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END OF THE BEGINNING OR BEGINNING OF THE END? SYNTHETIC BIOLOGY'S STALLED SECURITY AGENDA AND THE PROSPECTS FOR RESTARTING IT

Stephen M. Maurer*

Last year, synthetic biology celebrated its tenth anniversary by creating a bacterium around an artificial genome. But a second milestone may have been just as important. Over the years, synthetic biologists have devoted enormous effort to identifying security risks and debating solutions. At the same time, they knew that any debate would be pointless unless it ended in practical action. In the end, members pursued two strategies. The first was traditional and asked government to write regulations. The second asked industry and academics to govern themselves. Prior to 2009–2010, there was no way to know whether either strategy would produce useful results. Optimists and pessimists could see what they wanted.

Today, we know much more, and the news is discouraging. Almost everyone agrees that the security agenda's first and most urgent task is to keep would-be terrorists from buying synthetic DNA. But just how hard should companies investigate customer orders before filling them? Mainstream security experts have long agreed that many threats do not appear on any list, let alone the U.S. government's list of officially regulated "Select Agents." For the foreseeable future, the only way to detect these threats is for human experts to compare each customer request against similar published sequences that have well-known biological functions. In November 2009, gene companies around the world announced that they would indeed pay human experts to do this. One might have expected the U.S. government to endorse this result. Instead, the Department of Health and Human Services ("HHS") announced draft guidelines that encouraged companies to adopt a weaker procedure ("Best

* Berkeley Law School and Goldman School of Public Policy, University of California at Berkeley. I thank Rob Carlson, Rocco Cassagrande, George Church, Robert Cook-Deegan, Susan Ehrlich, Andrew Ellington, Drew Endy, Markus Fischer, Michele Garfinkel, and Henry Metzger for helpful conversations. I also thank the Carnegie Corporation of New York for generously supporting this work under Grant No. B7943.R01. I am solely responsible for any errors or omissions.

Match”) that can only detect sequences derived from Select Agents. The guidelines became final in October of 2010.

Surely, this is a modest return for ten years of effort. Worse, it signals that the U.S. government will shelter industry from strong biosecurity standards even when industry has already agreed to them. If so, synthetic biology’s security agenda has been so much wasted effort. Clearly, it is time for a closer look. This Article examines what synthetic biologists have done to improve biosecurity over the past decade and asks how much additional progress can be expected. Parts I through III introduce synthetic biology, the economic and scientific forces that have driven it for the past decade, and the pressures that persuaded the community and eventually the U.S. government to promise improved biosecurity. The Article then turns to the familiar argument that attempts to regulate technology are hopeless. To the contrary, Part IV argues that many of the weapons of mass destruction (“WMD”) technologies developed over the last century were eminently predictable and could have been blocked by policymakers. Part V reviews synthetic biologists’ extended debate over when and how to control so-called “experiments of concern” that might lead to new and better weapons. Parts VI and VII review synthetic biologists’ parallel debate over how to deny the field’s existing technologies, including synthetic DNA, to terrorists. Part VIII reviews the community’s failed attempt to implement these ideas through a combination of self-governance and formal government regulation. Part IX looks at the prospects for additional private standards and government regulation in the foreseeable future. Part X identifies practical reforms that would allow synthetic biology to revive its stalled security agenda. Part XI provides a brief conclusion.

I. INTRODUCTION: SYNTHETIC BIOLOGY AT THE CROSSROADS

“Synthetic biology,” like most phrases beloved of funding agencies, is an elastic term. That said, it is almost always used to describe experiments that can only be done with artificial DNA or at the very least would not otherwise be affordable. According to this definition, synthetic biology has existed as a distinct discipline since approximately the year 2000.¹ This dating is particularly satisfying because it makes the

¹ This date is inevitably arbitrary. Nevertheless, it would be hard to argue that the field existed much before the first gene synthesis companies began operations in 1999. Stephen

field's tenth anniversary coincide with J. Craig Venter and associates' announcement that they had created a cell entirely controlled by artificial DNA.² However, 2010 also marked a second anniversary. Since 9/11 and the Washington anthrax attacks, synthetic biologists have devoted enormous energy to identifying security threats and debating policy responses. These activities were only meaningful if government or the community was willing to implement them. This, however, could only be judged on the basis of concrete results, and for most of synthetic biology's first decade there were none.

Today we know much more, and the news is discouraging. Synthetic biology's security priorities have almost always included denying synthetic DNA to terrorists. But just how hard should gene-makers examine customer orders before filling them? Academic synthetic biologists called on industry to implement meaningful screening programs as early as 2006. In April 2008, a European trade association, the International Association Synthetic Biology ("IASB"), began developing a private standard that required human experts to examine incoming customer orders for threats. But there was opposition. Indeed, two large gene-makers tried to derail IASB's standard at the last minute by promoting what they called a "fast" and "cheap" alternative that would have replaced human experts with computers. This led to a dramatic, Silicon Valley-style standards war over biosecurity. Like most such wars, the market delivered its judgment decisively. By November 2009, more than eighty percent of the industry's installed capacity—including the same companies that had previously agitated for fast and cheap solutions—had adopted the IASB Code or an equivalent standard. Furthermore, IASB's Code had spread across the world to include companies in Europe, the United States, and even China.³

M. Maurer et al., Making Commercial Biology Safer: What the Gene Synthesis Industry Has Learned About Screening Customers and Orders (Sept. 17, 2009) (unpublished working paper), available at http://gspp.berkeley.edu/iths/Maurer_IASB_Screening.pdf. Conversely, the field was clearly self-aware by the time that Professor Bustamonte coined, or at least independently reinvented, the phrase "synthetic biology" in 2001. Luis Campos, *That Was the Synthetic Biology That Was*, in *SYNTHETIC BIOLOGY: THE TECHNOSCIENCE AND ITS SOCIETAL CONSEQUENCE* 5 (Markus Schmidt et al. eds. 2009); see also Rob Carlson, *Synthetic Biology 2.0, Part IV: What's in a Name?*, *SYNTHESIS* (May 23, 2006, 11:50 PM), <http://www.synthesis.cc/2006/05/synthetic-biology-20-part-iv-whats-in-a-name.html>.

Both considerations suggest that it is reasonable to date the field from 2000.

