CHAPTER

4

Responsible Stewardship of Powerful Biotechnologies

The dual use nature of biology greatly complicates strategies to prevent the development of biological weapons.

The life sciences are inherently "dual use" in that a great deal of the scientific knowledge, materials, and techniques required for legitimate, beneficent biological research could also be used to make a biological weapon. As an example, laboratory research conducted to uncover critical information about how a pathogen manipulates the human immune system to cause disease could be exploited to make a disease harder to treat.[129]

This dual use nature of biology greatly complicates strategies to prevent development of biological weapons. Bioweapons development cannot be prevented using the same strategies developed to prevent nuclear terrorism

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because, unlike highly enriched uranium, the building blocks of biological weapons are globally accessible. Pathogens can be harvested from sick people and animals, found in laboratory freezers, and collected in the natural environment.[130] Like most information on biological research, information on how to find and genetically manipulate pathogens is widely available on the Internet, and training in legitimate life sciences research yields skills equally useful for development of biological weapons.

Fortunately, and despite the wide accessibility of biological information and materials, countries rarely suggest they have biological weapons,[131] and there is no evidence that terrorist groups have subverted cutting edge biological science to make biological weapons. The potential, however, remains, and with the rapidly accelerating power of biological technologies, the consequences of misuse could increase over time.[132] Technologically advanced dual use research in aerosol technologies, synthetic viruses, or even antibiotic resistance could make a natural pathogen into a much more deadly weapon.[132]

The dual use dilemma of the life sciences was brought to policymakers' attention in 2001 following publication of a study done by a group of Australian researchers[133] who added a single gene, IL 4, to mousepox virus, a cousin of the human smallpox virus. The addition of that gene made the mousepox virus so much more pathogenic that it killed even the vaccinated mice. While it is not clear that adding IL 4 to smallpox virus would amplify the lethality of the virus in humans,[134] the implications were troubling. A popular cliché among infectious disease experts is that "Mother Nature is the worst bioterrorist,"[135,136] but the mousepox experiment demonstrated that it

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is indeed possible for a thinking enemy to make something worse than what could evolve naturally.

When published in 2001, the mousepox experiment also exposed the fragility of biodefense planning that relied on rapid development and deployment of vaccines. If an engineered smallpox virus were impervious to vaccine, there would be no defense that could save lives if the virus were used as a weapon. Creating a new vaccine or other type of medical countermeasure could take eight to ten years and could cost more than $800 million.[137]

Even worse, in 2001, most people under the age of thirty would not have had any immunity to smallpox, which kills 30 percent of its victims, because vaccination stopped in 1972 in the United States. People who had been vaccinated in the past but had not received booster shots since the 1970s would have had incomplete protection at best.[138] There were powerful reasons to prevent the misapplication of dual use scientific knowledge, difficult as that may have been, without harming legitimate science. Misuse could threaten the health and lives of many innocent civilians.

The question of how to manage the dual use dilemma is far from resolved.

Recognizing the inherently high stakes of dual use science, the Sloan Foundation funded a number of projects that sought ways to govern the life sciences responsibly without hindering essential, legitimate research. Sloan supported a National Academy of Sciences (NAS) committee in 2002–03 to consider the problem of dual use science; the resulting report ("the Fink Report") is considered the seminal reference in the field.[139] The foundation also funded a University of Maryland (UMD) to develop a prototypical mechanism for international governance of dual use science. While UMD's

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oversight system did not gain wide support among scientists, it did prompt the scientific community to develop a mechanism for self governance. The approach could not be a traditional "command and control" regulatory system because the dual use nature of the life sciences makes it almost impossible to precisely define "allowed" versus "prohibited" scientific activities. Moreover, the life sciences are international, change rapidly, and require in depth scientific expertise to evaluate risks. Due in part to Sloan's efforts, there now exists a National Science Advisory Board for Biosecurity (NSABB) to advise the US government on matters related to dual use research and its publication. Sloan's investment in synthetic biology, which continues, also yielded US government guidance for gene synthesis companies that need to screen orders for the genetic sequences of dangerous pathogens.[140]

THE BUILDING BLOCKS OF BIOLOGICAL WEAPONS ARE GLOBALLY ACCESSIBLE PATHOGENS.

