MEETING OF THE STATES PARTIES TO THE CONVENTION ON THE PROHIBITION OF THE DEVELOPMENT, PRODUCTION AND STOCKPILING OF BACTERIOLOGICAL (BIOLOGICAL) AND TOXIN WEAPONS AND ON THEIR DESTRUCTION

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Consideration of oversight, education, awareness raising, and adoption and/or development of codes of conduct with the aim of preventing misuse in the context of advances in bio-science and bio-technology research with the potential of use for purposes prohibited by the Convention

OVERSIGHT OF SCIENCE

Submitted by the Implementation Support Unit

Summary

This background document introduces the concept of the oversight of science, and surveys current thinking and developments in the area. It outlines the need for oversight, the various problems and challenges, and several existing proposals for oversight frameworks. It also examines the requirements for effective oversight. Further details on proposed oversight frameworks are included in Annex I (in English only); lists of criteria for identifying high-risk activities and resources requiring oversight are included in Annex II (in English only).

I. Introduction

1. Although the oversight of science has not yet been specifically considered within the BWC, other organisations and institutions have considered why oversight might be necessary, and have begun to identify some of the outstanding challenges. Several stakeholder organisations have already produced policy statements endorsing the creation of frameworks to oversee the practice of science. Other organisations have gone further and started to develop detailed oversight mechanisms. Some frameworks advocate a top-down, government-regulated approach; others favour a bottom-up, self-regulated mechanism; some seek to balance top-down and bottom-up approaches; and others are issue-specific.

The need for oversight

2. A review of published works on the oversight of science finds six often-quoted reasons that such efforts are needed:

(i) To prevent the life sciences being used for malign purposes - As Resolution 20.54 of the World Health Assembly points out (in a similar vein to the preamble of the BWC) the international community is "deeply convinced that the scientific achievements, and particularly in the field of biology and medicine ... should be used only for mankind's benefit, but never to do it any harm."[1]

(ii) To ensure that the benefits of the life sciences are maximised while their risks are minimised – This need for a balance between security and peaceful use is a common theme and is summed up in a recent report by the US National Science Advisory Board for Biosecurity: "Science is a critical component of public health and well being, and therefore a precious resource that needs to be protected against misuse."[2]

(iii) To ensure that efforts to mitigate risks are proportionate and do not unduly restrict science for peaceful purposes – Concepts of oversight are not only confined to restrictions or regulations but also help to ensure future developments. As the WHO has noted, "Control mechanisms… for managing the risks associated with potential misuse of life science R&D could hinder the development of a science"[3]

(iv) To prevent any further undermining of public confidence in the life sciences or life scientists – As WHO notes "Strong public confidence must be maintained in science and scientific advice for policy-making… Coping with uncertainty and risks in the life sciences will require improved communication and openness on these issues."[4]

(v) To adapt to the changing nature of science – Changes in the ways science is pursued have magnified certain possibilities for malign use.

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[1] WHO Resolution WHA 20.54, 1967.

[2] NSABB, Dual Use Issues in Life Science Research: A Roundtable on Strategies for Fostering International Engagement. Executive Summary http://www.biosecurityboard.gov/pdf/Intl%20Roundtable%20Brief%20Summary%20Oct07%20NSABBWeb.pdf.

[3] WHO, Life Science Research: Opportunities and Risks for Public Health, 2005, http://www.who.int/ethics/Life%20Science%20Research.pdf.

[4] Ibid.

(vi) To enhance awareness of issues related to the Convention – Awareness of the potential malign use of life science research has not fully penetrated the full membership of all relevant stakeholders.

Calls for oversight

3. Policy statements expressing support for developing a mechanism to address the possible malign use of the biological sciences have been released by a range of scientific organisations, including those that fund scientific endeavours, those that carry out scientific activities, such as national academies, and those that disseminate scientific information, such as journal publishers. In the United Kingdom, for example, a group of funding bodies – the Biotechnology and Biological Sciences Research Council, the Medical Research Council and the Wellcome Trust – released a joint policy statement urging the scientific community to "…take active steps to further develop mechanisms of self-governance, and through doing so the community can ensure that responsibly conducted research is not unnecessarily obstructed."[5]

4. In November 2005, the InterAcademy Panel on International Issues (IAP) released a *Statement on Biosecurity*. The statement was endorsed by 68 national and regional scientific academies, and included the following:

> "Scientists have a special responsibility when it comes to problems of 'dual use' and the misuse of science and technology… Scientists have an obligation to do no harm. They should always take into consideration the reasonably foreseeable consequences of their own activities… Scientists with responsibility for oversight of research or for evaluation of projects or publications should promote adherence to these principles by those under their control, supervision or evaluation and act as role models in this regard."[6]

5. In February 2003, 32 journal editors and authors' groups, representing many of the most prestigious scientific publications, agreed on a ***Statement on the Consideration of Biodefence and Biosecurity***[7]. This statement recognised that the biological sciences, and the scientific publications that they create, have the potential to be used for malign as well as beneficial purposes. It also recognised "that on occasions… the potential harm of publication outweighs the potential societal benefits". As a result, "scientists and their journals should consider the appropriate level and design of processes to accomplish effective review of papers that raise such security issues".

