

Fighting Proliferation: New Tools for New Challenges

New nonproliferation tools are beginning to emerge independent of international treaties and national regulations. These new tools are conceived, crafted, and implemented solely by the private sector, a distinct change from achieving national security through such traditional means such military and intelligence capabilities, diplomacy, economic strength, and threat reduction treaties crafted by nation-states. In contrast to the tangled web of national review boards, professional societies, government bureaucracies, and years of review and negotiation often involved in creating regulations and treaties, self-governance tools of the kind beginning to come from the private sector can be launched with comparative alacrity.

The concept of self-governance within the private sector and the scientific community, of course, is not new. With varying degrees of success, in advance of regulatory requirements industries and professional associations have acted to address societal concerns about a certain product or to police the conduct of practitioners of select disciplines.ⁱ The life sciences communities are currently coming to grips with how they would respond to a major challenge associated with the deliberate misuse of life sciences know-how, technology, materials, or equipment. In the nonproliferation arena, the pioneering examples of self-governance tools are aimed at preventing the abuse of dual-use life sciences capabilities. This article first provides an overview of developments in the life sciences that have intensified the need for new risk management mechanisms and then describes two self-governance tools designed to fill gaps in the biological weapons nonproliferation regime. The article concludes with observations about the status of these new self-governance tools and the possible implications of these latest additions to the nonproliferation toolkit.

The Double-Edged Sword of Life Sciences Revolution

The life sciences have myriad beneficial applications in medicine, environmental remediation, renewable energy, agriculture, and other areas. For example, four of the nine fundamental technological breakthroughs likely to occur by 2025 that the National Intelligence Council contends could have a transformative impact across the globe will lean heavily on biotechnology: clean water technology, biogerontechnology (health aids for seniors), biofuels, and human cognitive enhancement technologies.ⁱⁱ As the term dual-use implies, however, today's cutting-edge life sciences techniques, knowledge, materials, and equipment can be deliberately or inadvertently misapplied, and a series of controversial experiments sparked discussion about the need for stepped-up oversight of life sciences research. In a prominent case in point, Australian researchers inserted the IL-4 immunosuppressant gene and the egg protein gene into the mousepox genome, anticipating that the modified virus would subsequently sterilize mice. Instead, the modified virus was 80 percent lethal to mice. Many considered publication of this research a potential roadmap to increasing the lethality of smallpox.ⁱⁱⁱ Then, in 2002, scientists artificially created the polio virus, a killing, crippling scourge.^{iv}

The self-governance discussion among scientists that these developments prompted initially centered on the possible censorship of research that proliferators might usurp for nefarious purposes.^v On January 10, 2003, editors from thirty-two leading life sciences journals crafted a joint policy endorsing a security and safety review of potentially sensitive articles prior to publication, with revisions requested for papers deemed to have security implications. Journals might also decline to publish an article if reviewers judge that the potential harm from publication outweighs the societal benefits of the research.^{vi} Not all life sciences journals have followed suit. A survey of 28 international life sciences journals, including three Chinese and five Russian language publications, found that most had not established policies and procedures to screen submitted manuscripts for information that might raise security concerns.^{vii} Moreover, since the 2003 editors' meeting, referees for journals that have security screening procedures have seldom found reason to impose security restrictions on submitted manuscripts.^{viii}

Another uproar occurred in 2005 when one group of researchers sequenced the 1918 influenza virus, which may have killed as many as 50 million people, while a second research team recreated the virus and confirmed its high virulence in mice. Indicative of the speed of synthetic biology advances, the polio virus was synthesized in two years, but scientists recreated the more complicated eight-genome 1918 Spanish influenza virus in a few weeks.^{ix} The researchers who brought the 1918 influenza back to life sought permission from the then-Director of the Centers for Disease Control and Prevention, Dr. Julie Gerberding, and the head of the National Institute of Allergy and Infectious Diseases, Dr. Anthony Fauci. Also, meeting in emergency session about publication of the papers, the National Science Advisory Board recommended just prior to their publication that the authors add statements that the research was conducted safely and had important public health implications.^x