² See Daniel G. Gibson et al., *Creation of a Bacterial Cell Controlled by a Chemically Synthesized Genome*, 329 *SCI.* 52 (2010) (reporting the design, synthesis, and assembly of the *Mycoplasma mycoides* genome at the Venter Institute).

³ See *infra* Part VIII.B (discussing industry standards, including IASB's Code of Conduct).

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So far so good, but the U.S. federal government was also developing its own screening standard. Observers, including the editors of the prestigious science journal *Nature*, universally assumed that government regulation would inevitably be stronger than any private standard. They were wrong. Instead, HHS overruled the market by announcing non-binding guidelines that encouraged companies to use fast and cheap solutions after all. Despite criticism, HHS finalized the document—albeit in slightly watered-down form—in October 2010.⁴ It is not yet clear whether industry will take the hint and retreat from its commitment to human screening.⁵

Anyone who claims to take biosecurity seriously—and many scholars do⁶—should be thoroughly alarmed by this result. Following ten years of debate, the federal government has announced a policy that requires companies to spend almost nothing on screening. Worse, the government has overruled a significantly higher private standard to reach this result. This strongly suggests that the U.S. government is more allergic to regulation than industry itself. Were synthetic biology's security discussions a charade from the beginning? And what, if anything, should we expect in the future?

Clearly, it is time to take stock. This Article reviews synthetic biology's decade-long quest to invent and implement meaningful security measures and asks what, if anything, can be done to re-start its agenda. Part II provides a short history of synthetic biology and the economic forces that have driven it for the past decade. Part III discusses the various pressures that persuaded synthetic biologists and government regulators to promise improved biosecurity after 9/11. Part IV addresses and rejects the familiar argument that science is so unpredictable that any attempt to regulate synthetic biology is a fool's errand. Parts V through VIII review synthetic biologists' decade-long debate over security. Subtopics include proposals for managing so-called "experiments of concern" that could make biological weapons more powerful and easier to make (Part V), the debate over ideas for

⁴ Screening Framework Guidance for Providers of Synthetic Double-Stranded DNA, 75 Fed. Reg. 62,820 (Oct. 13, 2010).

⁵ See *supra* Part VIII.C–D (discussing government regulation of screening).

⁶ There is now extensive scholarly literature arguing that genetically engineered weapons pose realistic threats to American society. See, e.g., George W. Rutherford & Stephen M. Maurer, *The New Bioweapons: Infectious and Engineered Diseases, in WMD TERRORISM: SCIENCE AND POLICY CHOICES* 111, 128–38 (Stephen M. Maurer ed. 2009). By comparison, skeptics have been few and far between. For a rare counterexample, see MILTON LEITENBERG, U.S. ARMY WAR COLL. STRATEGIC STUDIES INST., *ASSESSING THE BIOLOGICAL WEAPONS AND BIOTERRORISM THREAT* (2005) (suggesting that terrorists' ability to create genetically engineered weapons has been overstated).

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keeping synthetic biology's existing capabilities, especially synthetic DNA, away from terrorists (Parts VI and VII), and the ultimately disappointing efforts of academic scientists, industry executives, and government regulators to turn these ideas into concrete action (Part VIII). Part IX reviews the prospects for further action at the start of synthetic biology's second decade. Part X asks what synthetic biologists, many of whom care deeply about security, can do to accelerate reform. Finally, Part XI provides a brief conclusion.

II. A SHORT HISTORY OF SYNTHETIC BIOLOGY

Scientists may soon look back on the genetic engineering of the 1990s with the same nostalgia that most of us reserve for wood-and-canvas biplanes. Just fifteen years ago, genetic engineering meant cutting and pasting DNA from different organisms. This limited engineers to whatever organisms existed in nature, or more precisely, whatever organisms they could get their hands on.

Help was on the way. Academic scientists had been learning how to create synthetic DNA molecules encoding arbitrary gene sequences since the 1970s.⁷ For many years, their progress was so slow that gene-length artificial DNA remained a curiosity. At the same time, each year saw a little more automation and affordability. By century's end, prices had fallen to about five dollars per base pair.⁸ This turned out to be a tipping point. Soon, scientists realized that they could perform some complex experiments more cheaply by replacing traditional cloning methods with synthetic DNA. This in turn created a virtuous cycle. Companies could now specialize in producing bulk DNA and invest the profits in better production processes. This led to even lower prices, more demand, and still more investment. A decade later, this process is only now reaching its technological limits. In the meantime, DNA prices have fallen by an order of magnitude and are hovering at roughly fifty cents per base pair.⁹

Cheap commercial DNA opened the door to large numbers of previously unaffordable experiments. Increasingly, these experiments were qualitatively different from what had come before. Suddenly, scientists could use synthetic DNA to write arbitrary DNA sequences

⁷ Har G. Khorana, *Total Synthesis of a Gene*, 203 SCI. 614 (1979).

⁸ See generally Maurer et al., *supra* note 1, at 1-5 (discussing the falling synthetic DNA prices). DNA's famous double helix consists of two strands linked together by molecules called "base pairs." Living things use the order in which different base pairs follow each other to encode genetic information. Synthetic genes typically include thousands or tens of thousands of base pairs.

⁹ *Id.*

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that had never existed in nature. But why should those DNA “blueprints” actually work? Here, researchers took a page from engineering by identifying short, well-behaved snippets of DNA (“standard biological parts”) that could be mixed and matched to make more complicated designs. This was more or less the same strategy that inventors had used to manage complex design problems since Samuel Colt opened his firearms business in the 1830s.¹⁰ Still, there were no guarantees. In particular, nobody knew how much new DNA could be packed into an organism without killing it. In 2004, University of California, Berkeley Professor Jay Keasling’s Amyris Corporation persuaded the Bill and Melinda Gates Foundation to invest forty-two million dollars in designing an organism that could make a molecule used in malaria drugs.¹¹ Despite its complexity, Keasling’s design succeeded admirably. This persuaded the National Institutes of Health (“NIH”) and venture capitalists to invest even more in the new technology and produced a second virtuous cycle, this time in funding.

