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Dual Use Biotechnology Research: The Case for Protective Oversight

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During recent years, there has been growing concern in the US and in other countries about dual use research.[1] Much of this has focused on the risk that advances in biotechnology could lead, either inadvertently or deliberately, to the creation of new pathogens more destructive than those that currently exist. This is not a future threat. Research with potentially destructive consequences is already being carried out in university, private sector, and government laboratories around the world.

Perhaps the most famous example of such research, and the one that first alerted some scientists and policy-makers to the potential risks from biotechnology research, was the mousepox experiment in Australia. In this work, published in February 2001, researchers trying to develop a means of controlling rodent populations inserted an interleukin-4 gene into the mousepox virus and in so doing created a pathogen that was lethal even to some mice that had been vaccinated against the disease (Jackson et al, 2001). US scientist Mark Buller later built upon this work, producing a mousepox virus so lethal that it killed all of the mice that had been infected, even those that had been both vaccinated and treated with antiviral drugs (MacKenzie, 2003). These projects and others that followed have led to concerns that the introduction of IL-4 into other orthopox viruses (such as smallpox) could have similarly lethal effects.

In another study funded by the US Department of Defense and published in July 2002, researchers from the State University of New York at Stony Brook created an infectious poliovirus 'from scratch', using genomic information available on the internet and custom-made DNA material purchased through the mail (Cello et al, 2002). Eighteen months later under a US Department of Energy grant, US Nobel laureate Hamilton Smith and colleagues reported that they had built a simple artificial virus in a record two weeks' time using commercially available DNA (Smith et al, 2003). These projects have raised concerns about the de novo synthesis of other, far more dangerous, pathogens.

Controversy also has surrounded research done by US army scientists and others with the 1918 influenza virus, which killed an estimated 20–40 million people in a single year. In 1997, researchers at the Armed Forces Institute of Pathology recovered fragments of the 1918 virus from preserved tissue samples. The genome was then sequenced. Since that time, researchers have used reverse genetics to reconstruct the 1918 virus and have done re-assortment studies with segments of the 1918 virus and the H5N1 avian virus (see, for example, Taubenberger et al, 1997; Taubenberger et al, 2005; Tumpey et al, 2005; Kash et al, 2006). Although the stated purpose of such research is to facilitate our understanding of, and preparations for, a future human influenza pandemic, the unintended release of the 1918 virus, or of a new hybrid containing segments of it, or the deliberate misuse of the associated research results could have catastrophic consequences.

This chapter considers how formalized oversight procedures might contribute to efforts to prevent the misuse of biotechnology research, focusing particularly on the US, where some of the most extensive discussion of oversight measures has taken place. It begins by examining the response of key US scientists and the US government to the growing concerns about advances in biotechnology. The chapter then outlines an alternative approach for managing the risks posed by this highly promising field of scientific endeavour. It concludes with a discussion of incremental measures that could help to lay the foundation for this more effective approach.

Confronting the dual use problem?

Spurred on, at least in part, by the mousepox experiment, the US National Academy of Sciences decided in the summer of 2001 to explore the possibility of creating an ad hoc committee to examine the adequacy of US oversight arrangements for dual use biotechnology research. Following the September 2001 terrorist attacks and anthrax mailings, the need for such a committee became even more apparent. In April 2002, the Committee on Research Standards and Practices to Prevent the Destructive Application of Biotechnology, chaired by Massachusetts Institute of Technology Professor Gerald Fink, was established. In October 2003, the Fink Committee, as it became known, issued its report – Biotechnology Research in an Age of Terrorism (NRC, 2003).

The Fink Committee report made two significant contributions to the US debate on dual use research. First, it clearly articulated the threat, stating unequivocally that biotechnology research is dual use and has the capacity 'to cause disruption or harm, potentially on a catastrophic scale' (NRC, 2003, p1). Coming from the pre-eminent scientific advisory body in the US, this was a judgement that could not be taken lightly.

In addition, the Fink Committee report acknowledged a serious gap in the existing domestic US and international oversight arrangements for dual use research. As the report made clear, current regulation of biotechnology research is concerned primarily with protecting laboratory workers and the environment

from dangerous pathogens, or with preventing unauthorized access to such pathogens. Only very limited efforts have been made thus far to ensure that legitimate research does not lead to destructive consequences.

