

UNDERSTANDING BIOSECURITY

**Protecting Against the Misuse of Science
in Today's World**

NATIONAL RESEARCH COUNCIL
OF THE NATIONAL ACADEMIES

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FOREWORD

As a scientist who has worked for over 40 years to find cures for infectious disease, I find the idea that terrorists would use biological agents as a weapon to be anathema. It violates the fundamental values of the life sciences that I and my colleagues hold dear: that science is a vital tool for improving life and the health of our planet and enhancing our understanding of the natural world.

My own work has focused on cholera, a disease responsible for the death of thousands of people around the world every year. During the past 40 years, research carried out through international collaboration of scientists has saved many thousands of lives.

Research with biological toxins and pathogens is both necessary and important, and our nation's health and security depend upon our understanding their mechanisms of virulence. At the same time, we are firm in the belief that this research should be conducted safely and responsibly. To date, the incidence of either laboratory workers or members of the public being infected, whether from laboratory accidents or intentional action, is extremely small. Nonetheless, through the years, safety and security practices and procedures have been developed that have successfully prevented accidental or intentional misuse of biological materials.

Scientists have not only demonstrated concern about these issues, they also recognize they have the most at stake should an incident occur. They are best able to identify potential risk, whether from a laboratory door left unsecured or the unusual behavior of a laboratory worker. It is for these reasons that we focus on promoting a culture of responsibility, enabling and empowering scientists to be vigilant stewards of their science. Care must be taken to avoid being overzealous and implementing procedures that don't make life sciences research more secure, only more difficult to conduct—with results that may diminish rather than strengthen security.

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Adapted from *Responsible Research with Biological Select Agents and Toxins* (NRC, 2009)



UNDERSTANDING BIOSECURITY

Protecting Against the Misuse of Science in Today's World

The life sciences offer tremendous promise for meeting many 21st-century challenges. Powerful new tools allow the collection and analysis of vast amounts of information about biological systems—from single cells to global cycles—invigorating the life sciences community and spurring innovation in numerous areas. Building on the knowledge and experience of generations of their predecessors, life scientists are developing information and technologies to improve human health, agriculture, energy, the environment, and applications in many other areas. Whether they are motivated to enhance the quality of life, inspired by the spark of discovery and innovation, or driven by the essential quest for deeper knowledge of our world, life scientists today face remarkable opportunities.

But with opportunities come responsibilities. An important aspect of scientists' responsibility to society is captured in the concept of biosecurity—the challenge to

move the life sciences forward for legitimate purposes while reducing the risks that some materials, knowledge, tools, and technologies could also be used to do harm. In

2001 shortly after the 9/11 terrorist attacks on the World Trade Center towers and the Pentagon, a series of letters containing lethal anthrax powder were sent through the mail

The Scientific Enterprise Is Built on a Foundation of Trust...

... for example, that researchers adhere to professional standards of science. Science is really a partnership between scientists and the greater society. Scientists rely on society for support of their work, whether from taxpayer funding of research or from public policy and regulation that encourage and sustain research. The public expects that scientific results—for example, the vaccines that eliminated smallpox and have nearly conquered polio—will deliver improvements in health and the quality of life. Because of that partnership—and their own commitment to advancing science for the public good—scientists must conduct research ethically and responsibly.

A critical cornerstone of the modern scientific enterprise is the essential exchange of information that enables scientists to replicate, verify, and build on the results of fruitful lines of research. This fundamental principle and practice also depends on public support. Open access allows scientists to evaluate, interpret, adapt, and extend results from many fields of inquiry for use in their own work. It can speed the delivery of life-saving knowledge to medical practice. Yet open access may allow both beneficent and malignant uses of scientific information. As a result, scientists are called on to keep watch against the potential for misuse of their work. Policy makers also need to pursue security goals without restraining the ability of science to advance and deliver on its promises to society.



National Academy of Engineering, Institute of Medicine, and National Research Council—to introduce some of the issues at the intersection of science and security. Because this booklet is limited to the scope of the National Academies’ work, it is not a guide to the outstanding efforts of many other organizations and institutions in the United States and overseas, although some additional resources are provided at the end of the booklet for further reference. This booklet was developed by the Academies to serve as an educational resource for students and the scientific community, illuminate the importance of biosecurity, and explore how scientists, organizations, and governments at many levels can work together to minimize the threat.

to New York City, Washington, D.C., and other locations. Those letters, which resulted in five deaths and put thousands of people at risk, represent one example of the potential misuse of biology. Recent scientific progress, combined with the globalized nature of today’s society, has in some ways expanded vulnerabilities to such misuse and the potential magnitude of effects.

As scientific research evolves, so does its biosecurity context. Policy, governance, and oversight frameworks that affect research in the life sciences are also in a state of change. To inform decision making and support a productive dialogue, life scientists, the security

Biologists working in a lab designed to handle pathogenic materials.
SOURCE: NIAID/NIH.

community, policy makers, and the public need to be educated about the risks and their responsibilities to help mitigate them. Research institutions, scientific journals, professional societies, governments, and international bodies all have a role in addressing the biosecurity challenge. It is particularly important that today’s science students—the next generation of life scientists—are aware of the biosecurity context of their work.

This booklet draws from the work of the National Academies—the National Academy of Sciences,

“The standards of science extend beyond responsibilities that are internal to the scientific community. Researchers also have a responsibility to reflect on how their work and the knowledge they are generating might be used in the broader society.”

