BIORISK MANAGEMENT CASE STUDY: CENTRE FOR BIOSECURITY AND BIOPREPAREDNESS

CENTRE FOR BIOSECURITY AND BIOPREPAREDNESS

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SUMMARY

Centre for Biosecurity and Biopreparedness (CBB) is the Danish authority on biosecurity and biopreparedness. CBB's risk assessment and risk management processes exemplify practical, small-scale (small country) approaches to prevent the misuse of dual-use materials and technologies that could lead to the production or use of biological weapons. This case study provides insights on how to approach regulation of dual-use technologies in an inclusive but authoritative manner and on the types of expertise required for this process. CBB:

- has a **legal mandate** to regulate dual-use technologies, referred to in Denmark as "technologies with misuse potential."
- considers technologies related to work with controlled pathogens as well as **technologies that may have a strong enabling effect** on the development, production, or use of bioweapons.
- uses a **lean and flexible process** that emphasizes dialogue with researchers in academia and industry.

DISCLAIMER

Biosafety and biosecurity risk management practices can change over time. This case study represents one point in time and is a sample of an evolving set of risk management practices. For additional information on current practices please contact the organization directly.

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THE VISIBILITY INITIATIVE FOR RESPONSIBLE SCIENCE (VIRS)

The goal of the Visibility Initiative for Responsible Science (VIRS) is to share information about the value of biorisk management and how life science stakeholder organizations approach the issue. VIRS was conceived by a multi-stakeholder group during an April 2019 working group meeting of the Biosecurity Innovation and Risk Reduction Initiative (BIRRI) program of NTI Global Biological Policy & Programs. With support from NTI, Stanford University Bio Policy & Leadership in Society VIRS produced a set of Case Studies in biorisk management, and The Biorisk Management Casebook that provides cross-cutting insights into contemporary practices.

THE BIORISK MANAGEMENT CASE STUDIES

The Biorisk Management Case Studies describes biorisk management processes for a diverse set of life science research stakeholders. The collection serves to evaluate the feasibility and value of knowledge sharing among both organizations that have similar roles and those that have different roles in managing research. Case studies were developed in consultation with organizations through a combination of research based on public sources, interviews, and providing a template with guiding questions for organizations to complete directly. Additional analysis can be found in The Biorisk Management Casebook: Insights into Contemporary Practices[1] in this collection. Project Directors: Megan Palmer, Stanford University; Sam Weiss Evans, Harvard University.

CONTRIBUTORS

- Line Gylling, Head of Biosecurity Section, MSc (Biology), CBB
- Katja Nyholm Olsen, Former Head of Laboratory Section, Ph.d. (Microbiology), CBB
- Kathryn Brink, Stanford University

ORGANIZATION BACKGROUND

Centre for Biosecurity and Biopreparedness (CBB) is the national authority that administers Danish biosecurity legislation. CBB's risk management framework is composed of both preventive measures (biosecurity) and mitigation and response measures (biopreparedness), including a 24/7 response capability to counter biological incidents.[2]

CBB was created in 2001 under the Ministry of Health to establish biopreparedness capabilities and the organization is a part of Statens Serum Institut.[3] Seeking to fulfill its obligation to UNSCR 1540, and following the recommendations from a biosecurity survey conducted in Scandinavia in 2007,[4] the Danish government signed the Biosecurity Act on Securing Specific Biological Substances, Delivery Systems and Related Materials in 2008[5] and a relevant Executive Order (EO) in 2009.[6] Annex 1 of the EO specifies a list of controlled items, including:

- Biological substances, including human pathogens, zoonoses and toxins, associated genetic elements and genetically modified organisms
- Delivery systems, including certain spray or mist systems
- Related materials, including process equipment used in the handling and processing of biological materials and related technology which can be immediately used for biological weapons development, production, or use

The Danish biosecurity control list is nearly identical to the Australia Group Common Control List[7] and is harmonized with Danish Export Control. "The biological substances, delivery systems and related materials included in the Annex to the Executive Order may be held, produced, used and stored only if a relevant permit has been obtained."[6] **CBB issues permits to legally authorize individuals or entities to work with substances and technologies on the control list.**