Despite more than a decade of focused and thoughtful work on the issue, the question of how to manage the dual use dilemma of the life sciences is far from resolved. Since the results of the mousepox study were published in 2001, several other controversial papers have been published: a June 2002 paper described how a smallpox virus gene inactivated part of the human immune system,[141] and an August 2002 paper described re creation of polio virus through chemical synthesis.[142] In 2005, researchers published the genetic sequence of the 1918 pandemic influenza virus,[143] prompting fear of regeneration of that virus. Most recently, in 2011 12, two researchers sought to publish results of their studies of whether and how the H5N1 influenza virus (a "bird flu" virus) could become more transmissible.[144] In response to the H5N1 influenza studies, the NSABB took the unprecedented step

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of recommending against publication, then reversed course after several months of heated debate in the global scientific community.[145] The H5N1 study controversy was the likely impetus for the United States Government Policy for Oversight of Life Sciences Dual Use Research of Concern,[146] which was released on March 29, 2012. This new policy requires US government funding agencies to review all proposed and funded projects to identify dual use concerns and propose risk mitigation plans that could include voluntary redaction or classification of research publications.[146]

Even with screening and oversight, the questions of whether a paper should be published and who is authorized to make that decision will probably continue to be contentious. It is virtually impossible to know in advance which study results may be useful to a terrorist, leaving open to debate the degree of threat posed by many scientific papers. Many learned people may agree that specific research poses a dual use threat, but they may disagree about overriding public health or scientific value that would make it worthwhile to publish a paper in the open literature despite any potential threat.

Although it may not be possible to have a readily codified system of oversight for dual use research, there is a clear need to educate scientists about the dual use dilemma (and about biosafety). Before proceeding with scientific work, scientists should always consider the possibility that research results could be misused[147] and should always be able to explain laboratory safety procedures when asked.[148] To shore up education for scientists, the Sloan Foundation funded researchers from the English Universities of Bradford and Exeter to deliver seminars for scientists around the world. Sloan also provided support for the WHO to develop international guidance on

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biosafety and dual use considerations and underwrote efforts to create the International Council for the Life Sciences to help scientists and policymakers increase biosafety in Central Asia, the Middle East, and North Africa.

Like all education initiatives, the task of educating scientists must be continued indefinitely to update established scientists and engage new scientists. The Sloan Foundation's investments have produced important results, and it is crucial for the government and professional associations to continue this work.

Preventing the Misuse of Science

The Fink Report

In 2001, when the Sloan Foundation awarded a grant to the NAS to explore ways to prevent destructive applications of research in biotechnology, the dual use nature of biological research was not a concern of most life scientists. Biological weapons were the stuff of movies, fiction, and the distant past.[19,20,149] The US bioweapons program was dismantled long before most of today's graduate students, postdoctoral fellows, and assistant professors in the life sciences were born.[150] The idea of using scientific research results to do harm or to gain greater understanding of how to wield pathogens as weapons was anathema to scientists. That tacit moral boundary was proved illusory,

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though, when the extent of the former Soviet Union's bioweapons program was revealed. As concerns about bioterrorism grew, so did concerns that life scientists were inadvertently providing information that could be of use to bioweaponeers.[28]

In 2001, the Sloan Foundation provided support to help launch the Committee on Research Standards and Practices to Prevent the Destructive Application of Biotechnology, chaired by Gerald R. Fink, then professor of genetics at the Whitehead Institute for Biomedical Research at the Massachusetts Institute of Technology (MIT). Composed of life scientists, social scientists, lawyers, and bioethicists, the committee met between April 2002 and January 2003.[139]

The idea for a project to review existing US oversight of "potentially dangerous biotechnology research . . . to prevent the destructive application of biotechnology research while still enabling legitimate research to be conducted"[139] actually emerged before 9/11 and the anthrax letters. Jo L. Husbands, now a senior project director for the NAS Board on Life Sciences, recalls that the NAS assumed the study committee "would have the luxury of thinking this through quietly, presenting it, disseminating it, and talking with our international colleagues, because it's a tough problem. Then all of a sudden, we were in the headlights."[151]

How do you avoid making science and security into a zero sum game?