—On Being a Scientist (NRC, 2009)

THE BIOSECURITY CHALLENGE

The benefits of biotechnology and its applications in biomedicine, agriculture, and other areas have been great. Two scientific inquiries illustrate the rapid progress toward new and beneficial knowledge that biotechnology offers. They also highlight the unexpected biosecurity challenges new knowledge may bring.

New Science Seeks to Conquer “Old” Diseases

The virulent strain of influenza that engulfed the globe in 1918-1919, known as the “Spanish flu,” is estimated to have killed between 20 million and 50 million people in one of the most devastating health disasters in history. The 1918 flu virus has been the focus of a great deal of research over the years, and in 2005 a group of researchers broke new ground in the quest to understand the factors that contributed to the 1918 pandemic. The group did painstaking work to collect samples of genetic material from the 1918 flu strain, traveling to remote reaches of Alaska to exhume the bodies of flu victims buried in permafrost. The team used modern molecular tools to decode the virulent strain.

Many consider this research to be a significant achievement for

advancing our understanding of health and disease. The research was designed to illuminate the factors that made that strain—and possibly related strains—so lethal. Once the virus’s genetic sequence was published, however, it became freely accessible to everyone, including terrorists and developers of biological weapons. Some members of the sequencing team then went on to reconstruct the virus, an even more controversial step. For some, the existence of the deadly virus in laboratories raised concerns about the possibility of its accidental introduction into the human population. The actual risks posed by the reconstruction of the 1918 influenza virus are unclear—many factors combine to determine whether an infectious agent causes a pandemic infection—and potential

benefits must also be weighed against potential risks. Genetic research could propel rapid progress against deadly infectious diseases, as new information is discovered and as access to that information fosters additional innovative research.

Emerging Science Makes Security a Moving Target

Historically, biological weapons generally utilized naturally occurring viruses and bacteria. Advances in biotechnology, however, such as the advent of genetic engineering, have raised concerns that developing “designer diseases” and pathogens

Emergency hospitals were quickly set up to handle the huge influx of patients during the 1918 “Spanish” influenza outbreak. Scientists have reconstructed the virus that caused the pandemic.

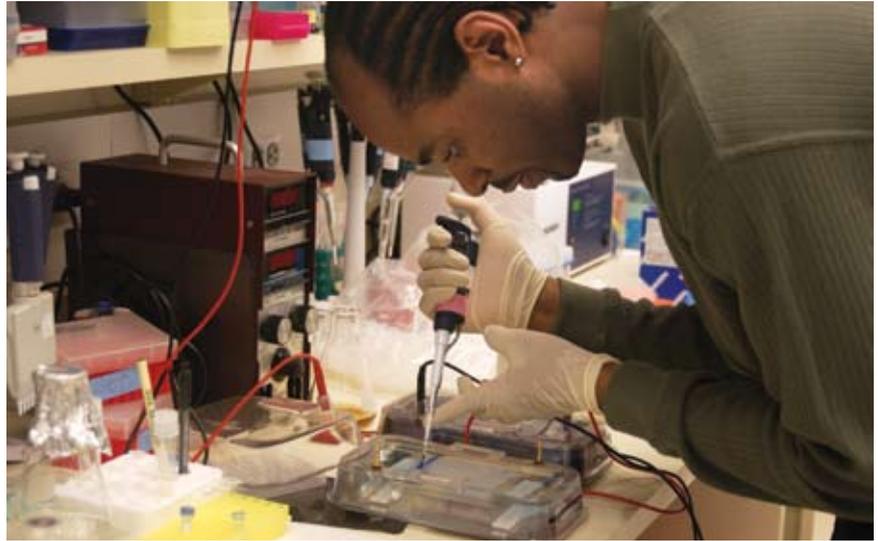


with increased weapons utility is becoming more feasible.

An unintended outcome of research by a team of Australian scientists drew attention to this potential in the late 1990s. In an effort to fight out-of-control mouse infestations in Australia, the researchers bioengineered a strain of *Ectromelia* virus (mousepox) that would render infected mice permanently infertile. But the genetic manipulation they used—incorporating the immunomodulatory cytokine IL-4 into the mousepox genome—unexpectedly turned the virus into an extremely effective mouse killer. The altered virus proved to be so virulent that 60 percent of infected mice died within weeks. Surprisingly, the researchers found that the IL-4 gene-expressing mousepox killed even vaccinated

“It is reasonable to anticipate that humans are capable of engineering infectious agents with virulence equal to or perhaps far worse than any observed naturally.”

—Globalization, Biosecurity, and the Future of the Life Sciences (NRC, 2006)



mice that were completely resistant to the parent virus.