To help fill this gap, the Fink Committee made three recommendations. The first was to add seven types of 'experiments of concern' to the National Institutes of Health Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines) – the oversight process that has been in place in the US since the 1970s to ensure the safety of recombinant DNA research. Specifically, the Fink Committee called for prior review of any experiment that would:

- demonstrate how to render a vaccine ineffective;
- confer resistance to antibiotics or antiviral agents;
- enhance the virulence of a pathogen or render a non-pathogen virulent;
- increase the transmissibility of a pathogen;
- alter the host range of a pathogen;
- enable evasion of diagnosis or detection methods; or
- enable the weaponization of a biological agent or toxin (NRC, 2003, pp4–6).

The purpose of this review is to consider whether the risks associated with the proposed research and its potential for misuse outweigh the potential scientific or medical benefits.

The committee also recommended the creation of an International Forum on Biosecurity to develop and promote harmonized national, regional and international measures for addressing the dual use issue, including systems for reviewing and overseeing relevant research. As the committee's report explained: 'Any serious attempt to reduce the risks associated with biotechnology ultimately must be international in scope because the technologies that could be misused are available and being developed throughout the globe' (NRC, 2003, p10).

Finally, the Fink Committee called for the establishment of a National Science Advisory Board for Biodefense to provide advice on the new domestic US and international oversight efforts, as well as on education and training programmes for scientists and other self-governance mechanisms (NRC, 2003, pp7–8).[2]

In March 2004, the Bush administration responded to the Fink Committee report, announcing the creation of a new body to advise US government agencies on how to reduce the risk that legitimate biological research will be misused for hostile purposes (US Department of Health and Human Services, 2004). The charter establishing this new body, known as the National Science Advisory Board for Biosecurity (NSABB), made clear that its advice is to apply to US government-conducted or supported dual use biological research only (Secretary of Health and Human Services, 2004). Classified research is also outside its purview.[3]

Notwithstanding the 2004 announcement, it took more than a year for the Bush administration to select the members of the NSABB and for the board to hold its first meeting. At this event in June 2005, the NSABB agreed to establish working groups in five initial areas: criteria for dual use research; communication of research results; codes of conduct; international collaboration; and synthetic

genomics. A sixth working group, on oversight of dual use research, was finally added a year later at the board's July 2006 meeting.[4]

At first glance, both the Fink Committee's recommendations and the efforts being undertaken by the NSABB seem to be an effective response to the challenges posed by advances in biotechnology. But on closer examination, both fall short in a number of important respects. First, both fail to include key segments of the biotechnology research community in their oversight arrangements. The Fink Committee has recommended adding experiments of concern to the NIH Guidelines. But only institutions that receive funding from the National Institutes of Health (NIH) for recombinant DNA research are required to adhere to the guidelines. This means that research at most US government and private labs would be outside the scope of any dual use oversight requirement under the Fink Committee's approach. The NSABB's oversight arrangements would go somewhat further in that dual use life sciences research at US government labs, or which is funded by the US government at private labs, would be covered. In a draft report in April 2007, the NSABB oversight working group recommended extending oversight still further to include all research at US government labs doing dual use research and at private labs receiving US government funding for dual use research (NSABB, 2007, p11). But even if this recommendation is adopted, this would still leave dual use research at private labs not receiving US government funding for such research, as well as classified research at both US government and private labs, outside the scope of the NSABB's proposed oversight plan.

Second, neither the Fink Committee approach nor that of the NSABB is legally binding. As the name implies, the NIH Guidelines, which are central to the Fink Committee's research oversight proposal, are exactly that: guidelines for researchers to follow when conducting certain types of recombinant DNA research. They have no legal effect. NIH can suspend, limit or deny funding for recombinant DNA research to any institution that fails to comply with the guidelines, or can require the institution to obtain NIH approval for other recombinant DNA research. But it is not clear whether this ever has been done. The NSABB, likewise, is developing guidelines for oversight of dual use research; nothing in the materials prepared either by the board or by its working groups thus far suggests that its proposed oversight arrangements will be legally based. Instead, in its April 2007 draft, the NSABB oversight working group appeared to draw from the NIH Guidelines enforcement procedures, proposing that compliance with guidelines for dual use research might be made a term and condition of funding. The working group also held out the hope that institutions not covered by the dual use guidelines would comply voluntarily (NSABB, 2007, p11).

