Viewpoint

In the Shadow of Anthrax: Strengthening the Biological Disarmament Regime

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One of the reasons that biological weapons (BW) have been employed rarely over military history is an innate human revulsion against the use of disease as a method of warfare. Despite this ethical norm, Japan is known to have dropped bombs containing plague-infected fleas on Chinese cities during World War II, and other alleged incidents of biological warfare have been reported.[1] The lethal anthrax spores sent through the U.S. mail in the fall of 2001 have also aroused new concern over bioterrorism.

Existing legal prohibitions on BW are flawed or incomplete. The 1925 Geneva Protocol bans the use of bacteriological agents in warfare but not their possession, and the 1972 Biological and Toxin Weapons Convention (BWC) prohibits the development, possession, stockpiling, and transfer of biological and toxin weapons but lacks formal measures to ensure that the 144 parties to the treaty are complying with their obligations. Article VI of the BWC offers only the weak option of petitioning the United Nations (UN) Security Council to investigate cases of suspected noncompliance, a measure that has been rendered ineffective by political disagreements. As a result, the BWC's lack of "teeth" has reduced the treaty to little more than a gentleman's agreement.

The objectives of biological disarmament are threefold: (1) to reassure law-abiding countries that potential enemies have also renounced BW; (2) to deter states that might consider acquiring BW from doing so; and (3) to contain the small number of "rogue" states, which either violate the BWC or remain outside the regime, with political, economic, or military sanctions. As defense analyst Brad Roberts has argued, "norms matter in international politics—not because they constrain the choices of the most malevolent of men but because they create the basis for consensus about responses to actions inconsistent with those norms."[2] At present, researchers, supported by U.S. government assessments, believe that roughly twelve countries have active biological warfare programs, including parties to the BWC such as Iraq, Iran, Libya, China, Russia, and North Korea. This level of noncompliance indicates that the moral and legal restraints enshrined in the treaty are not strong enough to prevent some governments from acquiring and stockpiling BW. Accordingly, it is essential to take concrete steps to reinforce the biological disarmament regime.

Because the materials and equipment used to develop and produce BW are "dual-use," or suitable both for military purposes and legitimate commercial activities, verifying compliance with the BWC to a high level of confidence is exceedingly difficult. For this reason, at the Second BWC Review Conference in 1986, States Parties sought to strengthen the treaty by adopting a set of confidence-building measures (CBMs) that were politically rather than legally binding. These measures included the exchange of information on research centers equipped with high-containment systems, and information on unusual outbreaks of infectious disease and similar occurrences caused by toxins. The Third BWC Review Conference in 1991, recognizing the value of CBMs and also their limitations, adopted additional transparency measures, including the declaration of vaccine production plants (which are easily diverted to production of BW agents), the description of past activities related to biological warfare, and the exchange of information on biodefense programs. Unfortunately, the level of participation in the CBMs has been poor. From 1987 to 1995, only 70 of the then 139 members of the BWC submitted data declarations, and only 11 took part in all rounds of the information exchange.[3]

In September 1993, a panel of government scientific and technical experts known as VEREX, which had been established to assess the feasibility of verifying the BWC, issued its final report. The VEREX group concluded that a combination of declarations and inspections to increase the transparency of dual-capable biological facilities, such as biodefense labs and biotechnology plants, could enhance confidence in BWC compliance and deter violations.[4] Accordingly, States Parties to the BWC established an Ad Hoc Group in September 1994 to negotiate a legally binding Protocol to the treaty that would include declarations of relevant biodefense and biotech facilities, routine visits to declared sites, challenge investigations of suspect facilities, and field investigations of the alleged use of BW or suspicious outbreaks of disease.

The "golden rule" of multilateral arms control is that the rights and obligations established by a treaty must apply equally to all of the participating states. For example, if the U.S. government wishes to inspect bioindustrial sites in countries of proliferation concern, such as Russia and Iran, it must be prepared to accept the same types of monitoring activities at plants on American soil. Thus, the key challenge facing the BWC Protocol negotiators was to design an on-site inspection system that was intrusive enough to give member states a reasonable level of confidence in compliance, while protecting legitimate national security information and the trade secrets of biotechnology and pharmaceutical companies. Problems arose when the Ad Hoc Group actually began to negotiate the draft Protocol, or "rolling text," in July 1997. Major differences among national positions meant that large portions of the text were not agreed by consensus and hence were set off in brackets.