Committee member and University of Louisville professor of biology Ronald Atlas explained: "We were dealing with a crisis situation. In responding to the threat of bioterrorism, the government was considering draconian measures actions like banning foreign scientists, banning foreign

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students from study in the life sciences, requiring government clearance to publish. Back then, there were those who argued that the scientific community just could not be trusted."[152] The fear that the government might act in a way that scientists would not like was echoed by Parney Albright, then a senior official in the White House Office of Science and Technology Policy and now director of Lawrence Livermore National Laboratory. In a 2003 forum, he said that "the science community ought to come up with a process before the public demands the government do it for them, and that will be driven by the rate at which controversial papers hit the streets."[153]

In October 2003, the National Research Council published *Biotechnology Research in an Age of Terrorism.* The document widely known as the Fink Report is considered foundational in the evolving discussion of science and national security. "The report showed that the scientific community recognized that this was a legitimate issue and was prepared to think through, in practical ways, what might be done," said Husbands. "The idea was, how do you avoid making science and security into a zero sum game?"[139]

The committee described an initial set of seven types of experiments of concern that, while not prohibited, would merit review and discussion before being undertaken or published in detail. Such experiments would do at least one of the following:

1. Demonstrate how to render a vaccine ineffective.
2. Confer resistance to therapeutically useful antibiotics or antiviral agents.
3. Enhance the virulence of a pathogen or render a nonpathogen virulent.
4. Increase a pathogen's transmissibility.
5. Alter the host range of a pathogen.

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6. Enable the evasion of diagnostic and/or detection modalities.
7. Enable the weaponization of a biological agent or toxin.[139]

In addition to recommending creation of programs to educate scientists about the dual use dilemma and their responsibility to reduce risks, the committee identified opportunities for review of scientific experiments and results throughout the research life cycle. This was to ensure responsible oversight of scientific advances that have the potential for dangerous misapplication.[139] The committee also called for creation of the NSABB to propose guidance and leadership for research oversight. Finally, the group recommended extending all US efforts in this realm to the global life sciences community.[139]

The US government swiftly adopted some of the Fink Report's key recommendations. The NSABB was created to offer advice, guidance, and leadership for the proposed system of review and oversight. Established in 2004 as a federal advisory committee, the NSABB has been chartered continuously at two year intervals by the secretary of HHS. The NSABB has offered guidance for handling dual use research of concern (DURC), a modified form of the Fink Report's experiments of concern, and has provided input on the publication of several papers, including one on the reconstruction of the 1918 influenza virus[154] and others that explored whether H5N1 could become transmissible among humans.[155-157]

Today, the Sloan funded Fink Report continues to shape thought and policy, "but we're a long way from a substantial culture change," admitted Husbands, who observed:

> There is still a general lack of awareness in the life sciences

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> community about possible security risks. Most life scientists genuinely believe that their work is about the benefits for humanity, broadly drawn. The concept that their research could have a dark side is difficult for people to accept. And there is a deep concern that this will mean increased regulation, at a time when, at least in the United States and most of the developed world, increased regulatory burden makes it harder and harder to actually do your science.[151]

US government actions taken after the 2011 12 controversies surrounding H5N1 experiments may prompt creation of a dual use research oversight system, the need for which was noted in the Fink Report. On March 29, 2012, the US government issued a policy for DURC oversight that requires federal government funding agencies to review all proposed and funded projects for DURC potential and propose risk mitigation plans for DURC research. Risk mitigation plans could include classifying or redacting information that might otherwise be published in the open scientific literature.[146]

It may be impossible to know whether efforts to prevent subversion of the life sciences are effective without what has been termed "extraordinary visibility" into the actions of a bioterrorist.[147] According to the Fink committee, biological scientists have an "affirmative moral duty to avoid contributing to the advancement of biowarfare or bioterrorism."[139] In short, scientists should do what they can to prevent misuse of their work.