The apprehensions voiced about life sciences run amok were reminiscent of the mid-1970s fears about genetic engineering, namely that recombinant DNA technology would harm laboratory workers, the public, and the environment. At that time, genetic engineers voluntarily agreed to suspend recombinant DNA experiments until governing mechanisms could be instituted. In 1975, scientists met in Asilomar, California, recommending institutional peer review processes for genetic engineering research and biosafety, which became the foundation for the U.S. guidelines to help ensure that research is performed responsibly and safely.^{xi} The centerpiece for oversight of recombinant DNA research is the Institutional Biosafety Committee (IBC), which consists of scientists who review pertinent research proposals. If needed, these committees are to require scientists to alter their proposed research design and strengthen biosafety measures to handle anticipated risks. They can also deny permission altogether for an experiment if the risks are deemed excessive. Institutional committees are to report any problems with approved research to the National Institutes of Health.^{xii}

A few countries (e.g., Germany, United Kingdom) have stipulated mandatory oversight panels for all facilities conducting recombinant DNA research. However, in the United States and many other nations, peer governance of scientific research is not

exercised comprehensively or evenly, and as is the case with any review process, these institutional oversight processes are only as assiduous as the scientists who sit on the committees. Some laboratories in the United States and other countries that conduct genetic engineering research have not even established institutional review panels. For U.S. laboratories that do not receive federal funding, observance of the guidelines for oversight of genetic engineering and biosafety research is voluntary. In contrast, all German facilities involved in recombinant DNA research, whether government, commercial, or academic institutions, must comply with German oversight regulations, which carry criminal penalties for violations.^{xiii} ✕

Evidence also indicates that, where they have been established, review committees do not always function effectively. Lackadaisical oversight can occur because often these panels are an unfunded mandate; some scientists are innately skeptical that a dual-use problem exists; reviewing scientists do not have knowledge of biological weapons or a feel for the wayward potential of proposed experiments; and, because “scientists hesitate to place any restrictions on each other’s work and regard oversight mechanisms largely as a bureaucratic burden.”^{xiv}

As the mousepox, polio, and 1918 influenza research controversies unfolded, national panels of esteemed scientists recommended heightened governance for life sciences research, again placing the onus on peer review of proposed experiments to assess dual-use risks. The U.S. National Research Council recommended peer review of proposals if the research would: 1) show how to defeat human or animal vaccines; 2) make a pathogen resistant to antibiotics or antivirals; 3) raise the virulence of a pathogen or make a nonpathogenic organism virulent; 4) compound the transmissibility of a pathogen; 5) change the natural host range of a pathogen; 6) make it more difficult to detect or diagnose a pathogen; and, 7) aid the weaponization of a pathogen. In 2007, the U.S. National Science Advisory Board on Biosecurity (NSABB) echoed this proposal and also recommended education for life scientists performing dual-use research and a code of conduct for life sciences.^{xv} One approach emerging from the private sector suggested a tiered system of institutional, national, and international oversight.^{xvi} In the area of synthetic biology, which involves the creation of new biological parts, devices, or systems or the redesign of existing biological systems, a group of experts pored over the chain of associated activities, evaluating their potential to serve as chokepoints to prevent misuse.^{xvii} Most efforts to reduce the ability to commandeer life science advances for malevolent purposes have to date concentrated on codes of ethics for and education of life scientists.^{xviii}

Corporate Screening for Suspect Orders of Genes and Oligonucleotides

One of the more remarkable life sciences advances is the ability to synthesize microorganisms *de novo*. Knowledge and technique aside, a key facet that puts this capability at the fingertips of trained scientists and even biohackers worldwide is the ability to order genes and short DNA fragments called oligonucleotides from commercial suppliers. Companies have been selling genes and oligonucleotides since 1999. Between 40 and 50 companies are presently engaged in this business. Each day, this industry receives thousands of orders for genes and millions for oligonucleotides. Consequently,

these companies face a challenge in flagging suspect sequence orders and evaluating which requests pose genuine dangers.^{xix}

By the mid-2000s, some, but not all, gene synthesis companies began erecting precautionary policies and procedures to prevent rogues from assembling dangerous pathogens. To illustrate, some companies screened gene orders against a regulated database such as GenBank® and also against a computerized database containing the sequences for pathogens of concern, namely those that nations previously weaponized or that were otherwise regarded as being at high-risk of misuse (e.g., Marburg, smallpox). When this initial automated screening identified suspect orders, company staffers with the appropriate credentials searched the scientific literature for additional technical data to determine whether the requested order posed a security risk. In addition, some companies guarded against sales to inappropriate customers by screening names of individuals and corporations against computerized watch lists and then confirming basic information about customers (e.g., professional affiliation, nationality) and/or the intended use of the requested genes or oligonucleotides. Order and customer screening varied across companies, with some observing more rigorous practices than others.^{xx}