Problems with oversight

6. Published works[8] on these issues also identify a number of difficulties and challenges which are yet to be overcome, including:

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[5] BBSRC, MRC, Wellcome Trust, Managing Risks of Misuse Associated with Grant funding Activities, http://www.bbsrc.ac.uk/organisation/policies/position/public_interest/misuse_of_research_joint.pdf.

[6] IAP, Statement on Biosecurity, 7 November 2005, http://royalsociety.org/displaypagedoc.asp?id=17463.

[7] Statement on the Consideration of Biodefence and Biosecurity, 20 February 2003, http://www.nature.com/nature/journal/v421/n6925/full/nature01479.html.

[8] In particular: WHO, Life Science Research: Opportunities and Risks for Public Health, 2005, http://www.who.int/ethics/Life%20Science%20Research.pdf; and NSABB, Dual Use Issues in Life Science

(i) Identifying what constitutes dangerous research, or at least activities relevant to the Convention that require oversight (some proposals for criteria to identify such activities are listed in Annex II, in English only);

(ii) Managing activities associated with possible malign use while not unduly impeding peaceful activities;

(iii) Dealing with the dynamic nature of science, especially scientific breakthroughs that might require new measures or flexible application of existing ones;

(iv) Dealing with issues that span the interfaces between science and security as well as the public and private sectors;

(v) Dealing with a broad and evolving range of actors: "a wide array of organisations with disparate memberships and mandates and a wide array of policy positions"[9];

(vi) The lack of dedicated resources for educating and training those to be involved in oversight.

II. Oversight frameworks

Existing proposals for oversight

7. The oversight frameworks described below have been proposed or developed by entities other than governments. Further details on each can be found in Annex I (in English only).

Controlling Dangerous Pathogens: A Prototype Protective Oversight System (Center for International and Security Studies at Maryland (CISSM))[10]

8. The CISSM model creates a conceptual categorisation of danger, ranging from tolerable, through potential concern and moderate concern, to extreme concern. Activities that would be classified as being of potential concern would be those that significantly increase the destructive potential of non-threat agents. Activities prompting a moderate concern would be those that involve listed agents or which make agents particularly suitable for use as a weapon. Extreme concern is reserved for activities that involve the most dangerous pathogens or which could result in the creation of a significantly more dangerous agent. Such an approach attempts to ensure that those activities most relevant to the Convention receive the greatest level of oversight, while placing as little as possible burden on the vast majority of research.

Research: A Roundtable on Strategies for Fostering International Engagement. Executive Summary http://www.biosecurityboard.gov/pdf/Intl%20Roundtable%20Brief%20Summary%20Oct07%20NSABBWeb.pdf.

[9] NSABB, Dual Use Issues in Life Science Research: A Roundtable on Strategies for Fostering International Engagement. Executive Summary http://www.biosecurityboard.gov/pdf/Intl%20Roundtable%20Brief%20Summary%20Oct07%20NSABBWeb.pdf.

[10] http://www.cissm.umd.edu/papers/files/pathogens_project_monograph.pdf.

Synthetic Genomics: Options for Governance (J. Craig Venter Institute (JCVI), Center for Strategic and International Studies (CSIS), and the Massachusetts Institute of Technology (MIT))[11]

9. This framework offers a series of measures which could be adopted by gene firms, oligo manufacturers, DNA synthesizers, and users. It assesses the measures on how well they enhance biosecurity, foster laboratory safety, protect the environment, as well as on other considerations such as cost, potential to impede research and to assist the transition to application. The approach outlines a range of possible options that can be combined in different ways to suit the precise requirements of settings and locations.

Proposed Framework for the Oversight of Dual Use Life Sciences Research: Strategies for Minimizing the Potential Misuse of Research Information (US National Science Advisory Board for Biosecurity (NSABB))[12]

10. The NSABB approach does not set out a series of guidelines but is intended to act as a framework for their development. It addresses the entire scientific process and looks at options for oversight at the project concept and design stage, during the funding application and award process, through institutional approval, throughout the duration of the research itself, while manuscripts or other research products are being developed, as well as for the public dissemination of the research findings or products. This approach is designed to ensure that all relevant activities are covered irrespective of where they fall in the development cycle.

DNA Synthesis and Biological Security (Bugl et al)[13]

11. This proposal is an example of an approach to the oversight of science that relies upon dealing with individual fields, disciplines or services. Such an ad hoc approach allows for the identification of areas within broader science practices that warrant extra levels of oversight, either due to an existing lack of oversight or because they are at particular risk of misuse. This model for an oversight framework for commercial DNA synthesis creates responsibilities for individuals, local oversight and governments. It requires a conceptual characterisation of danger like the CISSM model to allow for effective screening, deals with similar topic matter to the JCVI, CSIS and MIT model, and endorses the whole-life cycle nature of the NSABB model.

[11] http://www.jcvi.org/cms/fileadmin/site/research/projects/synthetic-genomics-report/synthetic-genomics-report.pdf.

[12] http://www.biosecurityboard.gov/Framework%20for%20transmittal%200807_Sept07.pdf.

[13] Bugl et al, DNA Synthesis and Biological Security, Nature Biotechnology, Vol.25 No. 6, June 2007. For more information on DNA Synthesis, see: BWC/CONF.VI/INF.4.