This case study focuses on CBB's approach to regulating technology with misuse potential (TMP), which is "[t]echnology, which can be directly used for the development of biological weapons or for offensive usage of biological weapons" (Annex 1, Section 3.i).[6] Technology should be understood as dual-use knowledge and skills. CBB distinguishes TMP from physical items, which are subject to slightly different risk management approaches. For a detailed description of CBB's overall approach to biorisk management, see its self-published guide "An efficient and practical approach to biosecurity."[8]

Supported by the legal framework, CBB's approach to TMP control is guided by a continuous threat landscape analysis. This analysis draws on the varied expertise of CBB's team, including not only biological knowledge but also insights into dual-use scenarios, military history, and technical weapons knowledge. CBB develops analyses in-house with support from open-source intelligence (OSINT), CBB's own expertise and analytical discoveries, and national and international collaborations.

CBB has adjusted its risk management approach to TMP over the years to incorporate feedback from dialogues with stakeholders and lessons learned from the governance of physical dual-use items. TMP cases have been rare, though, and although there is a good management framework in place, it has been difficult to get enough experience to test it.

In parallel to the legal regulation of both physical items and TMP, CBB makes efforts to raise awareness of biosecurity, the legal framework, TMP, and responsible research among life science students and researchers at Danish universities and encourages and supports biosecurity officers to establish a strong biosecurity culture in their workplaces.

Assessing and regulating TMP is difficult. CBB aims to participate in stronger national and international networks and possibly establish new partnerships to make progress on this issue. CBB sees biotechnology development as a future high-risk area in terms of dual-use potential, enabled and pushed forward by interactions with other emerging technologies.

PROCESS

Scope of risks considered

The 2009 EO gives CBB legal authority over any current and future dual-use technologies CBB deems to be directly useful to the development, production, or use of bioweapons. Thus, **CBB considers not only TMP involving work with pathogens directly, but also TMP that may have a strong enabling effect on the development, production, or use of bioweapons.** For example, CBB also evaluates TMP risks associated with spray drying or fermentation techniques, where highly specialized expertise is required for design, development, and troubleshooting. While all work in Denmark related to TMP is subject to review by CBB, most technologies that CBB reviews do not ultimately require a permit.

Overall sequence of steps

CBB uses a case-dependent approach to manage TMP risks, and risk mitigation can vary according to the type of TMP. The process from application to issuing a permit for work with TMP can last anywhere from 2–3 weeks up to three months, depending on the applicant and type of project or technology.

- The process proceeds as follows:
  CBB becomes aware of a TMP project that could benefit from risk assessment. This can happen in a few different ways, including: an institution self-reports TMP to CBB, CBB conducts an inspection of a facility that has an existing biosecurity permit related to other controlled items, or CBB visits a facility without a current permit but based on its research and publication portfolio. CBB plans to conduct more outreach to potential applicants that do not currently hold permits, pending available resources at CBB.
- CBB visits the research facility that may potentially require a permit (hereafter referred to as the applicant) and has a dialogue about the technology that the applicant is working with/pursuing.
- CBB performs a detailed risk assessment based on the dialogue with the applicant, CBB's own evaluation of the potential of the technology, and perhaps supporting documentation (e.g., project description) and decides whether a permit is required.
- If a permit is required, the applicant applies for a permit, which includes performing a vulnerability assessment and making a security plan. The individual(s) completing the application are biosecurity officers supported by e.g., researchers, project leaders, experts, and/or management. The vulnerability assessment consists of answering a standard set of questions, such as how many workers are involved in the project and the purpose and time frame of the project. The security plan details mitigation strategies to address the vulnerabilities identified in the assessment.
- CBB reviews the permit application and issues the permit. If CBB decides that a TMP permit is not necessary, CBB still offers risk mitigation and guidance according to the needs of the applicant.
- The applicant proceeds with its work following CBB's requirements and guidelines. Requirements will be mentioned in the permit and are supported by guiding documents available to the biosecurity officers.
- Every 2–3 years, CBB performs an inspection where it evaluates the project and discusses mitigation steps with the applicant. Some types of projects or technologies could involve more frequent interactions between CBB and the applicant, but this has not yet been necessary.
- Every five years the applicant must re-apply for a permit, which also provides an opportunity for CBB and the applicant to revisit risks and mitigation steps.