In April 2008, the International Association of Synthetic Biology (IASB), which represents several of the smaller European gene synthesis companies, began a project focused on a code of conduct to serve as the umbrella to coordinate the industry's approach to order and customer screening. At a meeting held in Munich, the IASB, together with the International Consortium of Polynucleotide Synthesis, its U.S. counterpart which has subsequently dissolved, articulated the first steps to establish a global biosecurity standard for the industry, agreeing to share information about customer and gene screening practices so that industry-wide best practices could be developed. The work plan called for companies to work on best practices to screen oligonucleotide orders after institutionalizing a gene screening standard.^{xxi} In 2008, the IASB issued several statements about the responsible sales practices it was shaping and invited gene synthesis companies in Asia and elsewhere to join its effort to harmonize gene and customer screening practices.^{xxii}

In another important step toward a collective screening standard, the IASB shepherded the development of a bioinformatics database to preserve the virulence factors gleaned from literature searches about suspect orders. Significantly, this database will allow gene synthesis companies to screen orders effectively and cost-efficiently above and beyond the standard computerized lists of high-risk pathogens because companies do not have to repeat labor-intensive literature searches about questionable orders. This database should be available to participating gene synthesis companies in early 2010. On November 3, 2009, several smaller gene synthesis companies, including by ATG Biosynthetics, Entelechon, Febit Synbio, PolyQuant, and Sloning Biotechnology sealed a formal code of conduct. Genray Biotech, based in Shanghai, also endorsed it.^{xxiii}

An interesting twist in the industry's journey toward a global standard occurred in mid-November 2009, when the five top gene synthesis companies, representing an estimated 80 percent of the industry's capacity, created a new industry consortium to

oversee and promote adherence to a harmonized screening protocol. The International Gene Synthesis Consortium's (IGSC) protocol sets standards in five core areas: the aforementioned customer and gene sequence screening; retention of records; refusal of suspect orders; reporting to the appropriate government authorities; and compliance with regulations. The five founding companies are DNA 2.0, GeneArt, GenScript, Blue Heron® Biotechnology, and Integrated DNA Technologies.^{xxiv}

This development revealed a schism between the larger and smaller gene synthesis companies as to the best approach to biosecurity.^{xxv} Putting the two standards side by side, the IASB's is more rigorous on gene sequence screening, the IGSC's is tougher on customer screening. The gene sequence screening practice in the IGSC's code aims only to stop shipments of items consistent with government lists for high-risk pathogens, but companies embracing the IASB's code aspire to ensure that whatever goes out the door is not dangerous, regardless of whether it is already on a government risk list. Arguably, the IASB's code sets a higher standard for gene sequence screening, but because gene sequence companies will have access to the bioinformatics database to facilitate this more rigorous screening, it need not impose exorbitant expense on the companies. As written, the IASB requires a "commercially reasonable" confirmation of a customer's identity, including validating that the customer's receiving address is consistent with a legitimate business or institution. The IGSC, in contrast, mandates screening customers against government compiled watch lists for terrorists, those abetting proliferation, denied and debarred individuals, and other untrustworthy people and organizations. Moreover, IGSC companies require customers ordering listed high-risk pathogens or DNA fragments to provide an end-use statement, after which the companies are obligated to confirm through independent means the customer's identity and whether the end-use statement is consistent with the customer's prior research. Companies adhering to the IASB and IGSC standards must report suspicious cases to the proper government authorities and store data related to gene sequence and customer screening for eight years, although they stipulate that different types of data be retained. Both the IASB and the Consortium established mechanisms to improve and update screening practices.^{xxvi} Ideally, at some point, the two standards will be merged with both large and small companies adopting the toughest possible gene and customer screening practices.

The U.S. government's introduction of voluntary screening guidelines for U.S. gene synthesis companies, however, may cloud prospects for a merger of the industry standards. Published on November 27, 2009, the draft government standard, a watered down approach, does not stipulate investigation of the potential dangers of orders for pathogens or DNA fragments unless they are on government high-risk lists.^{xxvii} Following a period for public comment on the draft guidelines, which ends in February 2010, the government presumably will revise and reissue the guidelines.