Whether oversight arrangements that do not have the force of law will be adhered to is open to doubt. In a study published in October 2004, the Sunshine Project revealed numerous instances of non-compliance by US institutions with a cornerstone of the NIH Guidelines – the requirement to establish and operate a local body, known as an Institutional Biosafety Committee (IBC), to review recombinant DNA research projects. According to this study, scores of US

biotechnology companies (including some three dozen companies conducting bio-defence research for the US government) had no IBC registered with NIH, and many of the US university and other IBCs that were registered either did not meet or issued blanket approvals, rather than review each specific research project (Sunshine Project, 2004).

Third, both the Fink Committee and the NSABB have limited their oversight proposals to the US. Although the Fink Committee called for the creation of an international biosecurity forum to help harmonize oversight arrangements nationally, regionally and internationally, its actual oversight proposal has a distinctly national focus. The NSABB has given even less attention to the international dimension of the dual use issue, setting its sights, at least thus far, on 'awareness-building' and 'information-sharing' at the international level (NSABB, 2007, pp29–30). Perhaps this should not be surprising considering the mandate given to each group; but as the mousepox experiment showed, the relevant research community is globally distributed. Of the nearly 14,000 manuscripts submitted to the American Society for Microbiology's 11 peer-reviewed journals in 2002, about 60 per cent included non-US authors from at least 100 different countries.[5] The adoption of a dual use oversight system in the US alone risks putting US researchers at a competitive disadvantage vis-à-vis their counterparts in other countries. It will also, in the words of the Fink Committee report, 'afford little protection if it is not adopted internationally' (NRC, 2003, p86).

An alternative approach

Even before the emergence of the Fink Committee report and the establishment of the NSABB, the Center for International and Security Studies at Maryland (CISSM) was pursuing a different approach to the problem of dual use biotechnology research. In a study first published in September 2003, CISSM outlined a prototype protective oversight system that applies comprehensively to all institutions conducting relevant research, whether government, private sector or academic, is legally binding and is international in scope.[6]

This prototype, known as the Biological Research Security System, includes two key elements. The first is national licensing of relevant personnel and research facilities. The personnel licensing requirement would extend to all scientists, students and technical staff proposing to conduct research covered by the oversight system. The purpose of the licensing would be to ensure that the affected individuals are technically qualified, have undertaken biosecurity training (and thus have been sensitized to the dual use potential of their work and educated about both national and international oversight rules) and have nothing in their background (such as a past biosafety violation) that would make it inappropriate for them to conduct consequential research. Receipt of a personnel license would be viewed as an acknowledgment of the individual's special status within his or her broader professional community. The facility licensing requirement would extend to all facilities where relevant research takes place,

and would be designed to ensure that such facilities meet existing safety and security standards.[7]

Similar processes are already being used in advanced biology to ensure that certain individuals and facilities meet specified security and safety requirements. For example, under bioterrorism legislation and regulations adopted in the US, background checks are required on any individual having access to certain dangerous pathogens and toxins (designated as 'select agents'), and relevant facilities must be registered.[8] Various regulations in the US and other countries also require licensing of facilities that produce drugs and other products derived from biotechnology to ensure their safety and efficacy. Outside of biology, there are other examples of licensing requirements for individuals and facilities engaged in activities that could affect substantial numbers of people – such as doctors, or laboratories that work with radioactive materials.

The second element is independent peer review of relevant projects prior to their initiation. Any individual interested in conducting research covered by the oversight system would be required to provide information about their proposed project to an independent oversight body for review and approval.[9] This is consistent with the Fink Committee approach, which recommended using local IBCs for the initial review of experiments of concern. Unfortunately, the NSABB oversight working group appears to be disregarding this advice and is instead proposing, at least for now, to rely upon individual researchers to evaluate the dual use potential of their own research (NSABB, 2007, p10). In addition to having a self-interest in seeing their research proceed, such individuals are also unlikely to have the security and other expertise necessary to recognize the possible dual use risks of their work.

As with national licensing, precedents for independent peer review of consequential research can also be found. Within the US, review bodies already exist at the local level for research involving recombinant DNA techniques, human subjects and animals. Nationally, the Recombinant DNA Advisory Committee (RAC) exercises oversight over two particular categories of recombinant DNA research. Internationally, a special committee of the World Health Organization has been given responsibility for reviewing and approving smallpox research at the two designated repositories for the smallpox virus in the US and Russia.