Different approaches to oversight

12. A useful summary of the relative advantages and disadvantages of the various approaches adopted in the systems discussed above can be found in the report **Ethical and Philosophical Consideration of the Dual-Use Dilemma in the Biological Sciences**[14]. (See also Annex I, in English only.) There is a spectrum of different options for oversight, ranging from the complete autonomy of individual scientists, through institutional control, a combination of institutional and governmental control, regulation by an independent authority, to strictly regulated government control. In other words, the spectrum runs from a purely bottom-up approach at one end to an entirely top-down approach on the other.

13. Top-down approaches can be quickly executed and are often considered more robust, being legally enforceable and providing penalties. They are sometimes perceived, however, as not being sufficiently flexible to keep up with highly dynamic areas, as placing a heavy burden on central government resources, and as lacking support from stakeholders. Bottom-up approaches, on the other hand, are based on changing the perceptions of the affected community and therefore can be slower to implement, can require more resources, and may not always be entirely successful. When achieved, however, they are more flexible and better tailored to the demands of the community, are self-sustaining, more easily harmonized, and can be more comprehensive (as every member of the community becomes an agent for enforcement).[15]

14. It is often claimed that the scientific community prefers a bottom-up model, while governments favour top-down approaches. For example, the 2007 report **Science and Security in a Post 9/11 World** asserts that "To date, the response of the scientific community largely has been to assert the value of open scientific dialogue and exchange of information, self-governance, and increased communication among all affected sectors."[16] Some advocacy groups go even further, and argue that no action should be taken on this issue without exhaustive public debate. For example, an attempt by scientists involved in synthetic biology to voluntarily adopt a series of measures to limit the possibility of their field being misused was derailed by activist organisations because the (public) discussions were "inherently exclusionary and intolerable"[17].

15. It has also been suggested that neither a top-down nor bottom-up approach in isolation would be as efficient as a combined effort. The justification for finding the correct balance between top-down and bottom-up approaches was elegantly outlined by Selgelid:

> "Politicians and security personnel would likely favour security and stability over scientific advances. And depending on their particular expertise, politicians and security

[14] Miller & Selgelid, Ethical and Philosophical Consideration of the Dual-Use Dilemma in the Biological Sciences, Science and Engineering Ethics, Vol.13, 2007 http://www.springerlink.com/content/n514272v537582vv/.

[15] See, for example, BBSRC, MRC, Wellcome Trust, *Managing Risks of Misuse Associated with Grant funding Activities*, http://www.bbsrc.ac.uk/organisation/policies/position/public_interest/misuse_of_research_joint.pdf; and Borrie, *The Dual-Use Dilemma in Life Science Research*, XVI Amaldi Conference on Problems of Global Security, Rome 2007.

[16] US NRC, Science and Security in a Post 9/11 World, 2007 http://books.nap.edu/catalog.php?record_id=12013.

[17] Maurer & Zoloth, Synthesizing Biosecurity, Bulletin of the Atomic Scientists, November / December 2007 http://thebulletin.metapress.com/content/g428752x47720025/fulltext.pdf.

personnel would often not be especially qualified to judge the scientific importance of findings they might want to censor.

Relying on voluntary self-regulation by scientists and editors, on the other hand, is unacceptable as well. First, because… an individual scientist's interest in career advancement may… conflict with his interest in national security. Second, just as governmental officials are likely to have values biased in favour of security over the promotion of science, scientists and science editors are likely to be biased in favour of the promotion of science over security. Third – and most importantly – scientists and science editors are not security experts."[18]

III. Requirements for effective oversight

16. Before considering what an oversight framework might entail, it is necessary to consider what it is expected to accomplish. Perhaps the clearest articulation of the goal of oversight was published in the June 2007 issues of the scientific journal Nature, which asserted that an oversight framework should:

(i) promote and later compel responsible behaviour on the part of users;

(ii) be sufficiently simple and robust to be adopted as best practice throughout industry;

(iii) enable common improvement of needed technologies and promote sharing of operational wisdom throughout industry and government;

(iv) build on existing practices; and

(v) foster and support international transparency and cooperation.[19]

Intangible Resources

17. Modern biology involves both tangible and intangible resources. Tangible resources, such as laboratory equipment, organisms, growth media and reagents, are often covered by existing licensing, regulatory and export control regimes. With the advent of bioinformatics, a discipline dedicated to biological information[20], rapid developments in DNA sequencing and synthesis, laboratory automation, and the creation of open-source libraries of genomic data, progress in the life sciences is increasingly dependent on intangible rather than tangible resources. Therefore, any oversight framework must consider how it will address intangible as well as tangible resources.

18. Some attempts have already been made to strengthen the oversight of certain types of information. For example, in 2004 the Board of Life Sciences of the US National Academies

[18] Selgelid, A Tale of Two Studies: Ethics, Bioterrorism and the Censorship of Science, Hastings Center Report 37, no.3, 2007 http://www.ingentaconnect.com/content/thc/hcr/2007/00000037/00000003/art00011.

[19] Bugl et al, DNA Synthesis and Biological Security, Nature Biotechnology, Vol.25 No. 6, June 2007.