This is where things stood in May 2010 when the J. Craig Venter Institute (“JCVI”) announced that it had created an entire artificial genome and used it to control a living, self-replicating bacterium.¹² Some dismiss this announcement as an essentially arbitrary Edmund Hillary (“Because it’s there”) moment. In this view, JCVI’s feat lay, at most, in making a DNA molecule that was longer and had fewer errors than any previous experiment.¹³ But commentators who argued that

¹⁰ Samuel Colt famously introduced standard parts to American industry. On the use of standard *biological* parts to control complexity, see Jason R. Kelly et al., *Measuring the Activity of BioBrick Promoters Using an In Vivo Reference Standard*, J. BIOMEDICAL ENGINEERING, March 2009, <http://www.jbioleng.org/content/pdf/1754-1611-3-4.pdf>.

¹¹ Randall Osborne, *Amyris Gets \$12 Million to Help in Bill Gates’ Malaria Effort*, BIOWORLD (Dec. 14, 2004), http://www.bioworld.com/servlet/com.accumedia.web.Dispatcher?next=bioworldHeadlines_article&forceid=34262.

¹² Press Release, J. Craig Venter Inst., *First Self-Replicating Synthetic Bacterial Cell* (May, 20, 2010), <http://www.jcvi.org/cms/press/press-releases/full-text/article/first-self-replicating-synthetic-bacterial-cell-constructed-by-j-craig-venter-institute-researcher/>.

¹³ Professors Cho and Relman emphasize that the creation of an entire bacterial genome, though “noteworthy,” reflects “incremental” past advances and is “primarily a matter of scale.” Mildred K. Cho & David A. Relman, *Synthetic “Life,” Ethics, National Security and Public Discourse*, 329 SCI. 38, 38 (2010). Similarly, the Presidential Commission for the Study of Bioethical Issues has emphasized that

[t]he [JCVI] announcement last May, although extraordinary in many ways, does not amount to creating life as either a scientific or a moral matter. The scientific evidence before the Commission showed that the research relied on an existing natural host . . . [and] does not represent the creation of life from inorganic chemicals alone.

PRESIDENTIAL COMM’N FOR THE STUDY OF BIOETHICAL ISSUES, *NEW DIRECTIONS: THE ETHICS OF SYNTHETIC BIOLOGY AND EMERGING TECHNOLOGIES* 3 (2010) [hereinafter 2010

JCVI's *Mycoplasma mycoides* was a straight copy of nature's design may have missed the point. This is because the same techniques can now be used to create special "chassis organisms" with deliberately small genomes that leave maximal room for standard biological parts. If so, we may be on the brink of synthetic biology's third virtuous cycle. Today, synthetic biologists insert standard parts into many different organisms. This makes it hard for them to share data and, in particular, to know when a design's failure is caused by the host. The rise of chassis organisms, on the other hand, will encourage researchers to converge on a relatively small number of shared organisms. Microbiologists have known since the 1950s that research communities built around "model organisms" find it easier to share data and are much more productive.¹⁴ JCVI's achievement promises to similarly accelerate synthetic biology.

It is hard not to see these advances as good news. At the same time, science is neither moral nor immoral. State programs have perverted classical biology to develop weapons since the 1940s.¹⁵ More recently, Soviet scientists worked hard to develop genetically engineered weapons in the 1970s and 1980s¹⁶ Given this history, it was only natural to worry that synthetic biology methods would also be abused.

The simplest threat was economic: the Soviet program had cost far more than any terrorist could afford. Synthetic DNA made many of these experiments cheaper than they were before. More ambitiously, synthetic biology meant that researchers were no longer limited to pathogens they already possessed or could borrow from colleagues.

COMMISSION REPORT], available at <http://www.bioethics.gov/documents/synthetic-biology/PCSBI-Synthetic-Biology-Report-12.16.10.pdf>.

¹⁴ Joachim Henkel & Stephen M. Maurer, *Network Effects in Biology R&D*, 100 AM. ECON. REV. 159, 159 (2010).

¹⁵ The United States, United Kingdom, Soviet Union, and Japan all conducted large-scale biological weapons programs during World War II. Except for Japan, most of these programs continued into the 1960s. Uniquely, the Soviet Union continued to pursue biological weapons into the 1990s. Unlike earlier Western programs, this work fully exploited the then-new science of genetic engineering. See, e.g., DEADLY CULTURES: BIOLOGICAL WEAPONS SINCE 1945 (Mark Wheelis, Lajos Rózsa & Malcolm Dando eds., 2006) (discussing the various use of biological weapons programs throughout the world); JEANNE GUILLEMIN, BIOLOGICAL WEAPONS: FROM THE INVENTION OF STATE-SPONSORED PROGRAMS TO CONTEMPORARY BIOTERRORISM (2005) (examining biological weapon use in the United States, United Kingdom, Japan, and Soviet Union).

¹⁶ For the classic account, see KEN ALIBEK & STEPHEN HANDELMAN, BIOHAZARD: THE CHILLING TRUE STORY OF THE LARGEST COVERT BIOLOGICAL WEAPONS PROGRAM IN THE WORLD—TOLD FROM THE INSIDE BY THE MAN WHO RAN IT (1999). Some American scientists have expressed quiet skepticism about Alibek's claims. See, e.g., Richard W. Titball, *An Elusive Serial Killer*, 430 NATURE 145, 145 (2004) (pointing out the skepticism of American scientists interviewed for Wendy Orent's 2004 book entitled *Plague: The Mysterious Past and Terrifying Future of the World's Most Dangerous Disease*). In fairness, Alibek himself admits that his most spectacular claims are based on inference.

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Instead, workers who wanted particular viruses (and eventually bacteria) could build them from scratch. And this included really dangerous organisms—most notably, smallpox—that only exist in heavily guarded government laboratories. Indeed, researchers had already resurrected two viruses—1918 influenza and polio—that were formerly extinct.¹⁷ Could smallpox be far behind? Finally, synthetic biology promised to make machine-like organisms unlike anything found in nature. At least in principle, could similar technologies be used to make so-called “advanced weapons” that targeted, say, certain ethnic groups while ignoring others?¹⁸

III. THE PRESSURE BUILDS

Synthetic biologists have always known that their technology poses security risks. Indeed, biologists have debated claims that genetic engineering could create epidemics since the mid-1970s.¹⁹ These concerns happened to be particularly prominent at the time synthetic biology was born. In 1998, Richard Preston published *The Cobra Event*,²⁰ a novel in which terrorists used genetic engineering to create a super-virus. Many readers—including then-President Bill Clinton²¹—found the book chillingly credible, especially because Preston had written extensively about real-life biological weapons. The following year, defector Ken Alibek wrote an even bigger best-seller claiming that the Russian military had created genetically engineered weapons unlike anything found in nature.²² These bestsellers were followed by a renewed scholarly interest in so-called advanced weapons.²³ News that

¹⁷ See *infra* note 83 and accompanying text.