Extensive research and consultations with scientists both in the US and in other countries were carried out by CISSM to develop illustrative categories of research activities for dual use oversight purposes.[10] A key consideration in developing these categories was the extent to which the research in question has the potential to expose very large numbers of people to lethal or otherwise debilitating effects. That is not to say that research that could affect smaller numbers of people is not important. But if the oversight system captures too broad a swath of research, the process will be unwieldy and research with the greatest destructive potential may not be reviewed promptly or effectively.

The resulting categorization developed by CISSM has a number of important features. First, it is narrowly focused in that only the most consequential types of dual use research are included. Most biomedical and agricultural research would be outside the oversight requirements. Second, it can be readily imple-

mented in that the types of research that must be peer reviewed are clearly defined and presented. Researchers would be able to determine easily whether and, if so, where their proposed work falls within the oversight system and therefore what steps they must take to meet their peer review obligations. This is critical for any oversight system that is legally binding. Third, it is responsive to the threat in that it covers not just specific pathogens, but also the research techniques applied to those pathogens. In so doing, CISSM's proposal combines the best of the agent-based controls enacted by the US in 2002 and of the activity-based approach reflected in the Fink Committee's proposed experiments of concern. Finally, it is based on a tiered design in that the level of risk determines the level of oversight. As discussed below, most research would be reviewed locally at the institutional level, with a smaller subset of research considered at a higher level. This categorization is reflected in Table 7.1.

At the top of the CISSM oversight system there would be a global standard-setting and review body or International Pathogens Research Authority.[11] This new body would be responsible for overseeing and approving activities of extreme concern – research with the most dangerous pathogens or that could result in pathogens significantly more dangerous than those which currently exist. This would 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 biological weapons programme.

Table 7.1 *Illustrative categories of research activities*

Activities of extreme concern (AECs)
• Work with eradicated agent*
• Work with agent assigned as BSL-4/ABSL-4
• De novo synthesis of above
• Expanding host range of agent to new host (in humans, other animals and plants) or changing the tissue range of a listed agent**
• Construction of antibiotic- or vaccine-resistant listed agent
Activities of moderate concern (AMCs)
• Increasing virulence of listed agent or related agent
• Insertion of host genes into listed agent or related agent
• Increasing transmissibility or environmental stability of listed agent or related agent
• Powder or aerosol production of listed agent or related agent
• Powder or aerosol dispersal of listed agent or related agent
• De novo synthesis of listed agent or related agent
• Construction of antibiotic- or vaccine-resistant related agent
• Genome transfer, genome replacement or cellular reconstitution of listed agent or related agent

Table 7.1 *continued*

Activities of potential concern (APCs)
• Work with listed agent – or exempt avirulent, attenuated or vaccine strain of a listed agent – not covered by AECs and AMCs
• Increasing virulence of non-listed agent
• Increasing transmissibility or environmental stability of non-listed agent
• Powder or aerosol production of non-listed agent
• Powder or aerosol dispersal of non-listed agent
• De novo synthesis of non-listed agent
• Genome transfer, genome replacement or cellular reconstitution of non-listed agent

Notes: * This would include, for example, activities with the 1918 influenza virus and chimeric influenza viruses with at least one gene from the 1918 influenza virus.
** This would include, for example, activities with chimeric influenza viruses with at least one gene from a human influenza virus and at least one gene from an avian influenza virus.

Table key:
Agent: fungus, protozoan, bacterium or archaeon, virus, viroid or prion; or genetic element, recombinant nucleic acid or recombinant organism.

Listed agent: select agents or toxins regulated by the Centers for Disease Control and Prevention (CDC) and Animal and Plant Health Inspection Service (APHIS).

Related agent: for fungi, protozoans, or bacteria or archaea, an agent that currently is, or during the last two years was, assigned to the same genus as a listed agent; for viruses, viroids or prions, an agent that currently is, or during the last two years was, assigned to the same family as a listed agent; for genetic elements, recombinant nucleic acids or recombinant organisms, an agent orthologous to a listed agent (this category includes any avirulent, attenuated or vaccine strain of a listed agent, if said strain is exempt under the CDC or APHIS regulations.