[20] For more information on bioinformatics see: Background Information Document on New Scientific and Technological Developments Relevant to the Convention, BWC/CONF.VI/INF.4.

published the report **Seeking Security: Pathogens, Open Access, and Genome Databases**[21]. This document reviewed the need for, and outlined an approach to, the oversight of genomic information. In addition, the US National Research Council has proposed the development of an international agreement on the processes used for pre-publication review of papers and articles in the biological sciences that might have applications relevant to the Convention[22].

Proportionality

19. Most of the literature dealing with science and biological weapons concludes that virtually all biological and life science resources have the potential to be used for malign purposes in one way or another, but that some resources would have much greater potential than others. There is also general agreement that it is neither practical nor desirable to attempt to control or regulate all biological resources.[23] The conclusion is that those resources and activities which would be of most relevance to the Convention should receive the most scrutiny. Ideally the majority of scientific activity would require little or no oversight, while a few "high-risk" resources or activities would receive increasing levels of attention. This, however, requires some mechanism to establish *which* resources or activities require elevated levels of oversight.

20. A number of different mechanisms for identifying high risk activities have been developed. Two were covered by the Background Information Document on New Scientific and Technological Developments Relevant to the Convention prepared for the Sixth Review Conference (BWC/CONF.VI/INF.4) – the list of experiments of concern developed by the Fink Committee in 2004, and a second list of activities included in the Australian national scientific and technological review prepared for the Review Conference. These lists are reproduced in Annex II (in English only), along with two further lists: the criteria developed by the NSABB, and the categories developed by CISSM.

Harmonized national approaches

21. Just as biology is becoming increasingly information-based, it is also becoming increasingly international. Even a brief review of the authorship of articles in scientific journals illustrates increasing levels of international collaboration[24]. Many scientific organisations argue that the continued development of the biological sciences depends on biological resources being freely circulated across national boundaries.

22. National oversight arrangements naturally need to be tailored to the specific circumstances of individual countries. But differences between the respective oversight frameworks of different countries may make it more difficult to do biology internationally, thus becoming a potential barrier to scientific and technological advancement. At least two approaches to harmonizing national oversight frameworks have been proposed to date. The United States NSABB has proposed the development of a common tool-kit of guidance,

[21] US National Academies, Seeking Security: Pathogens, Open Access, and Genome Databases, 2004 http://www.nap.edu/openbook.php?isbn=0309093058.

[22] US NRC, Science and Security in a Post 9/11 World, 2007 http://books.nap.edu/catalog.php?record_id=12013.

[23] See for example: WHO, Life Science Research: Opportunities and Risks for Public Health, 2005, http://www.who.int/ethics/Life%20Science%20Research.pdf.

[24] US NRC, Science and Security in a Post 9/11 World, 2007 http://books.nap.edu/catalog.php?record_id=12013.

guidelines and standards, which could be used in developing national frameworks[25]. The WHO, on the other hand, has called for the creation of "some form of international monitoring system, both in order for national measures to be effective and to minimise the risk of unilateral measures that might hinder biomedical research in other countries."[26]

[25] NSABB, Dual Use Issues in Life Science Research: A Roundtable on Strategies for Fostering International Engagement. Executive Summary http://www.biosecurityboard.gov/pdf/Intl%20Roundtable%20Brief%20Summary%20Oct07%20NSABBWeb.pdf.

[26] WHO, Life Science Research: Opportunities and Risks for Public Health, 2005, http://www.who.int/ethics/Life%20Science%20Research.pdf.

Annex I

[ENGLISH ONLY]

FURTHER DETAILS ON PROPOSED OVERSIGHT FRAMEWORKS

I. The CISSM approach

Controlling Dangerous Pathogens: A Prototype Protective Oversight System (Center for International and Security Studies at Maryland (CISSM))[1]

1. The CISSM model creates a conceptual categorisation of danger, ranging from tolerable, through potential concern and moderate concern, to extreme concern. Activities that would be classified as being of potential concern would be those that significantly increase the destructive potential of non-threat agents (those that fall completely outside of the various regulatory regimes). Activities prompting a moderate concern would be those that involve listed agents or which make agents particularly suitable for use as a weapon. Extreme concern is reserved for activities that involve the most dangerous pathogens or which could result in the creation of a significantly more dangerous agent. Such an approach attempts to ensure that those activities most relevant to the Convention receive the greatest level of oversight, while placing as little as possible burden on the vast majority of research. (See Figure 1.)