¹⁸ For a survey of possibilities, see Rutherford & Maurer, *supra* note 6.

¹⁹ SUSAN WRIGHT, *MOLECULAR POLITICS: DEVELOPING AMERICAN AND BRITISH REGULATORY POLICY FOR GENETIC ENGINEERING, 1972-82 passim* (1994).

²⁰ RICHARD PRESTON, *THE COBRA EVENT* (1997).

²¹ Margo Nash, *Where Terrorism Meets Optimism*, N.Y. TIMES, Nov. 24, 2002, www.nytimes.com/2002/11/24/nyregion/in-person-where-terrorism-meets-optimism.html (reporting that President Clinton “asked the F.B.I. to determine whether the events described in ‘The Cobra Event’ could really happen”).

²² See ALIBEK & HANDELMAN, *supra* note 16.

²³ See, e.g., Steven M. Block, *Living Nightmares: Biological Threats Enabled by Molecular Biology*, in *THE NEW TERROR: FACING THE THREAT OF BIOLOGICAL AND CHEMICAL WEAPONS* 39-75 (Sidney D. Drell et al. eds. 1999); RICHARD A. FALKENRATH ET AL., *AMERICA’S ACHILLES’ HEEL: NUCLEAR, BIOLOGICAL, AND CHEMICAL TERRORISM AND COVERT ATTACK* (4th prt. 2001).

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an Australian team had discovered a way to help pox viruses evade vaccines added to these concerns in the months before 9/11.²⁴

Given this background, it was natural for synthetic biologists to ask whether their field posed any special concerns. Indeed, one group discussed the fact that their laboratory could now synthesize, though not assemble, pox virus DNA as early as 1999. Despite this, no very detailed or practical discussions seem to have taken place until 2002–2003.²⁵

By then, a great deal had changed. First and foremost was 9/11 and the Amerithrax attacks that followed two months later. Suddenly, many officials, including the President, believed that a biological weapons attack was imminent or even underway.²⁶ This crisis atmosphere predictably led to various Executive Branch responses. These ranged from pressing researchers to suppress certain experimental results²⁷ to opening new dialogues with academic scientists. By 2002–2003, a wide variety of biosecurity experts including governmental staff and advisors were asking synthetic biologists to identify security threats and think about possible solutions.²⁸ Meanwhile, Congress passed the USA PATRIOT Act, which inter alia made it a crime to possess biological agents, toxins, or delivery systems.²⁹ Subsequently, the Agricultural Bioterrorism Protection Act of 2002 required people possessing Select Agent organisms³⁰ to undergo background checks and register with

²⁴ Ronald J. Jackson et al., *Expression of Mouse Interleukin-4 by a Recombinant Ectromelia Virus Suppresses Cytolytic Lymphocyte Response and Overcomes Genetic Resistance to Mousepox*, 75 J. VIROLOGY 1205 (2001).

²⁵ E-mail from Drew Endy to author (Mar. 1, 2011, 11:01 PST) [hereinafter Endy E-mail] (on file with author); accord Robert F. Service, *Synthetic Biologists Debate Policing Themselves*, 312 Sci. 1116, 1116 (2006) (stating that synthetic biologists started to consult ethicists and launch studies in 2004).

²⁶ See, e.g., GEORGE W. BUSH, DECISION POINTS 152–53 (2010) (recounting post-9/11 fears that the White House had been contaminated with botulinum toxin).

²⁷ See *infra* Part V.A.

²⁸ E-mail from Robert Carlson, Principal, Biodesic to author (Mar. 1, 2011, 11:07 PST) [hereinafter Carlson E-mail] (on file with author); E-mail from Andrew Ellington to author (Mar. 1, 2011, 11:04 CST) (on file with author); Endy E-mail, *supra* note 25; see also Drew Endy, *Strategy for Biological Risk and Security* (Oct. 2003) (unpublished working paper), available at <http://dspace.mit.edu/handle/1721.1/30595>.

²⁹ Pub. L. No. 107-56, § 817, 115 Stat. 272, 385–86 (2001) (codified at 18 U.S.C. § 175 (2006)); see also Select Agents and Toxins, 42 C.F.R. pt. 73 (2010) (implementing 18 U.S.C. § 175 by, inter alia, publishing the list of select agents and toxins). The Act contained an exception for “prophylactic, protective, bona fide research, or other peaceful purpose[s]”. Pub. L. No. § 817(1)(C), 115 Stat. at 385–86 (codified at 18 U.S.C. § 175(b)). The bill also made it a crime for illegal aliens and citizens of certain countries to possess, transport, or receive organisms found on the Centers for Disease Control and Prevention’s Select Agent list. *Id.* § 817(2), 115 Stat. at 385–86 (codified at 18 U.S.C. § 175b (2006)).

³⁰ Possession, Use, and Transfer of Select Agents and Toxins, 7 C.F.R. pt. 331 (2010) (implementing provisions of the Agricultural Bioterrorism Protection Act and listing agents

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HHS.³¹ These laws were immediately interpreted to include DNA molecules encoding sequences found in Select Agent organisms. However, the application of these laws to short and/or non-identical variant sequences remained unclear.

A. *Synthetic Biology Controversies*

The new laws re-focused commercial gene-makers' attention on security. They, in turn, introduced the issue to academic scientists.³² At this point, an intense debate was more or less inevitable. In part, this reflected synthetic biology's status as a new and highly publicized discipline. However, there were more specific reasons as well. In 2002, Professor Eckhard Wimmer used artificial DNA to make the world's first artificial polio virus.³³ Though widely criticized,³⁴ Wimmer defended his work as a deliberate wake-up call for scientists and society alike. Thereafter, activists³⁵ and a second incident in which researchers resurrected the 1918 influenza virus³⁶ kept the issue alive. In 2005, *New Scientist* magazine added still more fuel to the fire by reporting that at

and toxins that "have the potential to pose a severe threat to plant health or plant products"); Possession, Use, and Transfer of Select Agents and Toxins, 9 C.F.R. pt. 121 (2010) (implementing provisions of the Agricultural Bioterrorism Protection Act and listing agents and toxins that "have the potential to pose a severe threat to public health and safety, to animal health, or to animal products").