Risk assessment

CBB risk assessments draw on dialogue with the applicant, documentation related to the TMP project, and an internal CBB assessment. Some research institutions in Denmark also have their own dual-use research assessment procedures; these institutions apply for a permit and/or seek counseling from CBB as needed.

Ideally, 2–4 experts from CBB are involved in the risk assessment process for a given TMP project. All experts on this team discuss the project together and provide input into the decision-making process.

Depending on how well CBB knows the applicant and the nature of the project/technology, the assessment process can be finalized within a couple of weeks. CBB conducts 1–3 inspections or dialogues with applicants in person, in addition to phone and/or email correspondence. CBB has not yet encountered cases where modifications of a project would be required, but if this were the case, it would probably require additional communication with the applicant.

If CBB needs to ascertain whether an applicant works with TMP, the dialogue starts with very open-ended questions, such as "tell us about your ongoing research projects" or "describe the technologies that you are working with in your company." Later questions are more specific, delving into the project's purpose, methods, and expected results.

After discussing the specific technology and its dual-use capacity, CBB also investigates organizational aspects of the applicant, including the risk of technology transfer beyond the applicant institution. Questions at this stage include which people are involved, what is the security culture at the institution, what knowledge is exchanged with project partners, and what needs, or incentives exist for publication.

Overall, the questions that CBB asks are case dependent. CBB has previously used a questionnaire (Appendix A). While the questionnaire has proved useful in some cases, CBB

found that the questionnaire does not encompass the full spectrum of possible cases of misuse, and it leads too easily to binary answers.

The risk assessment is written up as a short (one-page) document that summarizes the potential for misuse and the decision from CBB about the need for a permit. Currently, the full assessment document is classified and for internal CBB use only, but the applicant gets an oral explanation of the outcome and receives a formal writing to begin the application process.

Risk mitigation

CBB draws on the information obtained through the vulnerability assessment and dialogue with applicants during the permit application process in deciding risk mitigation recommendations. **CBB can recommend and require a variety of mitigation strategies,** including:

- Screening, listing, or excluding people involved in projects who might have access to technological information
- Developing procedures for re-evaluating risks in the project at current and future stages
- Taking steps to secure technical data and/or technical assistance
- Developing project-specific procedures and/or longer-term processes for hiring personnel and/or engaging PhD students and external consultants where knowledge about or access to TMP is expected
- Raising awareness of risks and biosecurity
- Evaluating outside partners involved in the project
- Modifying the project design or methods
- Advising on the responsible publication of results
- Blocking the project

These mitigations are implemented by the applicant (e.g., screening new employees), with CBB providing guidance. Applicants have the opportunity to submit a new application or provide additional details to supplement their existing application (typically upon request by CBB) depending on the mitigation measures recommended by CBB.

Expertise required

CBB staff reviews all TMP applications internally. Reviewers have a good understanding of TMP governance and may also be experts in other relevant areas including microbiology, bioweapons dispersal or manufacturing processes, and synthetic biology. People with good interview skills are also essential during the inspection process.

Senior CBB staff members train new reviewers in-house. Reviewers develop a sense for commonly held views about risk management through their experience working at CBB, including through access to previous applications and reviews.

CBB does not specifically train applicants on the application process. Most applicants will already have a trained biosecurity officer whom CBB is in contact with during the process.

FEEDBACK

Minor modifications to the risk management process are made on a case-by-case basis, with larger modifications happening rarely and not on a scheduled basis.

Some examples of applicant feedback include:

- Difficulty understanding what TMP is and why CBB thinks that they are working with it
- Asking for help on how to brief co-workers (in which case CBB shares teaching materials or offers to do a tailored presentation)
- Concerns about having to take resource-demanding steps to implement changes requested by CBB

Sometimes reviewers encounter resistance from applicants around specific requirements. Additional communication with the applicant can help to resolve some of these issues.