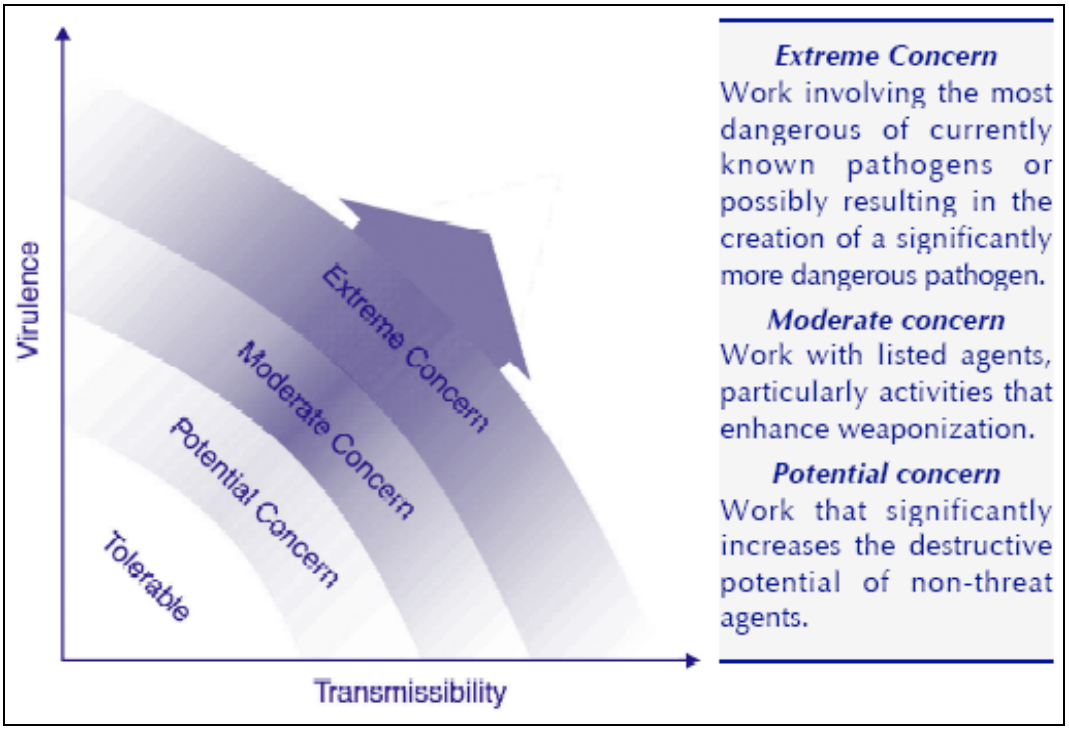


Figure 1: CISSM categorisation

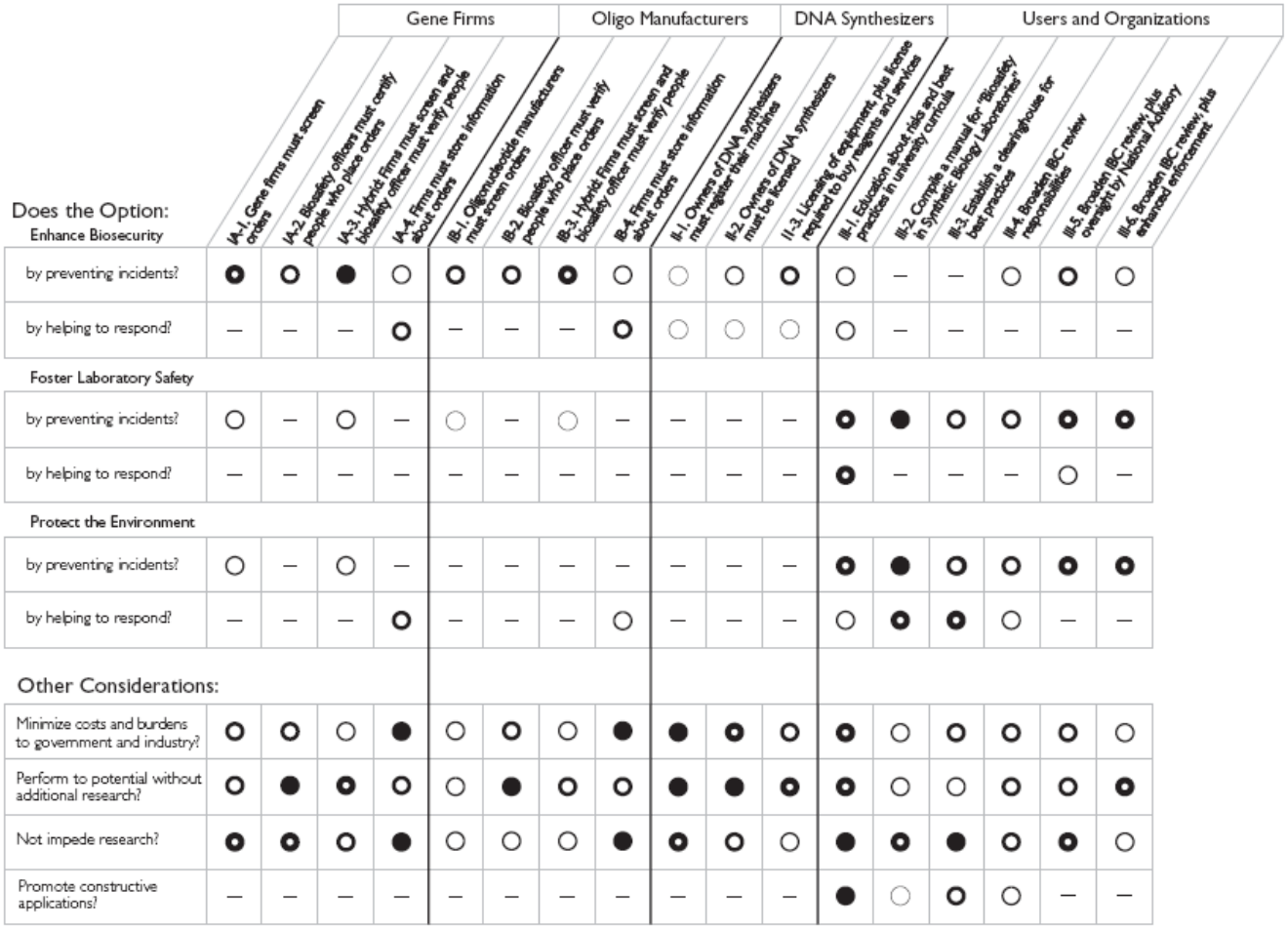
[1] http://www.cissm.umd.edu/papers/files/pathogens_project_monograph.pdf.