Non-listed agent: agent other than a listed agent or related agent.

Eradicated agent: agent previously in circulation in nature, but not within the last decade, as determined by human, animal or plant cases, or by isolation from humans, animals or plants, or by detection of antibodies to the agent from individuals younger than the time span elapsed since the last recorded isolation.

De novo synthesis: construction of agent using synthetic genomic nucleic acid (non-prion agents) or synthetic protein (prions), irrespective of whether said construction requires additional reagents, extracts, cells or 'helper' entities. For the purposes of this definition, 'synthetic genomic nucleic acid' refers to nucleic acid that corresponds to an agent genome and that is prepared using, in any step or set of steps, chemically synthesized oligonucleotides corresponding to at least 5 per cent of said agent genome.

Antibiotic: antibiotic of therapeutic utility against listed agent.

Vaccine: vaccine of therapeutic utility against listed agent.

Powder: powder other than lyophilized reference specimen (<10 milligrams).

Source: Center for International and Security Studies at Maryland

In addition to overseeing research activities of extreme concern, the global body would also be responsible for defining the research activities subject to oversight under the different categories and establishing standards for review and reporting. It would also develop rules to protect against the misuse of information reported as part of the oversight process. The global body would also help national governments and local review bodies to meet their oversight obligations by, for example, providing software and technical support for a secure data management system and by assisting in achieving international standards for good laboratory practices. This will be particularly important for developing countries, many of which have neither the biosafety rules nor the institutional mechanisms that could provide the basis for dual use oversight efforts. No existing organization currently fulfils all of these functions. The closest model is WHO, which not only oversees one specific type of highly consequential research, but also has developed international guidelines for laboratory biosafety and biosecurity.

At the next level there would be a national review body or National Pathogens Research Authority. This body is analogous to the RAC in the US. It would be responsible for overseeing activities of moderate concern – research that involves pathogens or toxins already identified as public health threats, especially research that increases the weaponization potential of such agents. This would include research that increases the transmissibility or environmental stability of a controlled agent or that involves production of such an agent in powder or aerosol form, which are the most common means of disseminating biological warfare agents. The national body would also be responsible for overseeing the work of local review bodies, including licensing qualified researchers and facilities, and for interacting with the global body.

At the foundation of the oversight system there would be a local review body or Local Pathogens Research Committee. This committee is analogous to the review bodies at universities and elsewhere in the US that currently oversee recombinant DNA, human and animal research. It would be responsible for overseeing activities of potential concern – research that increases the potential for otherwise benign pathogens to be used as a weapon or that demonstrates techniques that could have destructive applications. This would 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. Under the CISSM approach, the vast majority of microbiological research would either fall into this category or not be covered at all.

To ensure equitable treatment of all proposed research projects both within and between the different oversight levels, common criteria would be needed by the relevant review bodies for use in assessing the potential benefits of the work, as well as the possible risks.[12] A comparable risk–benefit assessment process currently is used in the US for reviewing human subject research. As in the review process for human subject research, the risk–benefit assessment of dual use biological research would apply to all relevant research, irrespective of whether it is carried out in a government, private sector or academic lab. In addition, the relevant review body would be required to consider certain issues as part of its deliberations and to document the discussion of those issues, as well as its overall risk–benefit assessment in its meeting minutes.

Based on a peer review simulation exercise of five hypothetical research projects,[13] CISSM developed dual use risk–benefit assessment criteria analogous to those used for human subject research. The first two issue areas, which focus on biosafety and the details of the proposed research plan, concern the conduct of the work. The remaining four issue areas relate to the justification for the work and cover public health, bio-defence, current necessity and potential impact. Similar issues and questions have been suggested by the British Royal Society for assessing dual use research (Royal Society, 2005). CISSM's proposed risk-benefit assessment criteria are listed in Table 7.2.