In June 2001, in an effort to move the stalled negotiations forward, Ad Hoc Group chairman Tibor Tóth proposed a 210-page "composite text" of the BWC Protocol that replaced the bracketed sections with compromise language designed to resolve the outstanding issues. Although most delegations were prepared to accept the chairman's text as a basis for further negotiations, the U.S. delegation declared that the draft Protocol could not be salvaged and withdrew from the talks on July 25, 2001.[5] Bush administration officials argued that the proposed inspection regime would have been ineffective at catching violators, creating a false sense of security, while imposing undue burdens on the U.S. pharmaceutical industry and potentially compromising government biodefense secrets. Other participating countries countered that the draft Protocol, while flawed, offered a reasonable balance between conducting on-site inspections intrusive enough to increase confidence in compliance and safeguarding legitimate national security and business information.

Because of the U.S. withdrawal, the Ad Hoc Group negotiations were formally suspended on August 3, 2001, bringing six and a half years of work to an abrupt halt. Although other countries considered proceeding with the talks without the United States, along the lines of the 1997 Ottawa Treaty on landmines, they quickly rejected this option because of the key role of the United States and its biotechnology industry. Instead, it was agreed that the mandate of the Ad Hoc Group would be retained so that the negotiations might resume at some point in the future.

The next opportunity for progress came four months later during the Fifth Review Conference of the BWC, which convened in Geneva, Switzerland, from November 19 to December 7, 2001. On the first day of the conference, the U.S. delegation tried to allay widespread anger over its rejection of the BWC Protocol by proposing an "alternatives package" of voluntary national measures to

strengthen compliance with the Convention. These measures included national legislation to criminalize the possession and use of BW, to extradite individuals accused of this crime, and to impose tighter restrictions on access to dangerous pathogens.[6]

Only two of the proposals in the U.S. alternatives package dealt specifically with monitoring compliance with the BWC and with the 1925 Geneva Protocol, which bans the use of BW in war. One proposed measure would expand the existing consultation procedures in Article V of the BWC by creating a "voluntary cooperative mechanism" for clarifying and resolving compliance concerns by mutual consent, through exchanges of information, visits, and other procedures. The other measure would strengthen an existing UN procedure for international investigations of alleged use of BW by requiring states to accept visits by expert teams dispatched at the request of the UN Secretary-General. In principle, such a mechanism would make it possible to investigate suspicious outbreaks of infectious disease, such as the 1979 epidemic of human anthrax in the Soviet city of Sverdlovsk. Although Soviet officials engaged in a systematic cover-up at the time, the cause of the anthrax outbreak was later revealed to have been an accident at a clandestine BW production facility.[7]

Other countries at the Review Conference welcomed the U.S. alternative proposals but argued that they did not go far enough, and that some type of legally binding agreement among BWC States Parties was necessary. On the last day of the Review Conference, however, the U.S. delegation unexpectedly put forward a proposal terminating the mandate of the Ad Hoc Group, the sole forum for negotiating multilateral measures to strengthen the treaty. This U.S. "killer" amendment, which had not been discussed in advance with close European allies, was unacceptable to most delegations and made it impossible for the Review Conference to reach consensus on a Final Declaration. In a desperate move to prevent the collapse of the meeting, the chairman adjourned it for one year, so it will resume on November 11-22, 2002.[8] During this "time out," the participating states should attempt to hammer out their differences.

Where Do We Go from Here?

With the suspension of the Ad Hoc Group negotiation and the failure—at least for now—of the Fifth BWC Review Conference, many countries and NGOs are wondering how best to bolster the regime at a time when the ethical norm against biological warfare has been seriously challenged by the anthrax-tainted letter attacks in the United States. The Bush administration's "à la carte" approach to strengthening the BWC, which emphasizes the negotiation of voluntary national compliance measures, does not effectively address the problem of noncompliance, which the U.S. delegation used as the justification for its decision to reject the draft BWC Protocol.