An Independent Web Portal to Review Experiments of Concern

A great many life science experiments are conducted every year; only a small percentage warrant security concern. Scientists, however, may lack the impartiality or biological weapons knowledge to scrutinize their own research proposals, and many research institutions not have a peer review process or have panels that, for whatever

reason, do not function as intended. A second, recently created new tool that deserves some attention, therefore, is an independent, impartial, expert peer review process, operating via a dedicated Internet portal. This free-standing peer review capacity is accessible to life scientists anywhere in the world. Any bench scientist, group of research collaborators, or even existing institutional biosafety committees can submit a proposal for a security sanity check at: gsppi.berkeley.edu/EoC/uc-berkeley-synthetic-biology-security-program/experiments-of-concern. A quartet of universities collaborated on the design and construction of the web portal, which the Goldman School of Public Policy at the University of California, Berkeley hosts.^{xxviii}

The review process is patterned on the type of scrutiny that an Institutional Biosafety Committee should provide. A panel of three experts, drawn from a rotating stable of multi-disciplinary volunteers who work at national laboratories, in academia, and at research institutions, will assess whether submitted research proposals would enhance the ability of states or terrorists to acquire bioweapons. A detailed response should be received within two weeks, with an explanation provided if the review requires more time. Those submitting inquiries can expect three basic replies: 1) proceed with the experiment as planned; 2) perform the experiment after making specific security and/or safety modifications; or, 3) do not conduct the experiment because it entails significant security and/or safety concerns. An explanation will accompany each review panel decision. To promote awareness and training for scientists and institutional oversight committees, a generic synopsis of the panel's decision will be posted online within a year. The synopsis, however, will redact information to protect intellectual property specific to proposed experiments and the identity of those requesting reviews. The library of review cases is intended to elevate the understanding of how an impartial, informed review process should function. Visitors to the website can also comment on posted cases.^{xxix}

Though it opened in late April 2009, the portal has received no proposals. Relatively few life sciences experiments with serious security implications are conducted annually, so Steve Maurer, director of the Information Technology and Homeland Security Project at the Goldman School, University of California at Berkeley, did not expect an immediate flood of proposals to the web portal. With a grant from the Carnegie Corporation of New York, Maurer facilitated the construction of the web portal and the drafting of a code of conduct via the IASB. Maurer presumes scientists will turn to the portal when they feel a need to do so, and he anticipates that gene synthesis companies will refer scientists who lack an institutional review of their proposal to the portal because responsible companies will insist on peer reviewed proposals as a prerequisite for approval of high-risk orders. In addition, Maurer observed that awareness of the need to utilize the portal would spike should controversial research conducted without a peer review again be published. Regardless, over time proposals will trickle into the portal, which was never intended as a high traffic zone. Rather, Maurer states, the portal was meant to give all life scientists easy access to independent, expert counsel.^{xxx}

Implications of Novel Biological Weapons Nonproliferation Tools

In the field on nonproliferation, the web portal and the screening code for the gene synthesis industry are ground-breaking endeavors. For the past few years, governments and the life sciences community have, to a certain extent, been vacillating, unable to identify or move forward with concrete and comprehensive measures to prevent intentional or inadvertent abuse of the life sciences. Meanwhile, breathtaking life sciences discoveries are occurring at a staccato pace and life sciences technology and know-how are reaching the farthest corners of the earth. In an age when far too many selfishly side-step any duty to the greater good, a small band of corporate and other nongovernmental actors have devised a pair of mechanisms that will make meaningful nonproliferation contributions. For that, these companies and scientists deserve the thanks of their governments and the public for erecting stopgaps to temper potentially wayward life sciences activities.

Constructive though these private sector mechanisms may be, however, governments can ill afford to abdicate biorisk management responsibilities to the private sector. Additional gaps in biorisk management remain. Existing national regulations need to be overhauled to keep pace with scientific developments for a formulation that is fair but strict,^{xxxii} including the proposed draft U.S. guidelines for gene screening. Moreover, new international biorisk management tools are sorely in need because now, more than ever, these are transnational issues. In two regards, governments and nonproliferation specialists alike might take inspiration from the enterprising approaches of the private sector. First, “outside of the box thinking” is not just an empty phrase; it is possible to add new implements to what has become a rather stale nonproliferation toolkit. Though many nonproliferation specialists gravitate automatically to the idea of international treaties, they should open their minds to the utility of letting market forces work for instead of against efforts to reduce security threats. In today’s global marketplace, most companies worldwide will heed standards driven by market forces, including standards with security objectives.^{xxxiii} Second, some traditional assumptions about the corporate sector’s role in managing security risks need to be reconsidered, specifically the stereotype that companies are recalcitrant partners in nonproliferation endeavors. Inviting the private sector into candid brainstorming sessions about how to contend with some of the more vexing biorisk management tasks might produce some fresh public-private nonproliferation tools that leverage the unique capabilities of both the private and public sectors to keep proliferators at bay.