II. The JCVI, CSIS and MIT approach

Synthetic Genomics: Options for Governance (J. Craig Venter Institute (JCVI), Center for Strategic and International Studies (CSIS), and Massachusetts Institute of Technology (MIT))[2]

2. This framework offers a series of measures which could be adopted by gene firms, oligo manufacturers, DNA synthesizers, and users. It assesses the measures on how well they enhance biosecurity, foster laboratory safety, protect the environment, as well as on other considerations such as cost, potential to impede research and assist the transition to application. The approach outlines a range of possible options that can be combined in different ways to suit the precise requirements of settings and locations. (See Figure 2.)

[2] http://www.jcvi.org/cms/fileadmin/site/research/projects/synthetic-genomics-report/synthetic-genomics-report.pdf.



Reading the evaluation diagrams

These diagrams found throughout the report allow for easy comparisons within and between options regarding their effectiveness in achieving the policy goals of biosecurity and biosafety, and their performance on other considerations.

Reading down the columns allows for an evaluation of the performance of a particular option on one goal relative to the other goals. Reading across the rows allows for comparison of the effectiveness of each option with respect to the others on any given goal or consideration. Those that perform better are indicated with circles that have more dark fill; those that perform worse have less fill.

These comparisons are qualitative: they only indicate that one option performs better or worse than another, but not by how much.

Figure 2: JCVI, CSIS and MIT approach

III. The NSABB approach

3. The NSABB approach does not set out a series of guidelines but is intended to act as a framework for their development. It addresses the entire scientific process and looks at options for oversight at the project concept and design stage, during the funding application and award process, through institutional approval, throughout the duration of the research itself, while manuscripts or other research products are being developed, as well as for the public dissemination of the research findings or products. This approach is designed to ensure that all relevant activities are covered irrespective of where they fall in the development cycle. (See Figure 3.)

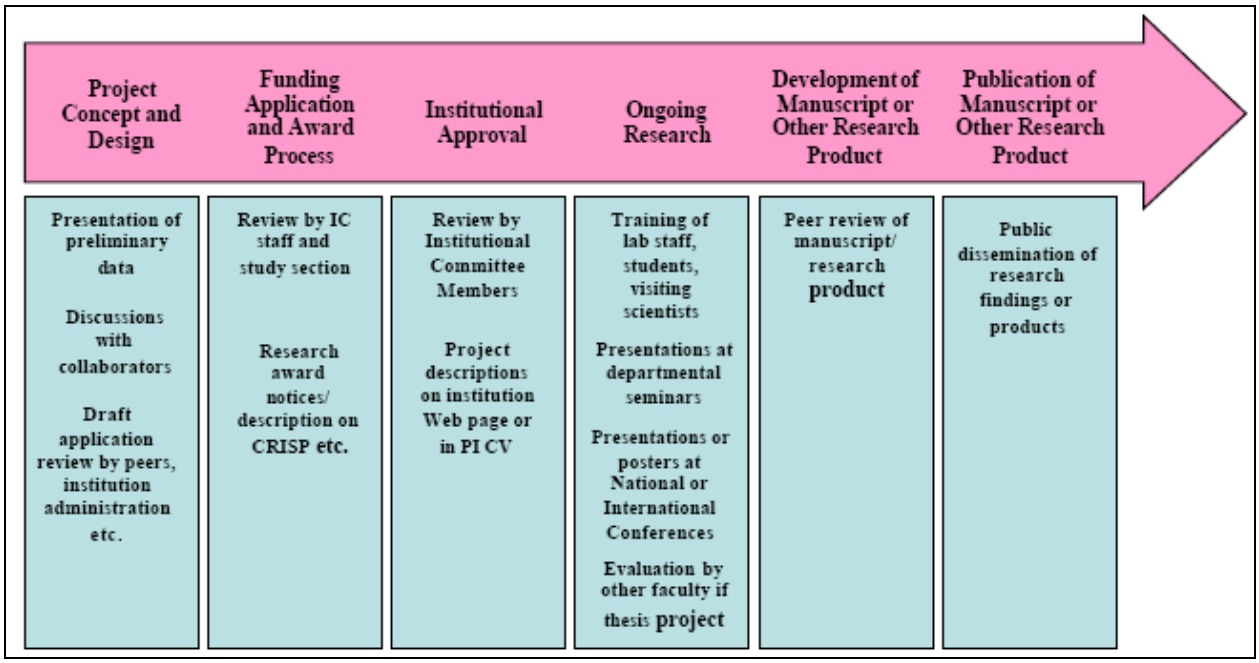


Figure 3: NSABB approach

IV. The issue-specific approach

4. Another approach to the oversight of science relies upon dealing with individual fields, disciplines or services. This ad hoc approach allows for the identification of certain themes within broader science practices that warrant extra levels of oversight either due to an existing lack of oversight or because they are at particular risk of being used for malign purposes.