The following sections examine three complementary approaches to reinforcing the biological disarmament regime: (1) measures within the framework of the BWC; (2) national measures to strengthen the regime; and (3) external measures to strengthen the regime. These approaches are mutually reinforcing and should be pursued in a coordinated manner.

MEASURES WITHIN THE FRAMEWORK OF THE BWC

Strengthen the Existing CBM Regime

Several politically binding CBMs have been in effect since the 1986 and 1991 Review Conferences, including annual exchanges of information of biodefense programs, relevant facilities, and unusual outbreaks of disease. Unfortunately, compliance with the reporting requirements has been poor. There are two reasons for this problem: (1) the fact that the CBMs are politically but not legally binding; and (2) the lack of a BWC Secretariat to remind and pressure States Parties to submit their annual data declarations. In the absence of a secretariat, national declarations are simply collated by UN staff and circulated to member states in the original languages. Because of these limitations, the two sets of CBMs have failed to achieve their stated goal of significantly enhancing openness and transparency with respect to BWC-related activities.

The European Union has proposed making some of the CBMs legally binding, which would increase the level of compliance significantly. In addition, creating a small professional Secretariat to assist countries with preparing their annual data declarations could greatly improve the effectiveness of the existing CBMs. Although the United States is unlikely to support or fund a BWC Secretariat, it might be financed through another mechanism, such as the United Nations Foundation, and staffed with officials from the UN Department of Disarmament Affairs.

Strengthen the UN Field Investigation Procedure

The idea of investigating the alleged use of BW under the auspices of the UN Secretary-General, as proposed by the United States at the Fifth Review Conference of the BWC, is not new. In a series of resolutions beginning in 1980, the UN General Assembly requested the Secretary-General to investigate alleged violations of the 1925 Geneva Protocol, the BWC, and other provisions of "customary international law." On November 30, 1987, the General Assembly went a step further by adopting Resolution 42/37, which grants the Secretary-General the authority to launch investigations of alleged use on his own authority.

To date, the UN has investigated four cases of the alleged use of chemical or biological weapons: (1) of fungal toxins ("yellow rain") by the Soviet Union and its allies against rebel groups in Southeast Asia and Afghanistan in 1980-83; (2) of chemical weapons (CW) by Iraq and Iran during the Iran-Iraq War in 1984-88; (3) of CW by RENAMO insurgents in Mozambique in 1992; and (4) of CW by Armenian forces in Azerbaijan in 1992. In some cases, cooperation was forthcoming (e.g., from both sides during the Iran-Iraq War) but in other cases it was not (e.g., during the "yellow rain" investigations in Laos, Cambodia, and Afghanistan). The investigations were successful only when they were carried out with the cooperation of the party on whose territory the alleged attack had occurred.

At the Fifth BWC Review Conference, the United States proposed requiring member states to accept UN investigations of alleged use on their territory without the right of refusal, but countries are unlikely to do so in the absence of a formal treaty that imposes legally binding rights and obligations. Moreover, the U.S. proposal only authorizes investigations of alleged use of BW and fails to address the need to prevent their acquisition in the first place. Thus, instead of relying on the existing ad hoc mechanism, BWC member states should negotiate a formal treaty that requires the participating states to accept UN field investigations on their territory and extends the authority of the Secretary-General to investigate suspect BW development and production facilities as well as use.

NATIONAL MEASURES TO STRENGTHEN THE REGIME

Criminalize BW Possession and Use

Although the United States has proposed that countries voluntarily pass national legislation criminalizing the possession and use of BW, countries that seek such weapons or that sponsor terrorism are unlikely to comply. Only a legally binding, multilateral regime would be effective in addressing noncompliance by imposing economic and other sanctions on violators and non-parties. To this end, BWC member countries should negotiate an international treaty branding the possession and use of BW as "crimes against humanity" under international law, so that even outlaw states such as Iraq would be bound by it. At the same time, participating states would agree to extradite individuals implicated in the acquisition and use of BW. The Harvard Sussex Program on Chemical and Biological Weapons (CBW) Armament and Arms Limitation has developed a draft international treaty to this effect.[9]