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International Oversight of Dual-Use Research

The Center for International Security Studies' Biological Research Security System

Biological scientists in the United States have laws, requirements, and regulations to follow, but there are no international authorities or regulations that govern their experiments unless they work on live smallpox virus.[158] To work with smallpox, scientists must receive permission from a WHO special committee of experts.[159] Because smallpox was eradicated from the natural world, this controlled system is to provide confidence that research is scientifically justified and conducted in a safe and secure manner.[158,160] Smallpox is a special case, but biological research with other dangerous pathogens could also be vulnerable to accident or misuse. That recognition led to the question of whether an international regulatory system similar to that governing smallpox research should be applied to bioscience research more broadly. John Steinbruner, director of the Center for International Security Studies at Maryland (CISSM), argued that it should, and the Sloan Foundation funded his work to develop an international framework to provide "systematic protection against misapplications of biotechnology."[161]

As Steinbruner and colleagues Elisa D. Harris, Nancy Gallagher, and Stacy Okutani wrote in *Controlling Dangerous Pathogens*,[162] the monograph

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that concluded their study, there are many benefits to be gained from advances in biotechnology, but there may also be grave dangers. "Hundreds of millions of lives might be enhanced, salvaged, manipulated, degraded, or terminated depending on how the same basic knowledge is applied. Little of that potential has yet been accomplished, but none of it can be dismissed as fantasy."[162] They argued that the optimal time to establish a regulatory system to protect society from those grave dangers is *before* any harmful powers of biology become commonplace.

The researchers' Sloan funded work began before 9/11, when they began to examine existing rules and laws governing biological research in the United States and other nations, particularly the United Kingdom. Steinbruner and colleagues then conducted a series of workshops around the world to explore the best ways to manage the risks of powerful biotechnologies, and they developed a network of scientists, arms control experts, information specialists, lawyers, regulators, and institutional experts to inform their draft oversight plan. In 2007, Steinbruner's group finalized the prototype Biological Research Security System (BRSS).[162] If implemented, they hoped it would protect the global population from any dangers of bioscience advances so "judgments are based on social consequences, not just scientific merit."[163]

Governance of science must be based on global public health interests, rather than national security interests.

Designed to encompass all biological research around the globe, the BRSS would require licensure for all biological scientists and peer review of all projects before they began. Projects would be placed into one of three categories based on the level of danger and degree of oversight required to assure safety; most research would require little oversight.[164] Local

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consultation, within a university, for example, would be recommended for low concern activities; national consultation would be required for research involving specific dangerous pathogens; and international consultation would be required for work "with the potential to create agents significantly more consequential than those currently known."[164] The group made a BRSS software package available for research centers that want to collect and analyze information about their biological research activities and have projects reviewed for dual use concerns.[165]

The prototype BRSS was controversial and was not embraced by the scientific community. In 2003, Ron Atlas, then president of the American Society for Microbiology, said that requiring scientists, institutions, and even experiments to be licensed "would have a devastating, chilling impact on biomedical research."[166] Some questioned whether it would be feasible to establish a global regulatory regime when one had never been established in a nation,[166] and many favored self governance or an institution based approach to mitigating risks of dual use biological science.[132,167]

Although many scientists did not agree with Steinbruner's approach, Olsiewski believes the group was able to "move the conversation,"[168] by showing that other approaches to research oversight, including those recommended by the NSABB, seemed more reasonable once compared with Steinbruner's BRSS.[169]

Although he believes that American scientists will not accept greater oversight, Steinbruner is hopeful about the international scientific community. In meetings and workshops held in Africa, East Asia, Russia, and the Middle East, non US scientists have not reacted as negatively as US scientists to the idea of greater oversight. Despite US resistance, Steinbruner