Publication of the experiment's results in 2001 sparked concern and debate throughout the scientific and political spheres. Some saw the paper as dangerous because it illustrated how to construct an IL-4-expressing orthopox virus, potentially providing a “roadmap” for sophisticated bioterrorists to engineer a more virulent strain of smallpox that could affect even vaccinated individuals. Others supported the research and its publication, pointing to its significant contributions to knowledge of health and disease. Some argued that it was important to recognize the possibility that even vaccinated individuals may be killed by a virus that has been spontaneously or intentionally altered. Knowledge of these experiments allows the scientific community to explore how to

Scientist loading DNA into a gel.
SOURCE: Maggie Bartlett , NHGRI.

overcome such engineered viruses. The authors were sensitive to the biosecurity issues involved in their work and had consulted with their peers about whether the results should be submitted for publication. When the authors did submit the paper to the *Journal of Virology*, reviewers and editors at the journal did not express concern about possible misuse of information in the manuscript, and the article was accepted for publication. After publication, concerns were raised about biosecurity. The editor in chief conducted a retrospective review and concluded that the journal was correct in its decision to publish. Ultimately, the controversy led to termination of the research because of concerns about its dual use potential.

The Biosecurity Challenge: Examples of Research with Dual Use Potential

A concept related to biosecurity—*dual use*—refers to the fact that research intended for legitimate purposes may also have a potential to be misused in the development of bioweapons. The debates sparked by the publication of data related to the reconstruction of the 1918 “Spanish” influenza virus¹ (as explained on page 4) illustrated how scientific achievements may also generate security concerns. Additional recent research endeavors that have been identified as having the potential for misuse include:

- *Synthesis of infectious poliovirus.*² Researchers sought to resolve the unusual nature of poliovirus, which behaves as both a chemical and a “living” entity. They succeeded in recreating the virus by chemically synthesizing a cDNA of its genome. Some critics assert that the publication of their methods provided a recipe for terrorists by showing how one could create any virus from chemical reagents purchasable on the open market. The researchers acknowledged this potential but noted that a threat of bioterrorism arises only if mass vaccinations against polio end.
- *Development of “stealth” viruses that could evade the human immune system.* These viruses are being developed to serve as molecular means for introducing curative genes into patients with inherited diseases. However, the research has raised questions about whether they could potentially be induced to express dangerous proteins, such as toxins.³
- *A method for the construction of “fusion toxins” derived from two distinct nontoxic chemical predecessors.*⁴ This technique was originally investigated for the purpose of killing cancer cells, but some argue that it might be redirected to develop novel toxins that could target the normal cells of almost any tissue when introduced into a human host.
- *Genetic engineering of the tobacco plant to produce subunits of cholera toxin.*⁵ Because tobacco is easy to engineer, it is a likely candidate for producing plant-based vaccines. The technique could be used



The technique for modifying tobacco (shown above) and other plants, such as lettuce, to express the cholera vaccine offers a likely prospect for quick and efficient production of the vaccine. However, some critics suggest that it may also have a potential for misuse, illustrating the central conflict involved in biosecurity concerns. The tobacco seeds on the left have been successfully engineered, or “transformed,” to express cholera vaccine; those on the right are untransformed.

SOURCE: Professor Henry Daniell, College of Medicine, University of Central Florida.

to produce large quantities of cholera toxin cheaply and relatively easily, paving the way for fast and efficient vaccine production. Concerns have arisen that it might also have a potential for misuse.

- *Development of new technologies for delivering drugs by aerosol spray in individual doses.* Some have expressed concern that this development, intended to improve the ease of use and rate of compliance among diabetic users of insulin, could be adapted to allow aerosol sprays to cover wider areas in an attack.⁶

Nonlaboratory research may also lend itself to possible misuse. Investigation of the potential effects of a deliberate release of botulinum toxin into the U.S. milk supply recommended aggressive pursuit of early detection measures and new research on means to inactivate the toxin. Publication of the studies pinpointed weaknesses in the system that critics argue could help direct a terrorist to the most vulnerable points in the milk supply.⁷

ADDRESSING THE CHALLENGE

Scientists, security professionals, and society as a whole support adopting active approaches to biosecurity challenges, without unnecessarily hindering scientific innovation. Vital, practical steps to improve oversight of research and provide education can give people the tools to conduct science responsibly. Reports and activities from many sources have examined current regulations and practices and recommended ways to improve approaches to oversight, governance, and education for biosecurity.

The Role of Scientists

In some ways, scientists are the “front line” of defense against misuse of biological research. Working together, scientists can develop effective guidelines and standards that deter misuse without inhibiting the exploration of new and important lines of research. Such guidelines have become a model for dealing with other potential threats. They can also help decision makers who focus on security concerns understand both the potential biosecurity implications and the benefits of new developments.

As noted in the National Research Council report *Biotechnology Research in an Age of Terrorism* (2004), biologists have a moral duty to avoid

contributing to the advancement of biowarfare or bioterrorism. Individuals cannot be expected to ensure that the knowledge they generate will never be used for malevolent purposes, but the report concludes that scientists can and should take steps to minimize this possibility. It is each scientist’s responsibility to consider the dual use potential of his or her own work, make informed decisions on whether or how to proceed, and conduct the work using the principles of responsible scientific practice.

The report proposes a “cradle-to-grave” system in which reviews of experiments at various stages in the research life cycle—from proposal and grant evaluation to publication and communication—would identify and assess potential biosecurity risks. The report recommends that this system involve a mix of voluntary self-governance by the scientific community and expansion of the existing regulatory process, in part based on the approaches to oversight of research using recombinant DNA. That model of self-governance engages the personal responsibility and accountability of the researcher, establishes local oversight by the research institution through a committee of peer researchers

and professionals, and looks to a nationally convened advisory group for recommendations on oversight strategies and guidelines. The National Research Council report *A Survey of Attitudes and Actions on Dual Use Research in the Life Sciences: A Collaborative Effort of the National Research Council and the American Association for the Advancement of Science* (2009) found a basis of support among U.S. life scientists for measures that could lead to a system of self-governance on dual use research.