Restrict Access to Dangerous Pathogens

Would-be bioterrorists who are skilled in microbiology might be able to culture deadly germs from natural sources, but it would be far easier to obtain them from microbial culture collections in academic or industrial laboratories or commercial biological supply houses. Few of these culture collections are adequately secured and regulated. In the United States, facilities that possess cultures of anthrax bacteria are believed to number in the hundreds, including universities, private institutes, hospitals, veterinary clinics, and public health agencies. The precise number is unknown, however, because the federal government does not maintain a central registry of dangerous pathogens owned by academic and private institutions. Unfortunately, simply banning laboratory stocks of dangerous pathogens is not an option. Access to anthrax bacterial cultures, for example, is vital for scientists studying the disease, which causes serious outbreaks in livestock in many parts of the world.

Some controls on dangerous germs are already in place, but they are far from universal in their coverage. The United States and 32 other like-minded governments control national exports of certain pathogens to countries suspected of pursuing BW through an informal coordinating mechanism known as the Australia Group (AG).[10] Nevertheless, states pursuing biological arms have employed

numerous strategies to circumvent these controls, such as transshipment points and shell companies. Some countries that do not belong to the AG also engage in unregulated trade in dangerous pathogens. New measures are clearly needed to control "germ commerce," both within countries and among them.

In 1996, the U.S. Congress passed legislation tightening controls on shipments of dangerous pathogens and toxins within the United States.[11] This move followed revelations that a leading biological-supply house near Washington, D.C. had sold cultures of bubonic plague bacteria to an Ohio lab technician with links to the Aryan Nations, a violent white-supremacist organization. Under U.S. regulations that came into force in 1997, anyone intending to ship or receive agents on a list of 36 microbial pathogens and toxins must register with the federal Centers for Disease Control and Prevention and demonstrate a legitimate medical or scientific use for the material. Violations are punishable by prison terms and fines of up to $500,000.[12] In the aftermath of the September 11 attacks, Congress has moved to close loopholes in the existing law by extending the rules to cover possession as well as transfer of listed pathogens.

Even so, tighter U.S. regulations, while desirable, will not significantly reduce the global threat unless such controls are implemented internationally. Hundreds of labs and companies overseas work with dangerous pathogens, yet restrictions on access vary from country to country. According to the World Federation for Culture Collections (WFCC), a loose association of 472 repositories of living microbial specimens in sixty-one countries, 46 germ banks—in countries as diverse as Germany, India, and Iran—have stocks of anthrax bacteria. Although the federation recently urged its members to establish tighter rules for who is granted access to dangerous microbes, it does not have the authority to force compliance. Moreover, less than a third of the more than 1,500 microbial culture collections worldwide belong to the WFCC.[13]

To "harmonize" the uneven patchwork of national regulations, the United States should advocate the immediate negotiation by the UN General Assembly of an international agreement imposing common limits on access to dangerous pathogens and uniform standards of biosafety and physical security. Possession of deadly biological agents by unauthorized individuals should also be made a crime under international law. Negotiating such an agreement would not be as ambitious as it sounds. All governments have a common interest in preventing deadly microbes from being used against civilian populations, and regulating the germ trade would put significant obstacles in the path of would-be bioterrorists.

EXTERNAL MEASURES TO STRENGTHEN THE REGIME

Expand the Cooperative Threat Reduction Program

Until at least 1992, the former Soviet Union and then Russia had the world's largest and most sophisticated biological warfare program. It included four military microbiological institutes run by the Ministry of Defense and a vast complex of ostensibly civilian pharmaceutical facilities, known as Biopreparat, that was secretly engaged in offensive BW development and production. After the breakup of the Soviet Union in 1991, the culture collections, former production facilities, and specialized know-how associated with former Soviet biowarfare facilities in Russia, Kazakhstan, and Uzbekistan began to pose serious proliferation threats. The U.S. government has addressed this problem to some extent under the Department of Defense's Cooperative Threat Reduction program, the Department of Energy's Industrial Partnership Program, and the International Science and Technology Center in Moscow. Nevertheless, far more must be done to convert former biowarfare facilities into commercially viable enterprises and to keep former weapons scientists gainfully employed in peaceful research activities, so that they are not susceptible to recruitment by proliferators and terrorists. The United States, Japan, and the European Union should make a substantial financial commitment to dismantle the residual BW production capacity in the former Soviet Union, to employ former bioweapons scientists, and to enhance the physical security, control, and accounting of collections of dangerous pathogens.