CBB has found that applicants often think that risk management will be more burdensome than it is in practice. For example, some companies believe that risk management is anti-competitive. As a result, CBB takes care to explain to applicants that they do not want to stall their work, that biosecurity should be seen also as a provision to protect their business/research, and that guidelines and requirements are implemented on a case-by-case basis.

SHARING

Specific risk assessments and mitigation steps are not shared outside of CBB as the organization has a duty of confidentiality.

However, **CBB shares its overall procedures for managing biosecurity risks widely** in relevant communities and in more specific detail with relevant companies. This sharing is necessary to provide applicants with a basic understanding of technology with misuse potential and relevant legal oversight measures. Sharing these processes is also important for receiving input from applicants. CBB is open to their suggestions for process improvements.

REFLECTIONS

"Working with TMP governance has been a long and educational process. We have worked with slightly different approaches with valuable lessons learned. The general experience is that TMP is an exciting, however, difficult subject to manage. In a small organization such? as CBB the work is also very vulnerable to staff change. It requires experience and insight to handle TMP. Detecting or receiving cases to work on and to gain experience from has also been a challenge. Researchers are often unaware that they are working with TMP and fail to notify CBB by themselves, thus it requires more outreach from CBB which is very resource demanding." —CBB Staff

CBB staff offers the following reflections on their experience performing TMP management to date:

- Having biosecurity legislation that includes technology control is a huge advantage. CBB has a mandate to contact companies and institutions.
- A legal framework that requires further interpretation and case-by-case expert reviews is highly burdensome to administer, however, that also makes it future-proof. It goes against the inherent nature of technology if you try to narrow it down to specific pathogens or practices.
- Even with legislation, dialogue is paramount. Reviewers should take the time to explain why a specific project/technology has dual-use potential and what the consequences of a lack of security could be.
- The application process should be as smooth and lean as possible. Too much bureaucracy will push people away.
- Adapt requirements to the needs and infrastructure of the institution.
- Establish a fixed group of reviewers with different expertise. It takes time to understand which technologies have dual-use potential and it takes even longer to learn to evaluate and manage risks associated with these technologies.
- There could be significant challenges to expanding CBB's model while maintaining centralized reviewing expertise. Smaller hubs of experts could be established, but this will only work if there is a clear (legal) framework, sufficient training of experts, and sharing of expertise.

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APPENDIX A: QUESTIONNAIRE ABOUT DUAL-USE RESEARCH OF CONCERN FOR COMPANIES, PROJECT MANAGERS, ETC.

Note: CBB uses this questionnaire as support to their TMP risk management approach, but it is not a stand-alone tool.

List of technologies that require special attention.[1] Fill out the questionnaire to clarify whether the company conducts activities with dual-use potential. If one or more criteria are met, CBB is to be contacted for further evaluation.

CRITERIA	YES	NO
Do you expect enabled or enhanced transmissibility of microorganisms?		
Do you expect an increase in virulence of microorganisms or a lowered LD50 for		
toxins?		
Do you expect an increase in the durability/survivability of		
microorganisms or toxins?		
Do you expect that the absorption of toxins will be made easier?		
Do you expect an increased resistance of microorganisms to therapeutic or		
prophylactic antimicrobial or antiviral substances?		
Do you expect an increase in the potential for dispersal of		
microorganisms or toxins?		
Do you expect a reduced immune response towards the microorganisms?		
Do you expect a change in host tropism of microorganisms?		
Do you expect an increased receptivity of a host organism?		
Do you expect that entirely new pathogens are created or that extinct		
pathogens are recreated?		
Do you expect that the absorption of a biological agent is made easier?		
Do you expect a reduction in the efficiency of medical countermeasures or		
decontamination towards the agent?		
Do you expect that diagnostic methods can be circumvented?		
Do you expect to publish/disseminate your research results?		

Assessed by:

Name of responsible researcher

1 The list follows RKIs *Bewertung des Dual-Use-Potenzials von Forschungsvorhaben entsprechend der Dual-Use Hausverfügung vom 25.03.2013 im Robert Koch Institut*