a clearly defined and agreed-upon endpoint is reached (e.g. a condition is met such that communication no longer poses the same degree of risk).

c) Distribution

i) No limit on distribution

ii) Limit access to selected individuals on a “need to know” basis. It will be necessary to identify categories of individuals who should have access and under what circumstances.

iii) Recommend that the product not be published or otherwise made accessible to the public.

APPENDIX K: METHODS FOR CALCULATING PROBABILITIES

From the International Risk Governance Council report "White Paper on Risk Governance" 2005

In general there are five methods for calculating probabilities:

• Collection of statistical data relating to the performance of a risk source in the past (actuarial extrapolation);

• Collection of statistical data relating to components of a hazardous agent or technology. This method requires a synthesis of probability judgments from component failure to system performance (probabilistic risk assessments, PRA);

• Epidemiological or experimental studies which are aimed at finding statistically significant correlations between an exposure of a hazardous agent and an adverse effect in a defined population sample (probabilistic modelling);

• Experts', or decision makers' best estimates of probabilities, in particular for events where only insufficient statistical data is available (normally employing Bayesian statistical tools);

• Scenario techniques by which different plausible pathways from release of a harmful agent to the final loss are modelled on the basis of worst and best cases or estimated likelihood for each consequence at each

APPENDIX L: REFERENCES, DOCUMENTS AND SOURCES ACCESSED AND CONSIDERED

1. Salerno R M, Gaudioso J, Frerichs R L, and Estes D. *A BW Risk Assessment: Historical and Technical Perspectives.* The Nonproliferation Review / Fall-Winter 2004.
2. Morrison M. *Proceedings from the Nanotechnology and Security Workshop.* Institute of Nanotechnology. February 23, 2007.
3. Van Aken J. *When risk outweighs benefit: Dual-use research needs a scientifically sound risk-benefit analysis and legally binding biosecurity measures*. EMBO reports 7, SI, S10-S-13 (2006) doi: 10.1038/sj.embor.7400726.
4. Trull MC, du Laney TV and Dibner M. *Turning biodefense dollars into products*. Nature Biotechnology / Volume 25 / Number 2, February 2007.
5. Oborne MW. *Managing Risk and Dual Use Technologies: The Case of Biotechnology.* December 2, 2005.
6. *Summary Report of Presentations and Participant Dialogue* (National Forum on Dual Use Biotechnology March 1-2, 2006 / Ottawa, Ontario). April 7, 2006.
7. McLeish C and Nightingale P. Paper No. 132 *The Impact of Dual Use Controls on UK Science: Results From a Pilot Study*. SEWPS, SPRU Science and Technology Policy Research, The Freeman Centre, University of Sussex, Falmer, Brighton, UK.
8. *Do no harm: reducing the potential for the misuse of life science research.* Report of a Royal Society – Wellcome Trust meeting held at the Royal Society on 7 October 2004
9. Chapter 3: *The Ongoing Scientific and Technological Revolution* from Biotechnology, Weapons and Humanity 11, 2004. BMA Science and Education Department.
10. *Biological Weapons & Codes of Conduct*, A Chronology of Development, University of Exeter, UK, http://www.projects.ex.ac.uk
11. The Biological and Toxin Weapons Convention Implementation Act, Government of Canada legislation, 2002
12. Corneliussen F. *Steps for Preventing the Misuse of Biological Research* (Voice of Industry Conspicuously Silent in Policy Discussions). Genetic Engineering News, Point of View January 15, 2006 (Vol. 26, No.2).
13. Committee on Advances in Technology and the Prevention of Their Application to Next Generation Biowarfare Threats, National Research Council, US National Academy of Sciences. *Globalization, Biosecurity, and the Future of the Life Sciences* http://www.nap.edu/catalogue/11567.html
14. World Health Organization. *Life science research: opportunities and risks for public health.* World Health Organization 2005.
15. US National Academies, National Research Council, Committee on Research Standards and Practices to Prevent the Destructive Application of Biotechnology. *Biotechnology Research in an Age of Terrorism: Confronting the Dual Use Dilemma.* Washington, DC, The National Academies Press

16. Steinbruner JD, Harris ED. Controlling Dangerous Pathogens. *Biological Weapons, Issues in Science and Technology* Spring 2003.
17. Schneidmiller C. Scientific Codes of Conduct Inevitable, Experts Say. *Global Security Newswire*. February 22, 2006.
18. The Royal Society Policy Document *The roles of codes of conduct in preventing the misuse of scientific research* 03/05
19. Presentation by David Heyman and Gerald Epstein, co-Directors of CSIS Biological Threat Reduction project (BTR), who presented a new approach to biological threat reduction to delegates at the Sixth Review Conference of the Bioweapons Convention in Geneva in November, 2006. Their briefing, titled "Governance for Biological Threat Reduction: A Comprehensive, Interdisciplinary, International Approach", described a new framework that could substantially advance steps on a global level to reduce the risk of bioterrorism or other misuse of biology.
20. Website and associated open source documents for: the US National Research Council and its subsidiary organization, the National Academy of Sciences
21. Website and associated open source documents for: the Monterey Institute's Center for Non-proliferation Studies, San Diego, California
22. Website and associated open source documents for: the International Risk Governance Council, Geneva, Switzerland
23. Website and associated open source documents for: the National Science Advisory Board for Biosecurity, USA

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(U) Following the 2006 National Forum on Dual Use Biotechnology, it was clear that a Canadian strategy and policy would be needed to provide guidance and leadership on this issue within Canada and to support Canadian advocacy and positions in international fora. It was also suggested that certain advisory, analytical and decision making tools and reference frameworks would be needed to support such a Canadian approach and among them, the idea of a threat assessment aid was raised. With this context, Defence Research and Development Canada decided to pursue the idea through a commissioned study that would consider the feasibility, applicability and potential design of a Threat Assessment Framework (TAF) concept. The study would scan current developments and trends in the governance and management of dual use biotechnology, identify the core issues that need to be addressed in such a threat assessment framework, explore core elements for the framework, and if deemed feasible, undertake a preliminary concept development for the framework.

(U)

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