Enhance Global Epidemiological Surveillance

BWC member states should fund the creation, under World Health Organization (WHO) auspices, of an improved international system for rapidly detecting and responding to unusual outbreaks of disease. Such a global system would not only help to contain natural epidemics but could have a deterrent effect on the covert use of BW. The greater likelihood that covert biological attacks would be detected could reduce the military utility of bio-

logical weapons and deter their use by increasing the risk of attribution and retaliation.

Because the WHO must be insulated from political pressures to perform its primary public health mission, the global epidemiological surveillance system should not be explicitly linked to the BWC compliance regime, although such a system would indirectly support the goals of the Convention. As a first step, the United States and like-minded countries should sponsor an effort to develop a comprehensive inventory of all disease-surveillance systems around the globe. WHO member countries should then develop a plan of action for funding and organizing an efficient global network, linked by satellite communications, of disease-monitoring stations, reference laboratories, and response teams.

Encourage Industry Self-Regulation

The international biotechnology industry should create a global association similar to the World Association of Nuclear Operators (WANO).[14] WANO was established in May 1989 by the international nuclear power industry in response to the accident at the Chernobyl nuclear power plant in 1986. This disaster forced nuclear operators to reassess the issue of safety and made them aware of the need for international cooperation to prevent future accidents.

WANO facilitates the exchange of operating experience among nuclear power plant operators, so that its members can work together to achieve the highest possible standards of safety and reliability. By creating a similar global organization, the pharmaceutical and biotech industries could work together to establish guidelines and best practices, reducing the risk that dual-use technology and production equipment will be misused for purposes of biological warfare and terrorism.

Foster an Ethic of Scientific Responsibility

Because scientists would play a key role in any offensive biological warfare program, it is incumbent on the scientific community to complement diplomatic initiatives to strengthen the BWC by taking concrete steps to reinforce the ethical norm enshrined in the treaty.[15] As a first step, specialists in the biological, biomedical, veterinary, and plant sciences should become more aware of the potential for misuse of advances in genomics and genetic engineering techniques. They should also be encouraged to develop a culture of professional responsibility with respect to potentially hazardous areas of research.

In the past, the U.S. scientific and medical communities have addressed ethical issues related to research involving human subjects by establishing the Nuremberg guidelines and Institutional Review Boards. Yet scientists have been largely silent about the threats of biological warfare and terrorism. There are two likely reasons for this lack of action. First, scientists are generally reluctant to contemplate the misuse of their research for nefarious purposes. Second, scientists are rarely rewarded by their peers—and, indeed, may be punished—for speaking out on sensitive public policy issues. It is critical, however, that scientists become more actively involved in reinforcing the ethical and legal norm against biological warfare.

As a standard element of the graduate curriculum in the biological and biomedical sciences, as well as in medical and veterinary schools, students should be educated about the risks of certain lines of scientific inquiry as well as the norms of scientific responsibility and personal integrity with respect to biological research. Courses or training modules should provide a basic familiarity with the threat of biological warfare and the provisions of the BWC. In addition, all students who complete an advanced degree in biology or biomedicine should be required to sign a pledge of scientific responsibility, similar to the Hippocratic Oath, stressing the importance of ethical guidelines in the conduct of research. This step would be particularly important with respect to the large number of foreign students—including some from countries of proliferation concern—who study at U.S. universities.[16]

Provide Oversight of Hazardous Research

In recent years, dramatic advances in the fields of molecular biology and biotechnology have yielded numerous benefits for humanity, including improved health and nutrition. Yet these scientific breakthroughs also have a dark side: the potential to create more deadly instruments of biological warfare and terrorism.[17] Accordingly, specialists in the biological, biomedical, veterinary, and plant sciences should take the difficult but important step of monitoring and even limiting research that could have direct applications in offensive biological warfare. Harnessing the powerful knowledge arising from the biological sciences in a manner that benefits humankind, while

preventing its misuse, will require the scientific community to regulate itself.