To help frame these cradle-to-grave reviews, *Biotechnology Research in an Age of Terrorism* (2004) identifies an initial seven classes of experiments that raise concerns about their potential for misuse. Proposed research in these categories should prompt thoughtful consideration of whether such experiments should be conducted or their full results published. “Experiments of Concern” include those that would:

- demonstrate how to render a vaccine ineffective;
- provide pathogens with resistance to therapeutically useful antibiotics or antivirals;
- enhance the virulence of a pathogen or render a nonpathogen virulent;

The Biosecurity Challenge: Using Disease as a Weapon

Human beings have been using biological materials to cause harm for centuries. In 600 B.C.E. the Athenian leader Solon poisoned the water supply in the city of Kirrha with the noxious roots of the *Helleborus* plant—a primitive but effective biological toxin. In 1763 during continued conflict after the French and Indian War in North America, the commander of besieged British troops at Fort Pitt infected Native Americans with smallpox by giving them blankets used by sufferers of the disease. But the entire concept of bioweapons changed in the late 19th and early 20th centuries when biologists developed techniques to identify, isolate, and culture pathogens under precisely controlled conditions. This ability spawned both weapons programs and continuing international efforts to prevent the use of bioweapons.

As many as two dozen nations have engaged in bioweapons research. All the major combatants in World War II had bioweapons research programs. Only Japan actually used a biological weapon, in the Sino-Japanese war that extended into World War II, by air-dropping plague-infested fleas in parts of China to create epidemics. The United States established an offensive bioweapons program during World War II to deter the use of bioweapons and to retaliate against an attack if necessary. Because bioweapons, if used, could spread to military and civilians alike and affect both enemies and allies, President Richard Nixon shut down the United States' offensive bioweapons program in 1969. Bioweapons stockpiles were destroyed and facilities were converted to other purposes, including research on defenses.



B. anthracis spores, taken from the letter sent to the *New York Post* and postmarked September 18, 2001, are prepared for analysis.

SOURCE: U.S. Department of Justice.



A government scientist tests samples for anthrax following the letter attacks in 2001.

SOURCE: U.S. Army Medical Research Institute of Infectious Diseases.

The fundamental international agreements not to use disease as a weapon are the Geneva Protocol, signed in 1925, which bans first use of biological weapons, and the Biological and Toxin Weapons Convention (BWC), signed in 1972. The BWC was the first disarmament agreement to ban an entire class of weapons. Building on those accords, United Nations Security Council Resolution 1540 (2004) adds a further binding international commitment. It requires that all U.N. member states adopt measures to prevent terrorist groups, clandestine procurement networks, and other nonstate actors from acquiring biological weapons or the means of their delivery.

Unfortunately, some countries have not honored their international commitments. Despite having sponsored the 1972 BWC, for example, the Soviet Union continued to carry out clandestine bioweapons programs. Russia continued to stockpile anthrax, smallpox, plague, and other pathogens until 1992, when Russian President Boris Yeltsin banned further bioweapons activities.

- increase transmissibility of a pathogen;
- alter the host range of a pathogen;
- enable the evasion of diagnosis or detection;
- enable the weaponization of a biological agent or toxin.

Following a recommendation in the report, the U.S. government established the National Science Advisory Board for Biosecurity, which developed additional criteria to identify experiments that could be considered “dual use research of concern.”⁸ (For more information on the advisory board, see page 13.)

The accelerating pace of research progress is expanding the concept of biosecurity risks in the life sciences beyond pathogens, according to the National Research Council report *Globalization, Biosecurity, and the Future of the Life Sciences* (2006). Rapid international diffusion of results produced by the life sciences and the relevance to the life sciences of research in other disciplines pose further challenges.

The National Research Council report *Responsible Research with Biological Select Agents and Toxins* (2009) affirms that misuse of biological materials is taboo in every corner of the scientific community. But disastrous results could follow actions by only a few individuals ignoring that taboo. As stated in the report, such individuals can

often be detected by watching for warning signs before they actually commit a malevolent or violent act. Active and sustained monitoring and management by scientists could recognize many of these signals, providing the basis for prevention. To minimize potential security and safety risks, the report urges implementation of programs and practices to develop and support a culture of trust and responsibility,

“Biological scientists have an affirmative moral duty to avoid contributing to the advancement of biowarfare or bioterrorism.”

—Biotechnology Research in an Age of Terrorism (NRC, 2004)

Scientific Self-Governance and the Asilomar Conference

A common message from many recent National Research Council reports is that the scientific community should take preemptive steps to protect the integrity of science and minimize its risks. A 1975 conference and the guidelines resulting from it provide an example of how scientists responded to one case where a promising technology also appeared to pose potential risks.

The 1975 Asilomar conference—named for the California conference center in which it was held—became a landmark example of the scientific community’s ability to lead the way in developing new technologies responsibly. The focus of the conference was recombinant DNA, then a novel technology of unexplored potential and uncharacterized risks. These discussions inspired the development of guidelines, issued the following year by the National Institutes of Health, to prevent the unintended creation of harmful organisms in work with recombinant DNA. The influence of the Asilomar conference has continued to inspire responsible conduct and self-governance among scientists to this day.