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thinks oversight is inevitable[170] and stresses that scientists "should anticipate that systematic oversight is going to be a requirement, work it out so it is not done in the wrong way–do it yourselves rather than having it done to you by upset and angry people."[170] Steinbruner has continued to recommend his oversight framework after the 2011 2012 controversy surrounding publication of the H5N1 papers, and he continues to emphasize that governance of science must be dominated by global public health interests rather than national security interests.[171]

Options for Governance of Gene Synthesis

Rational Guidance to Limit Access to Mail Order Pathogens

In July 2002, Eckard Wimmer, distinguished professor at the State University of New York at Stony Brook, associate professor Aniko V. Paul, and then postdoctoral fellow Jeronimo Cello made headlines when they created a polio virus from scratch.[142] In their *Science* magazine article, they described how they painstakingly strung together sixty base pair pieces of DNA, purchased from a made to order DNA supplier, to build DNA molecules encoding the ~7,500 base pair virus. Once the DNA was transcribed into RNA and translated into proteins in a test tube, they had infectious polio virus. It took three years to perform this work. In a follow up interview in the

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New York Times, Wimmer noted, "You no longer need the real thing in order to make the virus and propagate it."[172]

The publication immediately caused alarm among policymakers, especially when it became widely known that the genetic information for polio virus, as with most other viruses, is freely available on the Internet. As Wimmer reflected, "It was immediately predicted correctly that a similar method could be used to synthesize any virus, including smallpox. . . . Moreover, the question arises as to whether a virus whose 'formula' genome sequence is known can ever be eradicated."[173] He described the paper as a wake up call.[173]

Less than two years after the poliovirus paper was published, a research team based in the J. Craig Venter Institute (JCVI) published its de novo synthesis of the 5,386 bp bacteriophage X174 (polio was 7,500 bp), which took them just two weeks.[174] A little over one year later, another research team published an article about its resurrection of the Spanish influenza virus by chemical synthesis.[143] Then, in 2010, J. Craig Venter and colleagues synthesized an entire bacterial genome and "booted up" a synthetic cell.[175] Venter described the cell as "the first self replicating species we've had on the planet whose parent is a computer. . . . This is a philosophical advance as much as a technical advance."[176] The philosophical questions are likely to continue, especially if George Church from Harvard University and his colleagues from Pennsylvania State University are successful in developing the technologies required to change the 400,000 sites where an elephant genome differs from a woolly mammoth and bring an extinct animal back to life.[177-179]

These demonstrations of the power and speed of new technologies are coming from world class laboratories. Creating a viable pathogen from scratch is not technologically simple, and assembling the genetic material is

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just the first step in a complicated process. However, that process is now as difficult as it will ever be, and the tools needed to make both the short pieces of DNA that characterized the polio work and gene length DNA pieces of 52,000 bp are increasingly accessible. The number of companies providing those services is growing, and the price is falling as demand increases. DNA is needed for basic research, vaccine development, and development of other biotechnology products, including biofuels.[180,181]

Creating effective regulations that do not hinder positive uses of a rapidly evolving technology requires careful thought. To support that effort, the Sloan Foundation provided funding for commercial suppliers, government leaders, and other stakeholders to work together for nearly two years to examine the best options for governance. The group included Robert Friedman from JCVI; Michele Garfinkel, then of JCVI and now at the European Molecular Biology Organization (EMBO); Drew Endy, then at MIT, now at Stanford; and Gerald Epstein, formerly at CSIS, and now at DHS. The group assessed the current state of the technology, then identified risks and benefits to society and formulated options for governance.[182] Their final report, issued in October 2007, offered an array of policy options for regulating gene synthesis and described the advantages and disadvantages of each option.[182,183]

The policy interventions focused on commercial firms that sell synthetic DNA, the owners of laboratory "benchtop" DNA synthesizers, and DNA users and their research institutions. The group considered government regulations, self governance options for commercial suppliers, screening software to detect suspicious synthesis orders, and greater institutional review of synthesis orders by researchers. As Friedman explained: "Somebody

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had to take the time to look through each potential intervention point for opportunities to reduce risk."[184]

By 2006, the US government was interested in changing regulation of synthetic biology. The NSABB was asked to examine the security issues related to synthesis of regulated pathogens ("select agents") to provide advice on "whether current United States Government (USG) policies and regulations adequately cover the de novo synthesis of select agents or whether additional biosecurity measures are necessary."[185] Commercial gene foundries were proactive in considering the risks from gene synthesis and formed two international industry associations to develop standards for screening customer orders.[186,187] The governance of gene synthesis was also a major focus at some synthetic biology users' conferences, which also drew Sloan support.