³¹ 42 U.S.C. § 262a(d); see also 7 C.F.R. § 331.7 (requiring the U.S. Department of Agriculture to develop registration and inspection measures for facilities that handle enumerated plant and animal pathogens).

³² Endy E-mail, *supra* note 25; cf. Alan Pearson, Ctr. for Arms Control & Nonproliferation: Scientists Working Grp. on Biological & Chemical Weapons, Establishing a Responsible Biosciences Forum 6 (Jan. 26, 2007) (unpublished report) (on file with author) ("Similarly, a concern among DNA synthesis companies that they could be held legally liable for even unwittingly enabling illegal activity is generating attention to issues of misuse and responsible conduct within the synthetic biology community.").

³³ Jeronimo Cello et al., *Chemical Synthesis of Poliovirus cDNA: Generation of Infectious Virus in the Absence of Natural Template*, 297 SCI. 1016, 1016–18 (2002) (describing Wimmer's research results).

³⁴ John D. Steinbruner & Elisa D. Harris, *Controlling Dangerous Pathogens*, ISSUES SCI. & TECH., Spring 2003, available at <http://www.issues.org/19.3/steinbruner.htm>. Perhaps the highest profile criticism came from Craig Venter, who called the work "irresponsible" and called for new procedures to review similar experiments in the future. *Id.* University of Pennsylvania ethicist Arthur Caplan joined in Venter's call for oversight. *Id.*

³⁵ Activists at the Sunshine Project warned against synthetic pathogens in November 2003. Dirk Stemerding et al., *Synthetic Biology and the Role of Civil Society Organizations Shaping the Agenda and Arena of the Public Debate*, in SYNTHETIC BIOLOGY, *supra* note 1, at 155, 157.

³⁶ Terrence M. Tumpey et al., *Characterization of the Reconstructed 1918 Spanish Influenza Pandemic Virus*, 310 SCI. 77 (2005).

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least one gene-maker made no effort to screen incoming customer orders.³⁷

B. Promising Action

In the post-9/11 environment, simply identifying threats and possible responses was no longer enough. However tentatively, biologists began to talk about action. The earliest and most influential suggestion came from the National Academy of Science's Fink Committee.³⁸ It urged the Bush Administration to create a new National Science Advisory Board for Biosecurity ("NSABB") to propose regulations that the government could implement. Given post-9/11 politics, the Bush Administration could hardly refuse: it created the NSABB in April 2004.³⁹ This, in turn, established a clear expectation that the NSABB—and the federal government itself—would eventually take formal action, although how much action remained unclear.⁴⁰

So far, these responses were fairly conventional. However, many synthetic biologists see themselves as the heirs to computer science and the electronics industry. This made it natural to ask whether self-governance could grow out of the community's recurring "Synthetic Biology" or "SB" conferences in the same way that Web self-governance had grown out of the electronics community's "W3C" conferences.⁴¹

³⁷ Peter Aldhous, *The Bioweapon Is in the Post*, NEW SCIENTIST, Nov. 12, 2005, at 8. The article reported that nine of twelve DNA makers contacted failed to examine incoming orders on a regular basis. *Id.* However, this figure was somewhat misleading because only one of the non-screener was a gene-maker. The rest specialized in making shorter molecules called "oligos." *Id.* Screening short sequences produces large numbers of false alarms and remains challenging even today. *Id.* The *Guardian* newspaper later published a similar expose in which reporters purchased short segments of smallpox DNA from three U.K. companies. James Randerson, *Lax Laws, Virus DNA and Potential for Terror*, GUARDIAN, June 14, 2006, <http://www.guardian.co.uk/science/2006/jun/14/weapons-technology.uk/print> (U.K.).

³⁸ COMM. ON RESEARCH STANDARDS & PRACTICES TO PREVENT THE DESTRUCTIVE APPLICATION OF BIOTECHNOLOGY, NAT'L RESEARCH COUNCIL OF THE NAT'L ACADS., BIOTECHNOLOGY RESEARCH IN AN AGE OF TERRORISM (2004) [hereinafter FINK REPORT].

³⁹ Kerry Boyd-Anderson, *U.S. Creates Advisory Board for Biosecurity*, ARMS CONTROL ASS'N (April 2004), <http://www.armscontrol.org/print/1513>.

⁴⁰ The Fink Committee may also have thought that the NSABB would give government bureaucrats political cover by making strong, specific recommendations. This is, after all, a common Beltway political tactic. *See, e.g.*, David Wessel, *Panel on Cutting Deficit Paves Way for Politicians*, WALL ST. J., Feb. 17, 2011, at A4 (recounting how the Deficit Reduction Commission was established to give Washington insiders cover to cut entitlements and other spending). If so, they were disappointed. NSABB's eventual recommendations were much too vague to serve this purpose. *See infra* notes 112-13 and accompanying text.

⁴¹ *See* TIM BERNERS-LEE & MARK FISCHETTI, WEAVING THE WEB: THE ORIGINAL DESIGN AND ULTIMATE DESTINY OF THE WORLD WIDE WEB BY ITS INVENTOR (2000), for a first-hand description of W3C and Web governance. The analogy between Web governance and

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Here, the fact that the SB1.0 conference had already hosted the community's first public discussion of security issues in 2004 was clearly encouraging.⁴² This immediately led to expectations that the SB2.0 conference scheduled for May 2006 would take concrete actions.⁴³

By late 2005, both the public and academic sectors had committed themselves, however vaguely, to the principle of action. Not surprisingly, the first fruits were a renewed emphasis on collecting—and if possible, building consensus around—security measures that had already been proposed. On its face, it was naïve to think that two hundred synthetic biologists could produce meaningful consensus, let alone action, in the space of a three-hour meeting. On the other hand, SB2.0's failure to act would trigger a cycle of disappointment and low expectations for every SB conference thereafter. In order to prevent this outcome, the Carnegie Corporation of New York and MacArthur Foundations funded a University of California, Berkeley project to help community members identify and develop proposals in advance of the meeting.⁴⁴

By then, the Sloan Foundation had already funded its own \$570,000, fifteen-month program to develop options—though not formal recommendations—for policymakers to consider.⁴⁵ Because most of these options required government regulation, the Sloan study

synthetic biology was never very exact. This was because the Web could not move forward—indeed, could not exist—without some minimal set of standards. For this reason, failure to adopt standards would doom the entire enterprise. By comparison, academic and commercial synthetic biologists could continue practicing their trades with or without biosecurity standards. This made synthetic biology's self-governance problem much harder than the Web's. The extent to which synthetic biologists in academia and especially industry managed to overcome this inertia is remarkable.