5. For example, the June 2007 edition of Nature Biotechnology contained a proposal put together by a group of academics, industry executives and security experts for an oversight framework for commercial DNA synthesis[3] (see Figure 4). This model creates responsibilities for individuals, local oversight and governments and requires a conceptual characterisation of danger like the CISSM model to allow for effective screening, deals with similar topic matter to the JCVI, CSIS and MIT model, and endorses the whole-life cycle nature of the NSABB model.

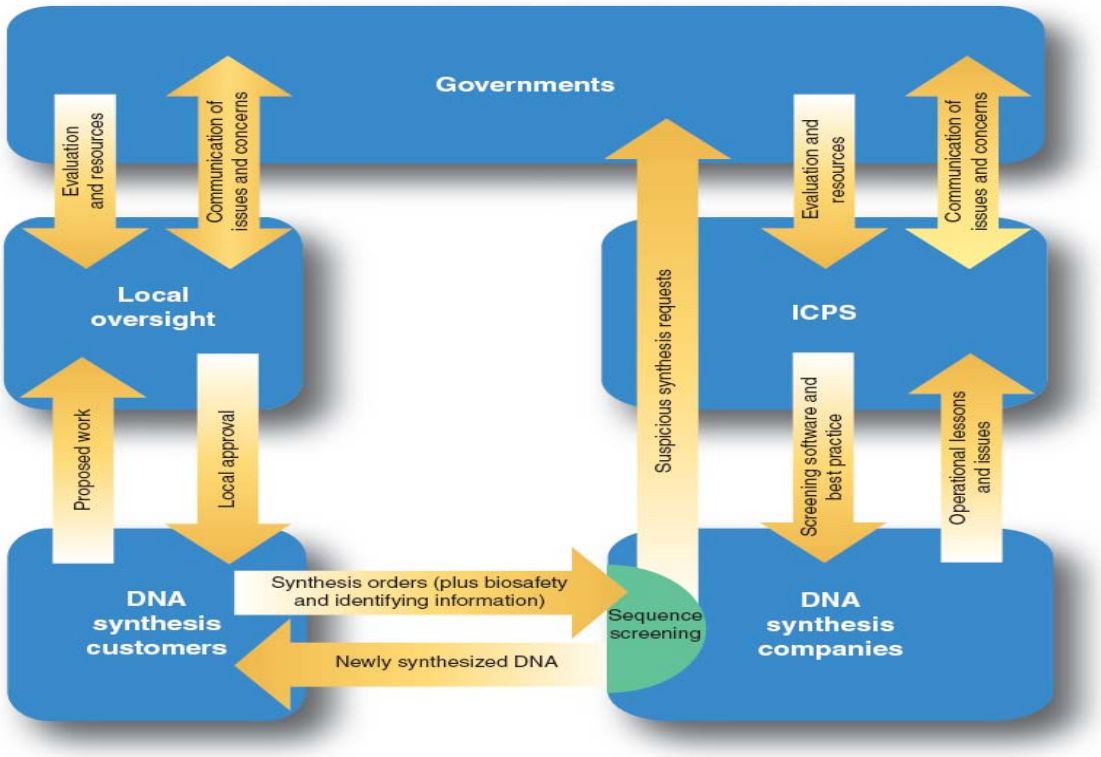


Figure 4: oversight framework for commercial DNA synthesis

[3] Bugl et al, DNA Synthesis and Biological Security, Nature Biotechnology, Vol.25 No. 6, June 2007.
For more information on DNA Synthesis, see: BWC/CONF.VI/INF.4.

V. Comparing approaches

6. A useful summary of the relative advantages and disadvantages of the various approaches adopted in the systems discussed above can be found in the report **Ethical and Philosophical Consideration of the Dual-Use Dilemma in the Biological Sciences**[4]. (See Figure 5.)

Decision-making for Dual-use Dilemmas in the Biological Sciences

Decisions	Options				
	Option 1—The Complete Autonomy of the Individual Scientist	Option 2—Institutional Control	Option 3—Institutional & Governmental Control	Option 4—An Independent Authority	Option 5—Governmental Control
Who are the Decision-makers regarding Im/ permissible Research?	Individual researcher	(i) Scientists in University (collegial) (ii) Corporation (iii) Govt Res. Centre	(i) Scientists in University (collegial) (ii) Corporation (iii) Govt Res. Centre	Independent Authority	Government
Should Compliance with Physical Safety & Security Regulation be Mandatory?	No	Yes	Yes	Yes	Yes
Should Dual-Use Technology be Licensed?	No	No	Yes	Yes	Yes
Should Education & Training be Mandatory?	No	No	Yes	Yes	Yes
Should Personnel Security Regulation be Mandatory?	No	No	Yes	Yes	Yes
Who are the Decision-makers regarding Censorship/Constraint of Material proposed for Dissemination?	Individual editor	(i) Individual editor (ii) Corporation (iii) Govt. Res. Centre	(i) Individual editor (ii) Corporation (iii) Govt. Res. Centre	Independent Authority	Government

NB: The decision-making in question pertains only to dual-use research in the biological sciences identified as potentially problematic by virtue of coming under one of the pre-established headings of Experiments of Concern

Figure 5: comparison of oversight options

[4] Miller & Selgelid, Ethical and Philosophical Consideration of the Dual-Use Dilemma in the Biological Sciences, Science and Engineering Ethics, Vol.13, 2007 http://www.springerlink.com/content/n514272v537582vv/.