As these criteria show, meaningful peer review would require the disclosure of detailed information to the relevant review body to use in assessing the potential benefits and risks of the proposed experiment. In rare cases, the review body might decide to approve a proposed project but to restrict the dissemination of information about the project or its results. This would require agreed guidelines for determining whether and under what circumstances information might have to be restricted or even possibly classified. It would also require an agreed process for determining who could be given access to controlled information.[14]

Table 7.2 Notional risk–benefit assessment criteria

Biosafety issues
1 Does the proposed research plan contain appropriate protections to minimize risk to the public or environment? • Proposals receiving a 'no' answer would have a low biosafety rating.
Evaluation of research plan
1 Are the proposed research plan and the stated rationale for the work consistent with one another? 2 Are the risks posed by the agent (either from a public health perspective or bioterrorism perspective) and the stated rationale for the work consistent with one another? 3 Is the proposed research plan logically sequenced? 4 Are there scientific reasons why the same outcome cannot be pursued through alternative means – for example, by using alternative methods (e.g. in vitro versus in vivo) or alternative materials (e.g. non-pathogenic versus pathogenic strains)? • Proposals receiving two or more 'no' answers would have a low research plan evaluation rating.
Public health considerations
1 Do agents to be constructed, or equivalent agents, currently exist in nature? 2 If not, are said agents expected to be generated by natural processes? 3 Will the research advance our understanding of the disease-causing properties of currently existing agents? • Proposals receiving 'no' answers either to questions 1 and 2 or to question 3 would have low public health rationale.

Table 7.2 *continued*

Bio-defence considerations
1 Do agents to be constructed, or equivalent agents, currently exist in other facilities?
2 If not, is the work being done in response to a 'validated threat' (i.e. one for which there is credible information) or 'theoretical' threat (i.e. one that is possible but for which there is no credible information)?
3 Will the countermeasures that are expected to result from the work significantly reduce the threat posed by the agent?
• Proposals receiving two or more 'no' answers would have a low bio-defence rationale.
Current necessity
1 Are countermeasures against agents to be constructed, or equivalent agents, currently unavailable?
2 Are there scientific reasons why countermeasures cannot be developed without access to such agents?
• Proposals receiving one or more 'no' answers would be of limited current necessity.
Potential impact
1 Will the proposed research contribute to new knowledge (e.g. by furthering our understanding of basic life processes or of pathogenesis) rather than primarily confirm work already done?
2 Are the research results likely to be definitive enough to inform policy decisions (e.g. on vaccination strategy)?
3 Are there significant obstacles to using the research results to develop a more dangerous pathogen or to overcome current countermeasures?
• Proposals with two or more 'no' answers would have a limited positive impact.

Source: Center for International and Security Studies at Maryland

To address this issue, CISSM proposed building upon the ideas outlined in an earlier report from a US National Academy of Sciences panel on scientific communication and national security chaired by former Cornell University President Dale Corson. The Corson Report, as it is known, concluded that US welfare, including US national security, is best served by allowing the free flow of all scientific and technical information 'not directly and significantly connected with technology critical to national security'. Accordingly, the report recommended that most fundamental research at universities should be unclassified; that a limited amount might require classification; and that a small grey area could require limited restrictions short of classification. It also suggested criteria for making classification decisions (NAS, 1982).[15]

Drawing on the criteria in the Corson Report, CISSM proposed that no restrictions should be placed on basic or applied biotechnology research or research results at university, private sector or government labs unless all of the following criteria are met:

- The technology is developing rapidly and the time from basic science to application is short.
- The technology has identifiable direct military applications, or it is dual use and involves process- or production-related technologies.
- The transfer of technology would give a biological weapons proliferator (e.g. national or sub-national level) a significant near-term capability.
- There are no other sources of information about the technology, or all of those that could also be the source have effective systems for securing the information.
- The duration and nature of the proposed restrictions would not seriously compromise the work of those directly responsible for public health.

The requirement to take account of the public health implications of any proposed restrictions was not part of the original Corson panel approach. But because legitimate applications of biotechnology research could have a profound impact on public health, considering only the security implications of such research would be insufficient. For similar reasons, in situations where certain research results might need to be restricted, individuals with a legitimate need to know for research or public health purposes would have access to the relevant information.