In January 2001, an inadvertent discovery highlighted the potential risks associated with the new genetic technologies. Australian scientists developing a contraceptive vaccine for controlling field mouse populations sought to enhance its effectiveness by inserting the gene for the immune regulatory protein interleukin-4 (IL-4) into the mousepox virus, which was being used as a delivery system for the vaccine. Although IL-4 is a substance that is normally produced in mice, insertion of the IL-4 gene into the mousepox virus unexpectedly transformed it into a virulent strain that shut down the mouse immune system and killed all the animals in the experiment. In addition to rendering mousepox lethal in mice that were genetically resistant to the disease, the inserted gene made the mousepox vaccine ineffective; the recombinant virus killed even those mice that had previously been vaccinated.[18] The Australian team debated for months over the wisdom of publishing their disturbing results but finally decided to do so as a means of warning the scientific community.

The mousepox experiment demonstrated that the novel gene combinations produced by genetic engineering can, on rare occasions, accidentally yield a more virulent pathogen—a possibility first raised in the 1970s by scientists concerned about the safety of gene-transfer experiments.[19] The Australian finding also highlighted the potential of genetic engineering to create new and more lethal instruments of biological warfare. Indeed, since human beings possess the interleukin-4 gene, it is possible that inserting this gene into a poxvirus that infects humans, such as smallpox or monkeypox, could create a highly lethal strain that would be resistant to the existing smallpox vaccine.

Inadvertent discoveries of this type, as well as deliberate efforts to employ the new genetic technologies for nefarious purposes, may become increasingly common as biological research continues to generate a flood of new information about the structure and function of microorganisms at the molecular level and the host response to infection. According to a recent commentary in the scientific journal *Nature Genetics* by Claire M. Fraser, director of The Institute for Genomic Research, and Malcolm R. Dando, a policy analyst at the University of Bradford in England, "The ever-expanding microbial genome databases now provide a parts list of all potential genes involved in pathogenicity and virulence, adhesion and colonization of host cells, immune-response evasion and antibiotic resistance, from which to pick and choose the most lethal combinations."[20]

Revelations about the Soviet/Russian biological warfare program indicate that the potential exists for the deliberate creation of "designer pathogens." Until at least 1992, military scientists working at the Biopreparat institutes employed genetic engineering techniques to develop more lethal strains of anthrax bacteria, smallpox virus, and other biological warfare agents. According to Ken Alibek, a senior Biopreparat official who defected to the United States in 1992, the Soviet germ warfare program included efforts to develop "advanced" biological agents by engineering bacterial pathogens to be resistant to multiple antibiotics and vaccines. Soviet scientists also created hybrid ("chimeric") viruses through the transfer of genes for protein toxins and virulence factors, and developed incapacitating and behavior-modifying agents through the manipulation of natural brain chemicals.[21]

Unclassified reports on some of this research were later published in the Russian scientific literature. In 1997, for example, scientists working at the State Research Center for Microbiology at Obolensk, near Moscow, reported that they had developed a strain of anthrax bacteria containing an inserted gene for a foreign toxin, rendering the agent resistant to the existing Russian anthrax vaccine.[22] In addition, scientists at the State Research Center for Virology and Biotechnology "Vector" in Koltsovo, near Novosibirsk, did a number of experiments on vaccinia, a virus closely related to the causative agent of smallpox that serves as a vaccine against the disease. One research group at Vector identified a site in the vaccinia DNA where they could insert foreign genes without disrupting the ability of the virus to infect and replicate.[23] A second group at Vector spliced into vaccinia a gene from the Ebola virus coding for a viral protein called "vp24." When the recombinant virus was injected into guinea pigs, the Ebola gene was successfully expressed as a protein and induced the formation of specific antibodies.[24] According to Alibek, the ultimate goal of the Vector research was to create a hybrid of the smallpox and Ebola viruses that would combine the contagiousness of the former with the lethality of the latter. It appears, however, that gene-transfer experiments with the smallpox virus itself were never carried out.