SOURCE: From the Dr. Donald S. Fredrickson Papers, NLM.

within which potential personnel issues can be identified and addressed.

The Role of Research Institutions (Private Laboratories, Universities, and Others)

Institutions that house biological research facilities—such as universities, government research campuses, and the laboratories of private companies—have a responsibility to protect the safety and security of their workers, those living in the surrounding environment, and the public at large. These institutions must be aware of and comply with rules governing research activities and be prepared to actively educate their employees and students about relevant requirements and responsible practices for safety and security.

The research institutions in which most scientists conduct their work have established formal oversight mechanisms, some of which stem from specific legal obligations. Bodies such as Institutional Biosafety Committees, Institutional Review Boards, and Institutional Animal Care and Use Committees may, to some extent, oversee research that also involves biosecurity. Depending on the institution's structure, such committees review research at many stages, such as assessing grant applications and reviewing experimental approaches.



SOURCE: NIH/NIEHS (Steve McCaw, Image Associates).

Research institutions can also play an important role in facilitating useful exchanges among scientists and others. For example, constructive dialogue between scientists and members of the national security community is needed to create a system that is responsive to the risks but also credible to and feasible for researchers. To help address this gap, the National Research Council report *Science and Security in a Post 9/11 World* (2007) recommends that universities work closely with federal agencies to develop opportunities for scientists to participate in policy fellowships at intelligence and national security agencies and, conversely, to develop opportunities for members of the intelligence and national

security community to participate in fellowships at universities.

The Role of Journal Editors

Peer-reviewed journals serve as a hub for the exchange of scientific information. The editors of these journals, in turn, serve as gatekeepers that determine what should—or should not—be published. Recognizing that publishing information with dual use potential carries risks, journal editors have taken steps to mitigate the risk that information they publish will be misused. In 2003 following a workshop held by the National Academies and the Center for Strategic and International Studies, a group of scientists, journal editors, and security experts drafted a “Statement on Scientific



Recognizing that publishing information with dual use potential carries risks, journal editors have taken steps to mitigate that risk—for example, screening submitted articles for potential dual use implications.

SOURCES: Service, R.F. 2006. Biosecurity: synthetic biologists debate policing themselves, *Science* 312:1116, reprinted with permission from AAAS. Davidson, E.M. and R. Cook-Deegan, 2007. Science and security: practical experiences in dual-use review, *Science* 316:1432-1433, reprinted with permission from AAAS. Cover. 2007. *Proceedings of the National Academy of Sciences U. S. A.* 104(12). Cover. 2008. *Nature* 454(7201).

Publication and Security.” In the statement, editors of leading journals in the life sciences accepted responsibility for screening manuscripts to reduce the risk of misuse of scientific information, indicating that manuscripts would be rejected if “the potential harm of publication outweighs the potential societal benefits.” The statement was simultaneously published in *Science*, *Nature*, and *Proceedings of the National Academy of Sciences (PNAS)* and by the American Society for Microbiology. These and other

journals have now adopted formal policies on biosecurity.

Scientific journals are not the only place where science is communicated. All scientists are responsible for monitoring their communication to maximize the benefits and minimize the risks of their research. Biosecurity needs change rapidly as science develops, and much depends on both the scientists who conduct research and the editors who publish it. Their roles and attitudes on biosecurity

“It is an unfortunate reality that almost all advances in life sciences technology pose potential ‘dual use’ risks. But better science is the best protection against potential threats.”

—*Globalization, Biosecurity, and the Future of the Life Sciences (NRC, 2006)*

are explored in detail in the report *A Survey of Attitudes and Actions on Dual Use Research in the Life Sciences* (2009).

In addition, policies in the United States must be considered in their international context. Journals in the United States publish papers from scientists in other countries, and thousands of journals publish life science research outside of U.S. borders. *Biotechnology Research in an Age of Terrorism* (2004) identifies the need for cooperation among journal editors to develop international guidelines for the publication of manuscripts containing potentially sensitive information.

The Role of Professional Societies

Scientific professional societies provide crucial venues for scientists to discuss current issues and the evolving contexts of their work. These organizations also furnish

networks through which information can be shared among scientists working in academia, government, and industry. As such, professional societies are uniquely qualified to help raise awareness of biosecurity concerns among scientists and provide guidance to limit the risks.

Biotechnology Research in an Age of Terrorism (2004) called on professional societies to create educational programs about the potential risks of dual use research. In addition, *Seeking Security: Pathogens, Open Access, and Genome Databases* (2004) calls for codes of conduct for scientists to protect against misuse of scientific progress that would cause environmental or medical harm and to conduct their research in ways that minimize the risk of misuse of life science research for destructive purposes.