⁴² See Service, *supra* note 25, at 1116 (remarking that SB1.0 moved security issues “to the forefront”); Robert Carlson, *Synthetic Biology 1.0*, FUTUREBRIEF (2005), <http://www.futurebrief.com/robertcarlsonbio.pdf>. Carlson remarks that members were moved both by the actual threat and by “the potential public backlash it may incite.” *Id.*

⁴³ See Carlson, *supra* note 42 (“Synthetic Biology 2.0 is scheduled for June of 2006. We have an enormous amount of work to do before then.”); see also George Church, *Let Us Go Forth and Safely Multiply*, 438 NATURE 423, 423 (2005) (expressing confidence that SB2.0 meeting “should make significant progress” toward a code of conduct).

⁴⁴ The author served as principal investigator.

⁴⁵ Elizabeth Pennisi, *Synthetic Biology Remakes Small Genomes*, 310 SCI. 769, 770 (2005); Craig Venter Institute Release: *Major New Policy Study Will Explore Risks, Benefits of Synthetic Genomics*, BIOSPACE (June 28, 2005), http://www.biospace.com/news_story.aspx?NewsEntityId=20467320. The report ultimately took twenty months and included reports from a core group of fourteen experts. The centerpiece of the effort included three invitation-only meetings—an ironic procedure in a project designed to build public trust—several commissioned studies, and a final report. MICHELE GARFINKEL ET AL., SYNTHETIC GENOMICS: OPTIONS FOR GOVERNANCE, at i (2007), available at <http://www.synbiosafe.eu/uploads/pdf/Synthetic%20Genomics%20Options%20for%20Governance.pdf>.

considered a much broader range of issues than members could address at SB2.0. At the same time, the project would not be completed until 2007—long after SB2.0 ended. While this did not preclude community action at SB2.0, it almost certainly made it seem less urgent.⁴⁶ The main point as of early 2006, however, was that the community had committed itself to pursuing both private and public security initiatives. It remained to be seen whether either track would deliver meaningful results.

IV. IS BIOSECURITY POSSIBLE?

Anyone who listens to synthetic biologists debate security sooner or later will hear the claim that science moves too quickly to be regulated.⁴⁷ This argument surely deserves to be taken seriously. At the same time, it is good to be suspicious. As Herman Kahn pointed out fifty years ago, many people find the idea that a problem is hopeless strangely comforting because it makes hard choices unnecessary.⁴⁸ Clearly, there is no way to know for certain whether synthetic biology can be regulated. That said, it is important to try. Part IV.A addresses common assertions that existing synthetic biology technologies are, or soon will be, uncontrollable. Part IV.B tackles the harder question of whether science will inevitably produce new weapons of mass destruction (“WMD”) technologies faster than policymakers can regulate them.

A. *Controlling Existing Technologies*

As already discussed, the synthetic biology revolution depends on access to cheap commercial DNA. Regulating commercial sources will not work, however, if the same DNA can be readily obtained from other

⁴⁶ The European Commission funded a €235,000 counterpart to the Carnegie/MacArthur and Sloan projects in 2006. Unlike the American projects, SYNBIOSAFE was billed as a fact-finding exercise and exploration instead of a call to action. However, it too sought to identify something like a consensus around threats and eventual action. Huib de Vriend, *Constructing Life: Early Social Reflections on the Emerging Field of Synthetic Biology* (The Hague: Rathenau Inst., Working Doc. No. 97, 2006), available at http://depot.knaw.nl/4935/1/WED97_Constructing_Life_2006.pdf; *Safety and Ethical Aspects of Synthetic Biology*, SYNBIOSAFE, <http://www.synbiosafe.eu/> (last visited Apr. 10, 2011).

⁴⁷ Indeed, one survey of synthetic biologists has claimed “a consensus developing initially, according to which effective oversight of biology and protection from a biochemical catastrophe were impossible,” so that any kind of central regulation “would be useless.” Markus Schmidt et al., *SYNBIOSAFE E-conference: Online Community Discussion on the Societal Aspects of Synthetic Biology*, 2 SYSTEMS & SYNTHETIC BIOLOGY 7, 13 (2008).

⁴⁸ HERMAN KAHN, *THINKING ABOUT THE UNTHINKABLE* (1962).

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sources. In practice, there are at least three variants of this argument. It is surprisingly easy to marshal evidence for each of them.

First, skeptics like to say that genes can be made by undergraduates or even high school students.⁴⁹ However, this statement is only true in principle. In practice, even bright non-specialists make so many mistakes that success would take many years.⁵⁰

Second, some commentators argue that many academic and corporate labs already make genes. However, this ignores the fact that such work is almost always done for internal use or known customers. This implies that terrorists who try to obtain DNA from these sources will incur substantial—and often unacceptable—security risks. Historically, terrorist plots have frequently unraveled because companies reported unusual inquiries to authorities.⁵¹

Third, some synthetic biologists have argued that the complex skills needed to make genes will soon be replaced by easy-to-use tabletop synthesizers. Economically, this amounts to a bet that synthesizer technology will eventually become competitive with specialized workers operating in massive central facilities. No one can be sure whether this will happen. That said, it is worth pointing out that gene synthesis companies continue to make massive investments in plants and equipment. This implies a market judgment that tabletop devices are not imminent.⁵²

In addition to the foregoing technical objections, synthetic biologists sometimes advance various social or economic arguments that regulation is futile. For example, many synthetic biologists argue that even skills that are scarce—and hence regulable—today will inevitably become ubiquitous over time. This, however, ignores history. Indeed, some key biotech skills are markedly *less* common than they used to be. During the 1990s, many universities made oligos in-house. Today, however, most of these facilities no longer exist. Instead, researchers find it cheaper and more convenient to buy oligos on the open market.⁵³ This example shows that private skills can and do atrophy in the face of

⁴⁹ Mike May, *Seeking Security for Synthetic Genes*, SCI. AM. WORLDVIEW, <http://www.saworldview.com/article/seeking-security-for-synthetic-genes> (last visited Apr. 10, 2011) (“You can put all the guidelines you want on industry, but if ‘Mr. Evil’ wants to do something stupid, he can make it in a high school lab.” (quoting Claes Gustafsson, DNA2.0’s vice president of sales and marketing)).