To help protect against the unauthorized release of information, as well as to facilitate the peer review process, CISSM proposed the use of advanced information technology at each level of the oversight system. To illustrate how this might be done, a prototype data management system was built using open-source software and financial-grade security standards. The system has a tree-like structure in which each oversight node (i.e. local institutions, national authorities and the international body) would operate its own secure server for storing information under its jurisdiction. In a fully developed data management system, information required for licensing and peer review would be collected using questionnaires that meet dual use reporting requirements as well as other reporting requirements, such as those required for human subject or animal research.[16]

Next steps

A key issue both in the Fink Committee report and in the deliberations of the NSABB is the potential impact of new oversight requirements on the conduct of dual use biotechnology research in the US. To help address this issue, particularly the possible impact of its proposed oversight system, CISSM commissioned a survey of scientific journal articles published in the US between

2000 and mid 2005 (Kuhn, 2005).[17] The survey indicated that less than 1 per cent of US publications concerning bacteria, viruses or prions involved research that would have been subject to oversight had CISSM's proposed system been in effect. Overall, based on their publications, some 310 US facilities and 2574 US scientists engaged in research activities that fell within CISSM's system. Among those that would have been affected, only 12 of the facilities and 185 of the individuals would have been subject to international oversight – a tiny fraction of the American biotechnology research community. Fourteen facilities and 133 individuals would have been subject to national oversight; and 231 facilities involving 2119 individuals would have been subject to local oversight. Fifty-three facilities and 137 individuals would have encountered multiple oversight levels. Those numbers suggest that the development of local and national oversight arrangements could begin to cover much of the research that would fall within CISSM's more comprehensive, legally binding and globally harmonized system and could help to lay the foundation for the eventual adoption of such a system. Other measures could do the same, some of which are already being undertaken.[18]

For example, individual scientists and professional scientific organizations have been discussing applicable scientific codes (Rappert, 2004; Royal Society, 2005; see also Chapter 1 in this volume). Much of this discussion is focused on ethical codes, which describe personal and professional standards, or codes of conduct, which provide guidelines on appropriate behaviour. Virtually no attention is being given to codes of practice, which outline enforceable procedures and rules. In November 2005, the InterAcademy Panel on International Issues released a set of general principles to guide the development of codes of conduct by individual scientists and local scientific communities (IAP, 2005). In its initial work, the NSABB has outlined various considerations that professional societies and others could draw upon in developing a code of conduct for scientists and laboratory workers.

But it is not enough to simply have scientific codes, whatever the type. Both students and established scientists must be educated about the details of such codes and the potential for misuse of their work. They must also be informed about relevant laws and regulations governing the conduct of dual use research and be provided with training to enable them to meet the oversight requirements that are in place (see Chapter 3 in this volume).

These initiatives could be significantly reinforced if scientific funding agencies and journals required all of those with whom they interact on a professional basis to explicitly consider the dual use implications of their work, and if all research institutions made this a condition of employment. In September 2005, the UK's three leading bioresearch funding agencies, the Medical Research Council (2005), the Wellcome Trust and the Biotechnology and Biological Sciences Research Council, announced that they would now require grant applicants, reviewers and funding agency board members to consider whether the proposed research could be misused for harmful purposes.[19]

In addition to these measures, other interim steps could be taken by national governments that could more directly strengthen oversight of dual use research.

As suggested above, the US and other countries that follow the NIH Guidelines or similar oversight processes for recombinant DNA research could include specified dual use research activities in their national regulations and require mandatory adherence by all facilities undertaking such work. These national standards and regulations could then be harmonized among like-minded countries, perhaps beginning with the 30 nations that comprise the Organisation for Economic Co-operation and Development (OECD). This would be consistent with the OECD's efforts since 2001 to develop a harmonized approach to the management and security of culture collections and other biological resources, as well as its more recent interest in promoting responsible stewardship in the biological sciences and preventing the abuse of research (OECD, 2007). The OECD could develop a uniform list of dual use research activities to be subject to oversight, as well as standardized criteria for assessing the risks and benefits of such research. It could also establish a process for periodic reporting on national implementation of these measures by OECD member states.

Efforts such as this by the OECD or other like-minded countries could be facilitated by the WHO, which has a long history of providing technical information, guidance and assistance to the public, healthcare professionals and policy-makers on the control of dangerous pathogens.[20] In mid 2004, the WHO initiated an exploratory project on the governance of life sciences research and its implications for public health (WHO, 2005). Many of the issues that were highlighted in this exploratory work are now being considered in a new WHO project aimed at examining the implications of life sciences research for global health security (see Chapter 13 in this volume). In addition to raising awareness about the opportunities and risks of life sciences research, this project could also lay the foundation for the development by the WHO and other stakeholders of technical guidelines for overseeing dual use research.[21]

There are thus a variety of incremental steps that can be pursued by scientists, national governments and international organizations to help prevent biotechnology research from leading either inadvertently or deliberately to the creation of new, more destructive, pathogens. None is sufficient; but all of them can help to lay the foundation for the type of comprehensive, legally binding, global system outlined by CISSM.