CREATING A VIABLE PATHOGEN FROM SCRATCH IS NOT TECHNOLOGICALLY SIMPLE, BUT THAT PROCESS IS NOW AS DIFFICULT AS IT WILL EVER BE.

The discussions and identification of oversight options led to government action. On October 13, 2010, HHS released *Screening Framework Guidance for Providers of Synthetic Double Stranded DNA*,[140] which asks suppliers of double stranded DNA to screen orders against GenBank, the NIH genetic sequence database that is an annotated collection of all publicly available DNA sequences. The guidance calls for suppliers to screen customers as well, to ensure compliance with US trade restrictions and export controls. If sequence screening determines that a customer has requested genetic material available only to those with clearance to work with select agents, then the customer must be in compliance with select agent regulations.

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Some hoped the US government would impose stricter controls on DNA synthesis by, for instance, regulating oligos, which are single stranded pieces of DNA. George Church, a professor at Harvard Medical School and a leader in synthetic biology research, wrote years ago that all DNA synthesis should be more regulated, that the sales of the machines and supplies should be limited to licensed buyers, and that "all use of reagents and oligos would be automatically tracked and accountable (as is done for nuclear regulations)."[188] An NAS committee described a possible screening system that might eventually be useful for predicting the danger, or pathogenicity, of a sequence.[189]

However, stricter regulations would be difficult to put into practice without imposing greater burdens on US scientists performing legitimate research.[190] Gene synthesis is an international business, and companies outside the United States are not subject to US regulations. If it becomes too onerous to go through commercial suppliers, scientists may make the genes they need themselves, obviating the usefulness of regulation of commercial suppliers. A 2010 presidential commission examined the current approach to governance in synthetic biology more broadly and did not recommend increased controls at this time.[191,192]

Ensuring that regulation and guidance keep pace with rapid advances in DNA synthesis is a challenge, especially given the international availability of the technologies. By delineating all policy options shaped by scientific and security expertise, the Sloan funded governance project successfully steered US government policy in a rational direction.

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Educating Scientists about Dual-Use Science

Deliberative Seminars for Scientists Worldwide

Brian Rappert, a sociology professor at the University of Exeter, England, and Malcolm Dando, a biologist, international security professor, and arms control expert at the University of Bradford, England, have circled the globe to engage scientists and policymakers directly in conversations about mitigating the risks of dual use biotechnology.

Rappert and Dando began their work in 2005 in the United Kingdom with a series of modified focus groups that they called "deliberative seminars"; the seminars were funded by the Sloan Foundation. The pair's discussions with British life science researchers generally indicated that the scientists were not aware of and had not considered policymakers' concerns about dual use security issues.[193] Rappert and Dando questioned why scientists were not engaged in political discussions of dual use issues that required their input and affected their work, and they found that the subject was not part of scientists' education or training. Dando realized that "it would be very, very rare to meet any practicing life scientist who knew anything at all about the issues of concern to people like me who had contact with the security community."[194] Scientists may not have been concerned, but policymakers were, and the deliberative seminars proved useful for sparking dialogue

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and understanding across professional lines. The pair's experience with the seminars led Rappert and Dando to develop educational modules that could be incorporated into science education.

In a recent interview, Rappert said they have visited fifteen countries, including China, India, Israel, Japan, Kenya, the Netherlands, South Africa, Finland, and the Ukraine, where they have conducted more than 130 seminars on dual use concerns and held numerous meetings with government and professional policymakers.[193] Rappert described the seminars as having "a two fold purpose: to inform participants about current life science security debates and to generate discussion about how research findings should be communicated, whether experiments should be subject to institutional oversight, and how the funding of research is being affected by concerns about biothreats."[195]

Strengthening norms against misuse of biological science requires ongoing commitment.