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ⁱ For example, the alcohol industry has curbed advertisements aimed at minors. The American Bar Association has a code of behavior, buttressed by local peer review panels to investigate allegations of misconduct by lawyers, administering discipline, as appropriate. *Self-Regulation in the Alcohol Industry: A Review of Industry Efforts to Avoid Promoting Alcohol to Underage Consumers* (Washington, DC: Federal Trade Commission, September 1999). For more on the self-governance of the legal profession

in the United States, go to the Center for Professional Responsibility at:

www.abanet.org/cpr.

ⁱⁱ National Intelligence Council, *Global Trends 2025: A Transformed World* (Washington, DC: US GPO, November 2008), 47-8.

ⁱⁱⁱ Ronald Jackson et al., "Expression of Mouse Interleukin-4 by a Recombinant Ectromelia Virus Suppresses Cytolytic Lymphocyte Responses and Overcomes Genetic Resistance to Mousepox," *Journal of Virology* 75, no. 3 (February 2001): 1205-10.

Jackson and his colleagues consulted the Australian Defense Department prior to publication, and they intended their research results to serve as a warning to remind scientists that experiments can go dangerously awry. See also, Rachel Nowak, "Killer Virus," *New Scientist* (10 January 2001). Available at:

www.newscientist.com/article/dn3111-killer-virus.html. Rachel Nowak, "Disaster in the Making: An Engineered Mouse Virus Leaves Us One Step Away From the Ultimate Bioweapon," *New Scientist* 169, no. 2273 (13 January 2001): 4-5. With another controversial experiment, Ariella M. Rosengard et al., "Variola Virus Immune Evasion Design: Expression of a Highly Efficient Inhibitor of Human Complement," *Proceedings of the National Academy of Sciences* 99, no. 13 (25 June 2002): 8808-13.

^{iv} J. Cello, A. V. Paul, E. Wimmer, "Chemical Synthesis of Poliovirus cDNA: Generation of Infectious Virus in the Absence of Natural Template," *Science* 297, no. 5583 (2002): 1016-8. See also, Elizabeth Finkel, "Engineered Mouse Virus Spurs Bioweapon Fears," *Science* 291, no. 5504 (26 January 2001): 585. The World Health Organization spearheads a vaccination campaign to eradicate polio. For more, go to:

www.polioeradication.org.

^v Diana Jean Schemo, "Scientists Discuss Balance of Research and Security," *New York Times*, 10 January 2003. Available at:

www.nytimes.com/2003/01/10/science/10SECR.html. See also, Raymond A. Zilinskas and Jonathan B. Tucker, "Limiting the Contribution of Open Scientific Literature to the Biological Weapons Threat," *Journal of Homeland Security* (December 2002). Available at: www.homelandsecurity.org/journal/Search.aspx?s=Zilinskas. Elisa D. Harris and John D. Steinbruner, "Scientific Openness and National Security after 9-11," *The CBW Conventions Bulletin*, no. 67 (March 2005): 1-6.

^{vi} The journals adhering to this publication standard include: *Critical Reviews in Microbiology*, *Nature*, *Proceedings of the National Academy of Sciences*, *New England Journal of Medicine*, *Journal of Virology*, *Journal of the American Medical Association*, *Biochemistry*, *Biosecurity and Bioterrorism*, *Science*, *Neuron*, *Infection and Immunity*, *Journal of Clinical Microbiology*, *Nature Medicine*, *Journal of Immunology*, *Journal of Virology*, *Journal of Biological Chemistry*, *Molecular Biology of the Cell*. See "Statement on the Consideration of Biodefense and Biosecurity," *Nature* 421, (20 February 2003): 771.

^{vii} Jan van Aken and Iris Hunger, "Biosecurity Policies at International Life Science Journals," *Biosecurity and Bioterrorism* 7, no. 1 (20 April 2009): 61-72.