Scientific Community Oversight

The scientific community must address the problem of hazardous research, ideally through self-governance. Although many scientists view any restrictions on scientific inquiry as anathema, the alternative could be far worse. If a novel pathogen were created in the laboratory, the resulting public outrage could compel the U.S. Congress to impose draconian restrictions on scientific inquiry. In the interest of avoiding this outcome, scientists should act proactively to ensure that their research does not assist would-be bioterrorists.

A precedent for self-regulation by the scientific community already exists. In February 1975, some 140 biologists, lawyers, physicians, and journalists met at the Asilomar Conference Center near Monterey, California, to discuss the potential risks associated with recombinant DNA technology, which had only recently been developed. This conference resulted in a set of research guidelines administered by the National Institutes of Health and overseen by a Recombinant DNA Advisory Committee (RAC). The Asilomar analogy goes only so far, however. Whereas the 1975 conference focused on the possible *unintended* consequences of recombinant DNA research, the current concern is over the potential *malicious* use of this technology for harming or killing people and for attacking crops or livestock to cause economic damage.

In order to prevent the deliberate misuse of scientific knowledge for nefarious purposes, a system for "prudential review" of potentially hazardous research should be established. Because science is an inherently international activity, a regime focusing on the U.S. scientific community alone would not be effective; hence the oversight mechanism should be international in scope. Legitimate but high-risk projects would be reviewed by a scientific oversight board, which would be similar to the RAC but would operate at the international level. Research projects with direct offensive military applications would be forbidden outright, while others would be subject to close monitoring.

Regulated activities would constitute a small subset of scientific research in the fields of microbiology, infectious disease, veterinary medicine, and plant pathology. Areas of particular concern include the cloning and transfer of toxin genes and virulence factors, and the development of antibiotic- and vaccine-resistant strains of microorganisms and genetically engineered toxins. For example, the same technology used to create fusion toxins for the purpose of killing cancer cells could be redirected to produce novel toxins that target normal cells of almost any tissue.[25] Another area of potential concern involves the engineering of viruses to evade or manipulate human immune defenses. Gene therapists have sought to introduce curative genes into patients with inherited diseases by developing as molecular carriers "stealth" viruses that are not detected by the immune system. Yet such techniques could also be misused to convert pathogenic viruses into even more deadly warfare agents.[26]

The proposed review and oversight system should be capable of identifying hazardous lines of research, without being so intrusive as to have a chilling effect on legitimate scientific inquiry or to inspire attempts at circumvention. Because no universal set of criteria is possible, the judgments of the oversight board would have to be scientifically informed and made in the context of specific research proposals. Hazardous research that is justified for protecting public health or defending against biological warfare would be restricted to a few high-containment laboratories, as is already the case with research on the smallpox virus. All such work would be transparent and the results reported to the international oversight board on a regular basis. Inadvertent discoveries with dangerous implications, such as the Australian mousepox experiment, would also be reported to the oversight board, and advice would be sought on whether or not to publish the findings.

Because genetic engineering has become a burgeoning commercial business, many senior academic researchers have extensive ties to the private sector. Thus, to avoid gaping loopholes in the oversight mechanism, proprietary industrial information must not be exempt from coverage. To give but one example, a biotechnology company recently created a novel strain of *E. coli* bacteria containing an inserted gene for botulinum toxin and engineered for maximally efficient expression.[27] The goal of this effort was to boost commercial yields of botulinum toxin (trade name "Botox"), which has been a licensed drug in the United States for more than a decade and is used to treat neuromuscular disorders and to smoothe wrinkles for cosmetic purposes. Nevertheless, a genetically modified strain of *E. coli* capable of mass-producing a deadly toxin poses a potential biowarfare threat, particularly in view of the fact that *E. coli* is a common cause of food poisoning and is easily disseminated.