The pair has reached more than 3,000 scientists through global seminars and a website that offers training materials, articles, and books on dual use issues.[195] They built the website with colleagues at the University of Bradford to make publications and additional resources on the topic widely accessible.

It has long been recognized that life scientists should be more aware of security issues and that dual use science should be part of their education. The first recommendation of the 2004 Fink Report was for "national and international professional societies and related organizations and institutions [to] create programs to educate scientists about the nature of the dual use dilemma in biotechnology and their responsibilities to mitigate its risks."[139] In 2009, the National Security Council affirmed that "life scientists are best positioned to develop, document, and reinforce norms regarding the

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beneficial intent of their contribution to the global community" and that it would be part of the US strategy for prevention of biological threats to assist "professional societies and other representatives of the life sciences community in the development of relevant educational and training materials" for scientists.[196] It requires a lot of persuasion and work, though, to translate a general consensus that education is a desirable goal into the action required to accomplish that goal, and each country has specific needs. Rappert concurred: "Each country requires specific action. You need to assess country by country what might work. It can't be done alone by governments; it has to be done in collaboration with practitioners and professional organizations."[193]

Strengthening norms against misuse of biological science requires ongoing commitment to educating scientists in order to reach each new generation of researchers in every country and to keep practicing scientists up to date. Dando agreed: "Given the multitude of possible ways in which the life sciences can be misused in the future, I'm more and more coming to the opinion that strengthening the norm amongst practicing scientists is going to be one of the major restraints on misuse. We just can't rely on laws."[194] Rappert pointed out reason to hope that biosecurity education could become part of global science education: "Thirty years ago, the idea of biosafety training was met with resistance from many quarters. That attitude changed over time. How can we elicit the same change with biosecurity?"[193]

Rappert's and Dando's work in engaging scientists and policymakers internationally did help spur BWC action. In 2011, dual use education was discussed by the 165 States Parties of the BWC during the Seventh Review Conference. Working with several states they visited as part of their Sloan

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work, particularly Switzerland and Japan, Rappert and Dando helped secure a broad base of support for education initiatives.[197] The BWC had discussed the need for biosecurity education in 2005 and again in 2008,[198] but in the Final Declaration of the 2011 meeting, it was agreed that the topics of education, awareness raising, and training programs for scientists were important enough to be standing agenda items in the yearly intersessional meetings. Working in collaboration with governments and nongovernmental organizations, Rappert and Dando continue to push for meaningful biosecurity education activities and programs.

Setting International Priorities for Biosafety and Biosecurity

The International Council for the Life Sciences

The International Council for the Life Sciences (ICLS) began in December 2005 as a nonprofit, nonpartisan organization specializing in international biosafety and biosecurity, but focused mainly on the Middle East and North Africa (MENA) and in Central Asia and Russia. A grant from the Sloan Foundation allowed the organization to branch off the International Institute for Strategic Sciences to become a freestanding, membership based organization.

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The first major event for ICLS was the 2007 Biosafety and Biosecurity International Conference (BBIC) in Abu Dhabi,[199] which drew more than one hundred scientists and policymakers from twenty six countries.[200] This conference began what came to be known as the "BBIC process," in which ICLS serves as secretariat, but priorities for action are set by a region's scientists and policymakers.[200] The first priority for the Abu Dhabi meeting was to develop a regional biosecurity strategy for shared food and water resources.[200] Despite political differences, all MENA nations have common problems with food and waterborne diseases, especially shigella. "If you find the area of convergence of interest of these nations, then you can broaden that to expand to areas of interest that have more global benefits,"[201] explained Terry Taylor, president of ICLS. "The objective is to improve their processes for dealing with a broad spectrum of biological risks."[201]