^{viii} Phillip Campbell, "Dual-use Results and Scientific Journals," presentation (Washington, DC: National Science Advisory Board on Biodefense, 30 June 2005). Presentation available at:

oba.od.nih.gov/biosecurity/meetings/200506/Campbell%20NSABB30-6-05.pdf.

^{ix} Jeffrey K. Tautenberger et al., "Characterization of the 1918 influenza virus polymerase genes," *Nature* 437 (6 October 2005): 889-93; Terence M. Tumpey et al., "Characterization of the Reconstructed 1918 Spanish Influenza Pandemic Virus," *Science* 310, no. 5745 (7 October 2005): 77-80.

^x Donald Kennedy, "Better Never Than Late," *Science* 310, no. 5746 (14 October 2005): 195; "The 1918 Influenza Virus Is Resurrected," *Nature* 437 (6 October 2005): 794-5.

^{xi} Lawyers, government officials, and the media also attended the Asilomar meeting. Paul Berg, "Meetings that Changed the World: Asilomar 1975: DNA Modification Secured," *Nature* 445 (18 September 2008): 290-1. For a more in-depth description of Asilomar and the developments that led up to it, Michael Rogers, *Biohazard* (New York: Alfred A. Knopf, 1977).

^{xii} See *NIH Guidelines for Research Involving Recombinant DNA Molecules* (Washington, DC: National Institutes of Health, April 2002).

^{xiii} *Act on the Regulation of Genetic Engineering*, as revised (16 December 1993), Section 3 (4)(5)(6), Section 39. For an overview of the robust oversight system in the United Kingdom, see John Steinbruner, Elisa D. Harris, Nancy Gallagher, Stacy Okutani, *Controlling Dangerous Pathogens: A Prototype Protective Oversight System* (College Park, MD: Center for International and Security Studies, March 2007): 15-8.

^{xiv} Quote from, Jan van Aiken, "When Risk Outweighs Benefit," *EMBO Reports* 7, no. SI (2006): S13. Also, see Filippa Corneliusen, "Adequate Regulation, a Stopgap Measure, or Part of a Package?" *EMBO Reports* 7, no. SI (2006): S52-3; Malcolm R. Dando and Brian Rappert, "Codes of Conduct for the Life Sciences: Some Insights from UK Academia," briefing paper no. 16 (Bradford, United Kingdom: University of Bradford, Department of Peace Studies, May 2005). For more on scientists views about oversight, see *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* (Washington, DC: National Academies Press, 2009).

^{xv} See National Research Council, *Biotechnology Research in an Age of Terrorism* (Washington, DC: National Academies Press, 2004), 5-6. US National Science Advisory Board on Biosecurity, *Proposed Framework for the Oversight of Dual Use Life Sciences Research: Strategies for Minimizing the Potential Misuse of Information* (Washington, DC: National Institutes of Health, June 2007). See also, US National Research Council, *Globalization, Biosecurity, and the Future of the Life Sciences* (2006). Scientists in other countries also recognize the need to update governance mechanisms. See, for example, "Do No Harm: Reducing the Potential for Misuse of Life Sciences Research" (London: The Royal Society and Wellcome Trust, 7 October 2004).

^{xvi} Scientists from the US pharmaceutical industry first proposed a triple-tiered structure in Amy E. Smithson, ed., *Compliance Through Science: U.S. Pharmaceutical Industry Experts on a Strengthened Bioweapons Nonproliferation Regime*, Report no. 48 (Washington, DC: Stimson Center, September 2002), 61-5. Proposing an international body to review critical experiments and set standards, John D. Steinbruner and Elisa D. Harris, "Controlling Dangerous Pathogens," *Issues in Science and Technology* (Spring 2003): 47-54. With a tiered approach, John Steinbruner, Elisa D. Harris, Nancy Gallagher, Stacy Okutani, *Controlling Dangerous Pathogens: A Prototype Protective Oversight System* (College Park, MD: Center for International and Security Studies, March 2007): 21-48. Also suggesting a set of global standards for life sciences research and a strong role for scientific advisory panels, "Royal Society Submission to the Foreign and Commonwealth Office: Green Paper on Strengthening the Biological and Toxin Weapons Convention," policy doc. 25/02 (London: Royal Society, September 2002).