Some professional societies have incorporated education about biosecurity issues into their missions and are raising awareness and facilitating discussion about biosecurity through training programs and curricula, standards and guidelines, and professional development activities and conferences. For example:

- The American Association for the Advancement of Science (AAAS) convened a workshop in November 2008 to evaluate education on dual use research. The group called for teaching “the scientific, ethical, and

legal issues” related to dual use research to American and foreign scientists in the United States. Specific proposals emphasized establishing federal funding for such programs, developing guidance for scientists, and creating educational materials for scientists and nonscientists on the dual use dilemma.⁹

- The American Society for Microbiology (ASM) has called for biosecurity awareness to be a component of formal training for microbiologists, just as biosafety practices have been. The society holds annual conferences on



biodefense and emerging disease research.¹⁰

- The Federation of American Societies for Experimental Biology (FASEB) has issued a statement on biosecurity education, calling for integrating dual use education into the training scientists receive in the responsible conduct of research.¹¹

The idea to incorporate dual use issues into professional codes of conduct has also gathered considerable attention in recent years. The InterAcademy Panel on International Issues is a network of more than one hundred of the world’s academies of science. The group issued a *Statement on Biosecurity* in 2005 that provides principles that academies and other scientific bodies should consider in preparing codes of conduct. While codes of conduct cannot prevent those who are dedicated to carrying out malevolent acts from doing so, they can raise awareness and

Highly engineered Biosafety Level 4 (BSL-4) laboratories are equipped—and their personnel trained—to handle highly infectious biological agents. Here a scientist showers in a decontamination booth before exiting the sealed confines of the lab.

Increasingly, scientists receive information and training from professional societies as well as academic institutions not only in safety measures but also in recognizing and preventing situations that may give rise to biosecurity concerns.

SOURCE: Centers for Disease Control and Prevention.

sensitize practicing scientists to the risks of working with hazardous pathogens.

The Role of the Federal Government

The U.S. government addresses biosecurity concerns in part by setting basic policy for the conduct of science and by producing guidance and regulations to govern specific types of research. Communication between the scientific and security communities is important to ensure that policies balance increased security with continued scientific progress. Scientists thus have an essential role in using their knowledge to inform decisions.

The Select Agent Program

One of the primary mechanisms in place in the United States to oversee the use of dangerous pathogens in research laboratories is the Select Agent program, administered by the Centers for Disease Control and Prevention and the U.S. Department of Agriculture. Begun in 1997, the regulations governing the program were strengthened significantly in the aftermath of the anthrax mailings in 2001 and now provide a rigorous formal oversight system to decide who can possess microorganisms and toxins that could be used as weapons and how facilities that possess them will be protected. Individuals are subject to a background check to identify those on the list of “restricted

persons,” including convicted felons, illegal aliens, or those deemed ineligible for other reasons. Facilities must prepare security plans that include controlling access to laboratories that conduct select agent research and responding in the event of theft or accidental release. Select agent laboratories are also subject to inspection by the government agencies that oversee the program.

The National Science Advisory Board for Biosecurity

There is a gap—in language, goals, and understanding—between the scientific community and the national security community. Some in the national security community do not fully understand scientists’ need for openly sharing data and ideas, the importance of foreign students and scholars, or the extensive nature and benefits of international collaboration in science. Among university scientists, on the other hand, many do not

fully understand the concerns of the national security community about communication of scientific information or the significance of limits and responsibilities that security regulations place on scientists’ activities.

Several National Research Council reports, including *Science and Security in a Post 9/11 World* (2007), *Seeking Security: Pathogens, Open Access, and Genome Databases* (2004), and *Biotechnology Research in an Age of Terrorism* (2004), emphasize the need for closer partnerships among those involved in addressing the biosecurity challenge. As noted above, *Biotechnology Research in an Age of Terrorism* recommended that a science advisory board be established to serve as a point of continuing dialogue between scientists and security professionals to provide case-specific advice on the oversight and dissemination of life sciences research information.



SARS: Science in a Globalized Society

Today's society is truly a global village. Commerce and travel create a constant flow of people and materials around the planet. The severe acute respiratory syndrome (SARS) outbreak of 2002-2003 underscored the world's vulnerabilities to emerging disease outbreaks. Although it is not an example of the misuse of science—the virus occurred naturally—the SARS experience demonstrated how valuable unrestricted access to scientific information can be in a public health crisis.

The SARS outbreak was rapid and widespread. The virus that causes it is thought to have originated in an animal host in China. Shortly after the first few human cases occurred, people in five countries became infected within a 24-hour period; within six months, the disease had reached more than 30 countries, ultimately killing more than 700 of the estimated 8,000 people who were infected. During the outbreak, SARS was seen as having the potential to cause a more severe pandemic than even the 1918 flu.

Scientists in laboratories around the world raced to investigate the virus. Its genetic sequence was determined and within weeks was promptly published in the public domain. Dozens of companies and laboratories used this information to try to uncover the disease's pathogenic mechanism, develop diagnostic tools and vaccines, and determine what measures would be most effective to contain the spread of the virus.

Fortunately, the outbreak was contained and the feared pandemic did not occur. The factors responsible for its containment, as well as factors that might contribute to its reemergence, are still being studied. It is clear to many that research to investigate SARS was and continues to be necessary for the public good. On the other hand, the complete genome sequence of the virus that causes SARS, which is publicly accessible, could conceivably be used by a very sophisticated bioterrorist to synthesize a new version of the virus. The globalized nature of the scientific enterprise, in combination with the speed with which people—and pathogens—travel around the globe, increases the complexity of the biosecurity challenge, as well as the need for international collaboration in addressing it.



In response to the SARS infectious disease alert of 2003 in Asia, people moving around were screened for the disease, and measures were put in place at airports and other transport hubs to provide quarantine conditions for the public arriving from areas of infection.