⁵⁰ Maurer et al., *supra* note 1, at 3 n.10.

⁵¹ Probably the most famous is white supremacist Larry Wayne Harris’s attempt to obtain plague from a commercial repository.

⁵² The fact that at least one company has tried to develop a tabletop synthesizer and abandoned the effort as commercially impractical is also instructive. Maurer et al., *supra* note 1, at 3 n.9.

⁵³ GARFINKEL ET AL., *supra* note 45, at 4.

commercial competition. The effect is likely to be particularly important in synthetic biology, where economies of scale allow large companies to synthesize genes much more cheaply than anyone else.

Similarly, some synthetic biologists claim that strong regulation will breed rogue companies that specialize in defying the law.⁵⁴ This model only makes sense, however, if defying the law lets rogue companies (a) offer lower prices than the big firms that currently dominate the industry, or (b) make a living by selling high-priced DNA to undesirables. In fact, neither proposition is likely. On the one hand, no current or proposed screening standard is remotely expensive enough to erase the big firms' price advantage. On the other, the "undesirables" market is tiny; the prospect of one or two terrorist orders is not nearly enough to build a business.

Finally, some biologists, and even NSABB members,⁵⁵ worry that strong regulation could drive companies into foreign countries beyond the reach of U.S. law. This seems doubtful. If anything, economies of scale promise to increase the big U.S. firms' price advantage over competitors over time. No current or reasonably foreseeable regulation is remotely likely to change this.

Soon after Hiroshima, Manhattan Project physicist Richard Feynman argued that nuclear war was both imminent and inevitable. Sixty-five years later, this prediction remains spectacularly wrong.⁵⁶ It turns out

⁵⁴ See, e.g., Rob Carlson, *Tracking the Spread of Biological Technologies*, BULL. ATOMIC SCIENTISTS (Nov. 21, 2008), <http://www.thebulletin.org/web-edition/features/tracking-the-spread-of-biological-technologies>. Carlson argues that strong regulation will breed rogue gene-makers in the same way that the drug laws have bred illegal methamphetamine labs. *Id.* The analogy is doubtful. Criminals invest enormous time and effort learning to make methamphetamines because the illegal market is huge. By comparison, terrorists trying to obtain smallpox would presumably submit a single order. This is not nearly enough to support a business.

⁵⁵ See, e.g., Meredith Wadman, *U.S. Drafts Guidelines to Screen Genes*, NATURENEWS (Dec. 4, 2009), <http://www.nature.com/news/2009/091204/full/news.2009.1117.html> ("If we deter too much, the gene-synthesis industry will go outside the US and outside our purview, and it will come back to haunt us." (quoting NSABB Board member Stuart Levy)).

⁵⁶ Decades later, Feynman marveled at how wrong he had been:

I can't understand it anymore, but I felt very strongly then. I sat in a restaurant in New York, for example, and I started to look out at the buildings, and I began to think about how much the radius of the Hiroshima bomb damage was And I would go along and see people building a bridge, or they would be [building] a new road and I thought, they're *crazy*, they just don't *understand*. Why are they [building] new things? It's so useless. But, fortunately, it has been useless for [so many] years, hasn't it? So I've been wrong about it being useless to [build] bridges and I'm glad that those other people had the sense to go ahead.

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that it is not enough to know that atomic bombs are possible; difficulty also matters. Synthetic biologists should do more than point out that it is possible to evade regulation. They should also bear the burden of showing that such evasions are plausibly within terrorists' existing skill sets. Absent this showing, we should assume that regulation will be at least partly effective and move forward.

B. Predicting WMD Breakthroughs

Commentators often claim that science is inherently un-regulable because (a) discoveries are frequently unexpected, and (b) policymakers cannot control what they cannot predict. This section discusses whether the historical record justifies this assertion. We begin by presenting short case histories of how today's main WMD technologies were developed. These histories strongly suggest that policymakers could have foreseen most, though not all, of today's WMD threats in time to take meaningful action.

Case 1: Atomic Weapons. The discovery of radioactive decay and, soon after, the realization that the atomic nucleus contained enormous power was an unexpected result of late nineteenth and early twentieth century physics research.⁵⁷ This development could not reasonably have been foreseen or controlled by policymakers. For this reason, there was little or nothing they could do to suppress the concept of atomic bombs.⁵⁸ At the same time, no one knew how to release nuclear energy until academic researchers unexpectedly discovered the "chain reaction" principle, and two concrete strategies for implementing it, thirty years later.⁵⁹ Policymakers could easily have defunded the massive academic research programs that led to this result. Once chain reactions were discovered, however, nuclear weapons became a well-defined engineering problem. At this point, policymakers could do little to

JAGDISH MEHRA, THE BEAT OF A DIFFERENT DRUM: THE LIFE AND SCIENCE OF RICHARD FEYNMAN 160 (1994) (quoting Richard P. Feynman, *Los Alamos from Below*, ENGINEERING & SCI., Jan./Feb. 1976, at 11, 30).

⁵⁷ See ABRAHAM PAIS, INWARD BOUND: OF MATTER AND FORCES IN THE PHYSICAL WORLD 7–12 (1986) (describing nuclear research's origins in, *inter alia*, vacuum technology, spectroscopy, and electromagnetism research).