Notes

1 Portions of this chapter are drawn from Steinbruner and Harris (2003) and Steinbruner et al (2007).

2 The Fink Committee's other recommendations called for educating scientists about the dual use issue and their responsibility to mitigate its risks; reviewing publications for potential national security risks; ensuring adequate controls over access to dangerous pathogens and supervision of personnel working with such materials; and enhancing communication between the life sciences community and the national security and law enforcement communities.

3 Interestingly, this point appears to have been removed from the NSABB website, despite having been included in the original 'Frequently Asked Questions' section of

the website when it was accessed in March 2004.

4. Information on the NSABB's meetings is available on its website, www.biosecurityboard.gov/meetings.asp, accessed in April 2007.
5 Personal communication with Ron Atlas, president of the American Society for Microbiology, February 2003.
6 Successive versions of the study have been posted on the CISSM website since 2003. This chapter is based on the March 2007 version, which is available at www.cissm.umd.edu/papers/files/pathogens_project_monograph.pdf, accessed in April 2007.
7 The licensing process and requirements are discussed in more detail in Steinbruner et al (2007, pp27–28, 37, 67–70).
8 Select agents refer to specific human, plant and animal pathogens whose possession and transfer is regulated by the US government because they can be used for destructive purposes. The laws establishing this requirement and associated regulations are Public Law 107–188, 12 June 2002, 42 Code of Federal Regulations 73, 7 Code of Federal Regulations 331, and 9 Code of Federal Regulations 121.
9 The peer review process is discussed in more detail in Steinbruner et al (2007, pp28–30, 38–43, 71–78).
10 CISSM recognizes, as the Fink Committee did with its proposed experiments of concern, that its categorization is a starting point and that it will need to evolve to keep pace with emerging biological threats. The US select agent list, for example, is used for illustrative purposes only; an internationally agreed list would ultimately need to be developed and maintained.
11 The different research categories and corresponding oversight process are discussed in more detail in Steinbruner et al (2007, pp25, 37–43).
12 The risk-benefit assessment process is discussed in more detail in Steinbruner et al (2007, pp28–30).
13 The projects that were peer reviewed are Cloning of MHC I Immunomodulators into Vaccinia Virus; Enhancement of Virulence and Transmissibility of Influenza Virus; Immunosuppression and Immuno-transition in Plague-mouse Model; Manipulation of Temperate Sensitivity in Pospiviroidae; and Exploring New Non-lethal Incapacitation Options.
14 The issue of information disclosure is discussed in more detail in Steinbruner et al (2007, pp29, 31–32).
15 The rationale for using the Corson Report criteria is discussed in more detail in Steinbruner et al (2007, pp43–45).
16 The data management system is discussed in more detail in Steinbruner et al (2007, pp82–88).
17 As the working paper makes clear, these are rough estimates only: the author did not screen for all of the categories of research involving non-listed agents because of the overall number of papers and the absence of a suitable search strategy. The figures also do not reflect the broader definition of de novo synthesis used in the more recent version of CISSM's research categories table. At the same time, the author almost certainly included some scientists and facilities that were part of research projects outside of the US simply because they were American or affiliated with an American research facility. Although it is difficult to estimate, these factors could well increase the number of projects subject to local oversight, in particular, by 100 or more (see Kuhn, 2005).
18 For a more detailed discussion of these incremental measures, see Steinbruner et al (2007, pp45–48).

19 The Medical Research Council (MRC) appears to be using the Fink Committee's seven experiments of concern to define the types of research that should be reviewed for dual use risks; but it is unclear whether the other UK funding agencies are taking a similar approach. The MRC statement is at www.mrc.ac.uk/doc-bioterrorism_biomedical_research.doc, accessed in April 2007.
20 For information on the WHO's activities on the health aspects of biological weapons, see www.who.int/csr/delibepidemics/en/, accessed in April 2007.
21 This also was one of the priority areas identified by a scientific working group convened by the WHO in October 2006 (see WHO, 2007).

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