The World Health Organization promotes policies and actions in all countries to protect against potential biosecurity events and threats. Its *Laboratory biosafety manual* encourages countries to develop national codes of practice for safe handling of pathogenic microorganisms in laboratories. The third edition of the manual, published in 2004, stresses throughout the importance of personal responsibility. This version of the international biohazard warning symbol appears in the 2004 edition.

The National Science Advisory Board for Biosecurity (NSABB), chartered in 2004, has its headquarters at the National Institutes of Health. Providing federal guidelines and then relying on self-governance by research institutions are key to the board's proposed oversight system for dual use research. This system would require principal investigators to make an initial assessment of the potential for misuse of their research and would add biosecurity to the scope of reviews conducted by Institutional Biosafety Committees. The NSABB has developed criteria for identifying "dual use research of concern," proposed guidance on education and oversight issues,

and made recommendations on specific issues, including synthetic biology and proposals for personnel reliability programs for those doing research on dangerous pathogens.

The Role of International Coordination

In the global biological research enterprise, organisms, information, tools, and people are constantly crossing international borders, both on the ground and in cyberspace. Global cooperation among researchers speeds scientific advances—including progress in defenses against public health threats as well as bioterrorism. Individual scientists often have many opportunities to conduct, publish, and share their work in other countries, increasing the ability of researchers to make new connections and build on one another's work. Even within the United States, the scientific workforce is increasingly international: At the National Institutes of Health, for example, about half the technical staff is made up of non-U.S. citizens.

International coordination and cooperation will be necessary to make any effort to mitigate the risks of bioterrorism effective, according to *Biotechnology Research in an Age of Terrorism* (2004) and *Globalization, Biosecurity, and the Future of the Life Sciences* (2006). There are two main approaches to achieving international coordination on biosecurity:

"Top-down" efforts, such as formal international agreements, can set policies and standards, and international institutions can engage multiple stakeholders to set policy and guidance. "Bottom-up" networks of scientists and scientific organizations can work together to determine appropriate practices and mechanisms for research oversight and self-governance. Both types of efforts could be strengthened; many National Research Council reports and activities have explored ways for the international community to engage effectively on these issues.

Although prudence requires good stewardship of harmful biological materials, tools, and knowledge in the United States, as stated in

"Given the fundamentally international character of research in the life sciences, any serious attempt to prevent the misuse of research must include efforts at improving and harmonizing standards and practices internationally."

—Biotechnology Research in an Age of Terrorism (NRC, 2004)

Science and Security in a Post 9/11 World (2007), unnecessarily closing ourselves off from the world in a futile effort to protect ourselves will only isolate us from an increasingly integrated and competitive global community.

Recent international efforts have sought to supplement the deep and long-standing foundation of scientific self-regulation, voluntary standards, and associational accreditation with mandatory requirements on specific aspects of laboratory safety. A number of countries impose export controls on dual use equipment, pathogens, and toxins that could be used for biological warfare. In addition, agreements that are not



legally binding—such as those made by the Australia Group, an informal network of 40 member countries—work to harmonize national controls on the export of dual use materials and equipment. However, international regulation of biology is complicated by the lack of a multilateral consensus as to the basic security framework that would allow consistent application of controls.

In 2005 and 2008 the National Academies partnered with other scientific organizations in an international dialogue. As described in *The 2nd International Forum on Biosecurity: Summary of an International Meeting, Budapest, Hungary, March 30 to April 2, 2008*, participants at the forum identified views shared among many countries and issues on which they differ. Because countries may choose

to emphasize different strategies, participants supported developing a toolkit of multiple options for addressing education, oversight, and governance issues. For the bottom-up approach, participants identified key roles for international scientific organizations, such as the International Council for Science, the InterAcademy Panel on International Issues, the Academy of Sciences for the Developing World, and science unions, because these organizations are often perceived as neutral networks that can engage scientists from many countries. For the top-down aspects, participants particularly cited the Biological and Toxin Weapons Convention not only because it provides the fundamental norm against the misuse of the life sciences but also for its value as a convening mechanism to address topics relevant to the scientific community.

“The participants [in the Forum] came from all over the world because the life sciences are a genuinely global enterprise, and thus any policies must include international as well as national measures.”

—*The 2nd International Forum on Biosecurity: Summary of an International Meeting, Budapest, Hungary, March 30 to April 2, 2008* (NRC, 2009)

DOING SCIENCE RESPONSIBLY

Biology is advancing rapidly and powerful materials, tools, and knowledge are widely accessible throughout the world—indeed, the free exchange of scientific information was an essential factor in enabling the many scientific achievements of the 20th century. In parallel, current and future biosecurity threats could come as much from terrorists operating outside of traditional government frameworks as from the governments of other nations. Recognizing this reality, it is increasingly important that life scientists, and the organizations—funding agencies, professional societies, scientific journals, and others—that support their activities, take steps to ensure that the fruits of their work are not exploited for malevolent purposes. This will require that those working in

the life sciences achieve a greater appreciation of the dangers and a greater willingness to shoulder the responsibility to prevent misuse. On a global scale, a new ethos is required.

Life scientists also need to put forth, for the education of policy makers and the public, cogent arguments for the benefits of research for both health and security. The same developments serve biosecurity needs by providing therapies that would dramatically decrease the success of a potential biological attack. Concerted communication of this fact is needed to assure that policy makers and the security community do not impede essential research.