The BBIC process continued in Casablanca in April 2009, with a conference funded by the Kingdom of Morocco's ministry of education and Jordan's Royal Scientific Society.[202] One of the important outcomes of this meeting was the creation of the Moroccan biosafety organization in November 2009.[202] Jordan was the site of the 2011 BBIC, and the 2013 BBIC in Lebanon is being planned. In addition, the BBIC process includes technical workshops, assistance with development of national biosafety associations, advisory panels, and biosafety training. Each of the conferences has a theme; for 2011 it was affordable biosafety.[203]

The work done to bring the technical and political leaders of this region together is not easily accomplished by any government. "Sloan should be commended for being farsighted and seeing that this process had benefits," according to Taylor.[201] Having a record of involvement on both technical

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and political levels has allowed the BBIC process to continue over the years in times of greater political tensions. If anything, the political tensions have increased the desirability and importance of the BBIC process.

ICLS is now applying its skill in consensus building to a new topic synthetic genomics. In a Sloan funded effort, the group is helping different synthetic genomics professional associations develop and refine codes of conduct for responsible research.[201]

A Global Culture of Responsibility in the Life Sciences

WHO Guidance on Responsible Life Sciences Research

As the public health arm of the United Nations, the WHO provides global leadership on health concerns and technical assistance for member states in fighting disease and constructing sound health policies. Traditionally, the WHO had not led global discussions of biological weapons and divisive security issues. The organization's 1970 report *Health Aspects of Chemical and Biological Weapons* was not updated until 2004. This followed a 2002 World Health Assembly ruling (WHA55.16) that the WHO does indeed have responsibilities in a biological incident, "whether it is characterized as a

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natural occurrence, accidental release or a deliberate act," and urged member states to treat any deliberate use of a biological agent as a global health threat.[204]

WHA55.16 instructed the WHO to provide technical assistance to member states on biosecurity issues, but it was the Sloan Foundation's investment that enabled the WHO to help build member states' capacity to promote a culture of responsibility in the life sciences. The six year project, Responsible Life Science Research for Global Health Security, promoted a three pillar approach to building public health capacity: research excellence, sound ethics, and increased laboratory biosafety and biosecurity.[205]

Starting in 2004, Sloan Foundation support allowed the WHO to enhance its in house capacity to provide guidance and technical support to member states and establish contacts on global health security in the six regional WHO offices. In 2005, the WHO began pursuing a Sloan funded effort to develop a working paper on dual use issues in biotechnology: "Life Science Research Opportunities and Risks for Public Health: Mapping the Issues."[206] Next came the 2006 report *Scientific Working Group on Life Science Research and Global Health Security: Report of the First Meeting*, which outlined priority areas for WHO guidance, including raising awareness, advancing preparedness, assessing risk, building capacity, and overseeing research.[207]

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In 2007, the WHO held a meeting in Bangkok to bring together representatives from Asian Pacific countries and research experts in the life sciences. The meeting had several purposes: increase countries' understanding of the public health risks posed by advances in the life

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sciences and options for risk management; exchange information about and experience with related policies and best practices; identify countries' needs and priorities; and draft recommendations for research policy and management.[208]

In addition, the WHO and the US NSABB cosponsored an International Roundtable on Dual Use Life Sciences Research in February 2007.[209] The aim of this meeting was to start a dialogue about the management of dual use research among scientists from Australia, Argentina, Bulgaria, Georgia, India, Israel, Morocco, the Netherlands, the People's Republic of China, Poland, Spain, Switzerland, Uganda, and the UK and representatives from international organizations and scientific societies. The roundtable objectives included determining what various countries were already doing in this area and promulgating NSABB draft work products that included criteria for identifying DURC, elements of a code of conduct, and methods for the appropriate communication of dual use research.

The culmination of the WHO's Sloan funded multiyear, multifaceted project was publication of the report *Responsible Life Sciences Research for Global Health Security: A Guidance Document*.[205] Intended for a worldwide audience of life science researchers, laboratory managers, and research institution officials, the document includes a self assessment questionnaire for the WHO member states to evaluate their strengths and weaknesses in preparedness. As "there is no single solution or system that will suit all countries and all laboratories,"[205] the guidance steers the member states into crafting biosecurity solutions that can work for their unique situations.

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