^{xvii} Michelle S. Garfinkel, Drew Endy, Gerald L. Epstein, Robert M. Friedman, *Synthetic Genomics: Options for Governance* (Rockville, MD: J. Craig Venter Institute, October 2007). See also, Ali Nouri and Christopher F. Chyba, "Proliferation-Resistant Biotechnology: A Novel Approach to Improve Biosecurity," *Nature Biotechnology* 27,

no. 3 (2009): 234-6, US National Science Advisory Board on Biosecurity, *Addressing Biosecurity Concerns Related to the Synthesis of Select Agents* (Washington, DC: National Institutes of Health, December 2006).

^{xviii} Some professional societies have established codes of ethics specifically prohibiting bioweapons work (e.g., Australian Society for Microbiology). See also, British Medical Association, *Biotechnology, Weapons, and Humanity*, 2nd ed. (London: 2004). Education programs have also been created to heighten the awareness of scientists regarding the dual-use dilemma inherent in life science research have been created. On codes of ethics, Nancy L. Jones, "A Code of Ethics for the Life Sciences," *Science and Engineering Ethics* 13, no. 1 (March 2007): 25-43; Margaret A. Somerville and Ronald M. Atlas, "Ethics: A Weapon to Counter Bioterrorism," *Science* 307, no. 5717 (25 March 2005): 1881-2; James Revill and Malcolm R. Dando, "A Hippocratic Oath for Life Scientists," *EMBO Reports* 7, no. SI (2006): S55-60. For model education programs, see the web pages of the Federation of American Scientists at:

www.fas.org/biosecurity/education/dualuse/index.html, the Center for Arms Control and Non-proliferation at:

www.politicsandthelifesciences.org/Biosecurity_course_folder/base.html, and the University of Bradford/Exeter Project on Life Sciences, Biosecurity, and Dual-Use Research at:

projects.exeter.ac.uk/codesofconduct/BiosecuritySeminar/Education/index.htm.

^{xix} Hubert Bernauer et al., "Technical Solutions for Biosecurity in Synthetic Biology," Workshop Report (Munich: Industry Association of Synthetic Biology, 3 April 2008), 4. Available at:

www.synbiosafe.eu/uploads///pdf/iasb_report_biosecurity_syntheticbiology.pdf. See also, Stephen Maurer, "Grassroots Efforts to Impede Bioterrorism," *Bulletin of the Atomic Scientists* (5 March 2009). Available at: www.thebulletin.org/web-edition/features/grassroot-efforts-to-impede-bioterrorism. "Gene-Synthesis Firms Set Up Biosecurity Protocol," *Genetic Engineering & Biotechnology News*, 18 November 2009. Available at: www.genengnews.com/news/bnitem.aspx?name=68850005.

^{xx} Stephen M. Maurer, Markus Fischer, Heinz Schwer, Cord Stahler, Peer Stahler, and Hubert S. Bernauer, "Making Commercial Biology Safer: What the Gene Synthesis Industry Had Learned About Screening Customers and Orders," working paper (17 September 2009): 16-8. Available at:

gspp.berkeley.edu/iths/Maurer_IASB_Screening.pdf. Depending on a company's location and internal policy, gene synthesis companies used one or more of the following pathogen risks lists: the U.S. Select Agent list, the Australia Group list, and other national control lists. Hubert Bernauer et al., "Technical Solutions for Biosecurity in Synthetic Biology," 8-11; Maurer, "Grassroots Efforts to Impede Bioterrorism." GenBank®, maintained by the U.S. National Institutes of Health, contains all publicly available DNA sequences. For more, go to: www.ncbi.nlm.nih.gov/Genbank/.

^{xxi} Note that the IASB's American counterpart, the International Consortium of Polynucleotide Synthesis, participated in the Munich meeting, but this trade association subsequently dissolved. Hubert Bernauer et al., "Technical Solutions for Biosecurity in Synthetic Biology." See also, "DNA Firms Step Up Security Over Bioterrorism Threat," *New Scientist*, no. 2673 (14 September 2008). Available at: www.newscientist.com/article/mg19926733.500-dna-firms-step-up-security-over-bioterrorism-threat.html; Maurer, "Grassroots Efforts to Impede Bioterrorism." The activities of the code of conduct project can be found at: www.ia-sb.eu/go/synthetic-biology/. On 4 December 2006, a group of experts proposed an approach similar to the one taken by the IASB and the International Association of Polynucleotide Synthesis. See Hans Bügl et al., "A Practical Perspective on DNA Synthesis and Biological Security," available at: pgen.us/PPDSS.htm.