Annex II

[ENGLISH ONLY]

PROPOSED CRITERIA FOR IDENTIFYING HIGH-RISK ACTIVITY

I. Fink Committee criteria

1. The United States National Academy of Sciences included in its report **Biotechnology Research in the Age of Terrorism**[1], published in 2004, a list of seven experiments of concern, namely those which would:

(i) Demonstrate how to render a vaccine ineffective;

(ii) Confer resistance to therapeutically useful antibiotics or antiviral agents;

(iii) Enhance the virulence of a pathogen or render a non-pathogen virulent;

(iv) Increase transmissibility of a pathogen;

(v) Alter the host range of a pathogen;

(vi) Enable evasion of diagnostic and detection modalities;

(vii) Enable the weaponization of a biological agent or toxin.

II. Australian criteria

2. Australia provided the following list of experiments of concern in its contribution to the science and technology background paper for the Sixth Review Conference[2]:

(i) Rendering a vaccine ineffective;

(ii) Conferring resistance to therapeutically useful antibiotics or antiviral agents in pathogenic organisms;

(iii) Enhancing the virulence of a pathogen or rendering a non-pathogen virulent;

(iv) Increasing the transmissibility of a pathogen;

(v) Altering the host range of a pathogen;

(vi) Enabling the evasion of diagnosis and/or detection by established methods;

[1] USNAS, Biotechnology Research in the Age of Terrorism, 2004 http://books.nap.edu/openbook.php?record_id=10827&page=R1.

[2] BWC, Background Information Document on New Scientific and Technological Developments Relevant to the Convention, BWC/CONF.VI/INF.4.

(vii) Undertaking genetic sequencing of pathogens;

(viii) Synthesising pathogenic microorganisms;

(ix) Large-scale protein production employing heterologous expression systems (and associated production technology);

(x) Optimisation of live attenuated vaccine production processes;

(xi) Enabling the weaponisation of a biological agent or toxin;

(xii) Any experiment with the smallpox virus.

III. NSABB criteria

3. The NSABB **Draft Guidance Document on Criteria for Identifying Dual Use Research of Concern** asserts that careful consideration should be given to knowledge, products or technologies that[3]:

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

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

(iii) 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

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

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

(vi) Enhance the susceptibility of a host population

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

IV. CISSM criteria

4. In its report **Controlling Dangerous Pathogens: A Prototype Protective Oversight System**, CISSM is based upon a list of agents of particular concern and divides research activities into three illustrative categories: activities of potential concern (APC); activities of moderate concern (AMC); and activities of extreme concern (AEC) [4].

[3] NSABB, Draft Guidance Document on Criteria for Identifying Dual Use Research of Concern, July 2006 http://www.biosecurityboard.gov/pdf/NSABB%20Draft%20Guidance%20Documents.pdf.

[4] CISSM, Controlling Dangerous Pathogens: A Prototype Protective Oversight System, March 2007 http://www.cissm.umd.edu/papers/files/pathogens_project_monograph.pdf.

5. An activity of **potential concern** includes:

(i) Work with listed agents, or exempt avirulent, attenuated, or vaccine strain of a listed agent, not covered by AEC/AMC;

(ii) Increasing virulence of non-listed agents;

(iii) Increasing transmissibility or environmental stability of non-listed agents;

(iv) Powder or aerosol production of non-listed agents;

(v) Powder or aerosol dispersal of non-listed agents;

(vi) De novo synthesis of non-listed agents; and

(vii) Genome transfer, genome replacement or cellular reconstitution of non–listed agents.

6. An activity of *moderate concern* includes:

(i) Increasing the virulence of listed or related agents;

(ii) Insertion of host genes into listed or related agents;

(iii) Increasing transmissibility or environmental stability of listed or related agents;

(iv) Powder or aerosol production of listed or related agents;

(v) Powder or aerosol dispersal of listed or related agents;

(vi) De novo synthesis of listed or related agents;

(vii) Construction of antibiotic- or vaccine-resistant related agents;

(viii) Genome transfer, genome replacement or cellular reconstitution of listed or related agents.

7. An activity of *extreme concern* includes:

(i) Work with eradicated agents;

(ii) Work with an agent assigned to BL-4 / ABM-4;

(iii) De novo synthesis of eradicated agents or those assigned to BL-4 / ABM-4;

(iv) Expanding the host range of an agent to a new host (in humans, other animals and plants) or changing the tissue range of a listed agent; and

(v) Construction of an antibiotic- or vaccine-resistant listed agent.

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