Challenges Ahead

The process of developing an international mechanism to regulate hazardous "dual-use" research will be complex and difficult, requiring the active participation of a variety of stakeholders, including scientists, lawyers, and politicians from several countries.[28] It will be challenging to achieve consensus within the scientific community on a regulatory mechanism, and government policymakers will also be reluctant to grant an international body detailed, binding review authority over biodefense activities. Thus, simply agreeing to notify the oversight board that such activities are being conducted, and describing them in general terms, may be all that can reasonably be accomplished.[29] Because several years of negotiations will be required to hammer out a practical oversight system, preparatory work should begin as soon as possible.

In crafting an international regime for regulating scientific research of potential relevance to biological warfare, a number of difficult issues will need to be addressed. First, how will dangerous "designer pathogens" be identified in advance? What types of inserted genes or gene fragments would make a garden-variety microorganism declarable?

Second, how can one give the international oversight board the authority and power it requires to enforce the rules, while preventing it from becoming corrupt and autocratic? Because of the potential for abuse, the oversight board must be structured with checks and balances so that it does not unduly constrain scientific freedom or exploit its privileged access to sensitive and proprietary information. Obviously, the members and staff of the oversight body must meet the highest standards of professional ethics. Yet how can one ensure the reliability and integrity of the board members? Would they be subjected to a periodic vetting or clearance procedure?

Third, how can one alert the scientific community to potential biological warfare threats from research activities without creating self-fulfilling prophecies? Scientists from states with biowarfare programs should not be allowed to serve on the international oversight board, because of the possibility that they could be directly involved in clandestine weapons development. Yet making such distinctions would be politically difficult for national governments and would require the scientific community to adopt a "counterintelligence" mentality alien to its prevailing culture of openness.

Fourth, scientific journals should develop "opacity" policies for declining to publish articles that contain scientific information of direct value to potential bioterrorists or for removing certain technical details that could be misused for nefarious purposes.[30] Such decisions will require careful deliberation to avoid hampering legitimate scientific investigation. Given that the ethos of the scientific community is opposed to censorship of any kind, a strong professional consensus must support a decision not to publish research data because its dissemination could be harmful to society.

In sum, the international scientific community, working collaboratively through professional societies and national academies of science, should negotiate a set of rules and procedures for the oversight of potentially dangerous research. In developing such an oversight mechanism, public perceptions will play a key role. Even if the scientific community ultimately decides that controls on research are impractical, ill-advised, or do not meet risk-benefit criteria, it will be necessary to explain and justify these arguments to a skeptical public in an open and understandable manner.

Conclusions

The use of anthrax-tainted letters sent through the mail to kill and terrorize U.S. citizens has seriously eroded the norm against biological warfare and terrorism, making it imperative to strengthen the existing disarmament and nonproliferation regime. As described above, a number of complementary measures to strengthen the BWC should be taken at the international and national levels, with the involvement of governments, the biotechnology industry, the scientific community, and NGOs.

If nothing is done to strengthen the BWC and the international regime continues to unravel, the consequences could be grim. Widespread proliferation of the specialized know-how needed to develop and deliver designer pathogens would make mass destruction capabilities accessible to small groups of terrorists and even to mentally deranged individuals. To prevent this nightmare from becoming a reality, the international community should take concrete steps to reinforce the ethical and legal norm against biological warfare and to regulate hazardous research.

[1] Ken Alibek, for example, has asserted that the Soviet Union employed tularemia bacteria as a weapon against German troops during the Battle of Stalingrad in 1942. See Ken Alibek with Stephen Handelman, *Biohazard* (New York: Random House, 1999), pp. 29-31.

[2] Brad Roberts, "Implementing the Biological Weapons Convention: Looking Beyond the Verification Issue," in Oliver Thraenert, ed., *The Verification of the Biological Weapons Convention: Problems and Perspectives* (Bonn: Friedrich Ebert Stiftung, 1992), p. 104.

[3] Alexander Kelle, "Developing Control Regimes for Chemical and Biological Weapons," *International Spectator* 32 (July-December 1997), p. 141.

[4] Ad Hoc Group of Governmental Experts to Identify and Examine Potential Verification Measures from a Scientific and Technical Standpoint, *Summary Report*, Doc. BWC/CONF.III/VEREX/9, Geneva, September 24, 1993.

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