Researchers, policy makers, regulators, and the security

community are all grappling with biosecurity issues. Although much more can be done, a network of resources exists to guide scientists in making informed decisions. Within their institutions, researchers have oversight bodies to turn to; within their professional societies, they have access to training and other resources; within their state and federal governments, there are regulations and sources of guidance on broad issues. Together with networks at the international level, these resources—which continue to grow in number and type—can give scientists the information and tools they need to advance knowledge while doing their part to protect the safety and security of those around them: in short, to conduct science responsibly.

NOTES

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- ⁹http://www.aaas.org/news/releases/2008/1229dual_use.shtml.
- ¹⁰<http://www.asmbiodefense.org>.
- ¹¹http://opa.faseb.org/pdf/2009/FASEB_Statement_on_Dual_Use_Education.pdf.

WEB RESOURCES FOR FURTHER INFORMATION

National Academies Biosecurity Website

<http://nationalacademies.org/biosecurity>
This site aggregates information on studies and other activities at The National Academies on a wide array of issues related to biosecurity, both in the United States and internationally.

U.S. Government Interagency Biosecurity Website

<http://www.whitehouse.gov/administration/eop/ostp/nstc/biosecurity>
The White House has convened an interagency working group to coordinate biosecurity outreach and education across federal agencies. This website, developed by the working group, presents the biosecurity activities of the agencies and provides links to agencies, regulations, and reports being used to develop policies. Its goal is to reduce public confusion about U.S. biosecurity activities and, in the spirit of Open Government, have a transparent process for the interagency working group.

National Science Advisory Board for Biosecurity

<http://oba.od.nih.gov/biosecurity/biosecurity.html>
This official site of the National Science Advisory Board on Biosecurity contains information on their meetings and publications as well as background information on dual use issues.

American Association for the Advancement of Science (AAAS)

<http://cstsp.aaas.org/dualuse.html>
This site, maintained by the AAAS Center for Science, Technology, and Security Policy, contains information about dual use issues relevant to teachers and students.

The Virtual Biosecurity Center (VBC)

<http://virtualbiosecuritycenter.org>
A project of the Federation of American Scientists involving several scientific organizations, including AAAS and the National Academies, along with the Organisation for Economic Co-operation and Development, this site aggregates a wide spectrum of material on many aspects of biosecurity.

Biosecurity Codes Website

<http://www.biosecuritycodes.org/>
This site, developed by the International Futures Program of the Organisation for Economic Cooperation and Development, discusses and supplies numerous examples of biosecurity codes of conduct and international and national legislation. It also links visitors to resources throughout the international biosecurity community.

This booklet was prepared by the National Research Council based on the following reports:

Responsible Research with Biological Select Agents and Toxins (2009)

Sponsored by: National Institutes of Health

A Survey of Attitudes and Actions on Dual Use Research in the Life Sciences: A Collaborative Effort of the National Research Council and the American Association for the Advancement of Science (2009)

Sponsored by: Carnegie Corporation of New York, Alfred P. Sloan Foundation, and the National Academies Presidents' Circle Communications Initiative

The 2nd International Forum on Biosecurity: Summary of an International Meeting, Budapest, Hungary, March 30 to April 2, 2008 (2008)

Sponsored by: Carnegie Corporation of New York and Alfred P. Sloan Foundation

Science and Security in a Post 9/11 World: A Report Based on Regional Discussions Between the Science and Security Communities (2007)

Sponsored by: National Science Foundation and National Institutes of Health

Globalization, Biosecurity, and the Future of the Life Sciences (2006)

Sponsored by: Department of Homeland Security, Centers for Disease Control and Prevention, Food and Drug Administration, National Institute of Allergy and Infectious Diseases, National Science Foundation, and Intelligence Technology Innovation Center

Biotechnology Research in an Age of Terrorism (2004)

Sponsored by: Alfred P. Sloan Foundation and Nuclear Threat Initiative

Seeking Security: Pathogens, Open Access, and Genome Databases (2004)

Sponsored by: National Science Foundation

Additional Reports from the National Academies

Department of Homeland Security Bioterrorism Risk Assessment: A Call for Change (2008)

Sponsored by: Department of Homeland Security

An International Perspective on Advancing Technologies and Strategies for Managing Dual-Use Risks: Report of a Workshop (2005)

Sponsored by: Department of Homeland Security, Centers for Disease Control and Prevention, Food and Drug Administration, National Institute of Allergy and Infectious Diseases, National Science Foundation, and Intelligence Technology Innovation Center

Microbial Threats to Health: The Threat of Pandemic Influenza (2005)

Excerpted and updated from report sponsored by: Centers for Disease Control and Prevention's National Center for Infectious Diseases, Department of Defense, U.S. Agency for International Development, U.S. Department of Agriculture's Food Safety and Inspection Service, National Institutes of Health's National Institute of Allergy and Infectious Diseases, National Institutes of Health's Fogarty International Center, Ellison Medical Foundation, U.S. Food and Drug Administration, and U.S. Joint Institute for Food Safety Research

On Being a Scientist: A Guide to Responsible Conduct in Research, 3rd ed. (2009)

Sponsored by: National Science Foundation

Reports from the National Academies are available from the National Academies Press, 500 Fifth Street, NW, Washington, DC 20001; 800-624-6242; www.nap.edu. Reports are available online in a fully searchable format.

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