^{xxii} At an industry conference held in mid-October 2008 in Hong Kong, a special panel was convened to introduce the work in progress about a code of conduct and promote a dialogue on these matters. “SynBio 4.0: IASB Presents Security Report.” Available at: www.ia-sb.eu/go/synthetic-biology/activities/press-area/press-releases/press-release-on-synbio-40-iasb-presents-biosecurity-report-english.

^{xxiii} The creation of this database, called the Virulence Factor Information Repository, was a collaborative endeavor. The database was introduced at a conference in Cambridge, Massachusetts. Barry Bergman, “Goldman School Portal Takes Worry out of ‘Experiments of Concern,’” *The Berkeleyn* (2 April 2009). Available online at: www.berkeley.edu/news/berkeleyan/2009/04/02_concern.shtml; Hubert Bernauer et al., “Technical Solutions for Biosecurity in Synthetic Biology,” 12-13; Maurer, “Grassroots Efforts to Impede Bioterrorism;” “IASB Finalizes Code of Conduct for Gene Synthesis,” 23 November 2009. Available at: www.ia-sb.eu/go/synthetic-biology/activities/press-area/press-releases/iasb-finalizes-code-of-conduct-for-gene-synthesis.

^{xxiv} Yudhijit Bhattacharjee, “Gene Synthesis Companies Pledge to Foil Terrorists,” *Science Insider*, 19 November 2009. Available at: blogs.sciencemag.org/scienceinsider/2009/11/gene-synthesis.html; “Gene Synthesis Companies to Develop Biothreat Protocols,” *GenomeWeb Daily News*, 19 November 2009. Available at: www.genomeweb.com/synthetic-gene-companies-develop-biothreat-protocols. Also, “Gene-Synthesis Firms Set Up Biosecurity Protocol.”

^{xxv} Note that in August and September 2009, two of the consortium members presented a pathogen screening approach that differed significantly from the one being discussed by other industry companies in that human experts would not be required to investigate hits from the automated database screening. Erika Check Hayden, “Gene-makers Form Security Coalition,” *Nature News* (18 November 2008). Available at: www.nature.com/news/2009/091118/full/news.2009.1095.html; Meredith Wadman, “US Drafts Guidelines to Screen Genes,” *NatureNews* (4 December 2009). Available at: <http://www.nature.com/news/2009/091204/full/news.2009.1117.html>.

^{xxvi} For the IASB companies, note that a commercially reasonable inquiry could include identity confirmation via direct contact with the customer (e.g., emails, letters, phone conversations), consultation with others who know the customer, review of publicly available literature (e.g., web sites, industry information), ascertaining the awareness of the customer’s institution of the customer’s order and experimental plans, review of data on a customer’s grant awards or Institutional Biosafety Committee and license approvals, or the behavioral pattern of the customer’s prior orders. The IASB’s code of conduct is available at: www.ia-sb.eu/tasks/sites/synthetic-biology/assets/File/pdf/iasb_code_of_conduct_final.pdf. For the consortium protocol, go to: www.genesynthesisconsortium.org/Harmonized_Screening_Protocol.html.

^{xxvii} After publication for comment, a draft guideline may be revised prior to final publication. “Screening Framework Guidance for Synthetic Double-Stranded DNA Providers,” *Federal Register* 74, no. 227 (27 November 2009): 62319-27. Wadman, “U.S. Drafts Guidelines to Screen Genes.”

^{xxviii} Collaborators on the review portal project include Northwestern University, the University of Maryland’s Center for International and Security Studies, and Duke University.

^{xxix} E. Check Hayden, “Experiments of Concern to Be Vetted On Line,” *Nature* 457 (5 February 2009): 643; Bergman, “Goldman School Portal Takes Worry out of ‘Experiments of Concern.’”

^{xxx} Stephen M. Maurer, J.D., telephone interview with author, 1 December 2009.

^{xxxi} Along those lines, see “Pathways to Security,” *Nature* 455, no. 432 (25 September 2008). Available at: www.nature.com/nature/journal/v455/n7212/full/455432a.html.

^{xxxii} For more on the interaction of market forces with the security arena, Maurer, Fischer, Schwer, Stahler, Stahler, and Bernauer, “Making Commercial Biology Safer: What the Gene Synthesis Industry Had Learned About Screening Customers and Orders.”