⁵⁸ The popular press speculated extensively about both nuclear weapons and nuclear energy after radioactive decay was discovered in 1903. See, e.g., SPENCER R. WEART, NUCLEAR FEAR: A HISTORY OF IMAGES 18 (1988). H.G. Wells wrote a novel exploring atomic bombs and related arms control issues shortly before World War I. H. G. WELLS, THE WORLD SET FREE (Hogarth Press 1988) (1914).

⁵⁹ RICHARD RHODES, THE MAKING OF THE ATOMIC BOMB (1986).

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prevent some government, somewhere, from developing atomic⁶⁰ and, eventually, hydrogen weapons.⁶¹

Case 2: Radiological Weapons. The health effects of radioactivity were discovered accidentally⁶² and could not have been foreseen by policymakers. For a long time, however, radioactive isotopes were too scarce for practical use as WMD.⁶³ As with nuclear weapons, the turning point came three decades later with the discovery of chain reactions. In principle, policymakers could have defunded this research. Once scientists invented nuclear reactors, however, there was little policymakers could do to prevent some government, somewhere, from developing radiological WMDs. Strangely, no government seems to have done this. While the United States pursued radiological weapons in the early 1950s, the program was soon abandoned so that, uniquely, this particular form of WMD was never deployed.⁶⁴

Case 3: Chemical Weapons. Policymakers were deeply concerned by the rise of the chemical industry and its facilities for making poison gas by the late 1890s.⁶⁵ At the same time, normal industrial chemicals, such as chlorine, had only limited toxicity. This meant that their WMD potential was marginal. In principle, therefore, policymakers could have usefully delayed the development of more capable weapons by signing treaties that prevented governments from developing improved poisons. In practice, however, such treaties would have been hard to verify and would almost certainly have been ignored (like other weapons treaties) once World War I began. Even so, wartime progress was limited. Despite massive funding, government research and development

⁶⁰ Some have argued that only the U.S. government was rich enough to fund atomic weapons, and then only under the extreme conditions of World War II. This assertion is obviously not testable.

⁶¹ Research leading to fusion weapons (the hydrogen bomb) followed a similar trajectory. RICHARD RHODES, *DARK SUN: THE MAKING OF THE HYDROGEN BOMB* (1995).

⁶² See PAIS, *supra* note 57, at 93–100 (describing the tragic early history of academic and industrial exposure to radioactivity).

⁶³ The dirty bombs envisaged by the U.S. Department of Homeland Security and others since 9/11 would almost certainly cause very few casualties. Instead, their effects, if any, would be mostly psychological. Many experts privately point out that dirty bombs should not be considered WMDs at all, except somewhat sarcastically as “Weapons of Mass Disruption.”

⁶⁴ See Will Grover, *All the Easy Experiments: A Berkeley Professor, Dirty Bombs, and the Birth of Informed Consent*, *BERKELEY SCI. REV.*, Fall 2005, at 41–45 (discussing radiological warfare research in the 1940s).

⁶⁵ The first treaty against gas warfare was signed in 1899. Declaration on the Use of Projectiles the Object of Which is the Diffusion of Asphyxiating or Deleterious Gases, Hague Peace Conference of 1899, July 29, 1899, available at http://avalon.law.yale.edu/19th_century/dec99-02.asp.

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("R&D") programs only improved toxicity by a factor of thirty.⁶⁶ This improvement was miniscule compared to what commercial pesticide companies, whose R&D programs were supported by large markets over a period of decades, were able to accomplish after the War. By the mid-1930s, Hitler's Germany had exploited these discoveries to make weapons that were 2,500 times more toxic than chlorine.⁶⁷ Policymakers could have blocked this advance by making improved pesticides illegal. Such a ban would have immediately defunded commercial discovery programs in a simple and above all publicly verifiable way.

Case 4: Biological Weapons – Contagious Diseases. The idea of using contagious diseases as weapons has been known for centuries. In the modern world, however, smallpox is almost certainly the only pathogen capable of inflicting large-scale casualties.⁶⁸ The idea that terrorists could deliberately infect themselves to spread the disease was already widely known at the start of the twentieth century.⁶⁹ Policymakers could have done little to stop a determined government, and perhaps terrorists, from acquiring the pathogen and sending out human carriers to spread the disease.⁷⁰

Case 5: Biological Weapons – Anthrax. To work as weapons, pathogens that do not rely on human-to-human transmission must be able to survive for long periods on surfaces and the open air. This property is rare: among natural agents, only anthrax spores are simultaneously hardy and virulent enough to make useful weapons. Policymakers could do little to suppress this knowledge, which was widely discussed before World War II.⁷¹ Thereafter, Great Britain was able to develop effective anthrax bombs within a year or so while the

⁶⁶ The English program tested 150,000 chemicals. A similar American establishment tested 4,000 compounds and is said to have been the largest U.S. military R&D effort prior to the Manhattan Project. ROBERT HARRIS & JEREMY PAXMAN, *A HIGHER FORM OF KILLING: THE SECRET STORY OF CHEMICAL AND BIOLOGICAL WARFARE* 23, 35 (1982).

⁶⁷ For a detailed history of how Germany developed its Tabun and Sarin weapons, see HARRIS & PAXMAN, *supra* note 66, at 55–69; and JONATHAN B. TUCKER, *WAR OF NERVES: WORLD WAR I TO AL-QAEDA* 24–39 (2006). The British government similarly exploited postwar pesticide research to achieve an additional three-fold toxicity improvement for its VX weapon in the 1950s. HARRIS & PAXMAN, *supra* note 66, at 186–87; TUCKER, *supra*, at 158.

⁶⁸ Rutherford & Maurer, *supra* at note 6, at 114–15.

⁶⁹ See, e.g., H.G. Wells, *The Stolen Bacillus*, in H.G. WELLS, *THE STOLEN BACILLUS AND OTHER INCIDENTS* 11 (Westholme Publishing 2005) (1895).

⁷⁰ Strangely, they can do better today. The reason is that smallpox has been eradicated and no longer exists outside of a handful of heavily guarded laboratories. This assumes, of course, that terrorists cannot use synthetic biology to resurrect the disease.

⁷¹ The most famous use of the idea is found in Aldous Huxley's *Brave New World*, which describes what happens after Western civilization collapses under a rain of anthrax bombs. ALDOUS HUXLEY, *BRAVE NEW WORLD* (First Harper Perennial Modern Classics 2010) (1932).

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United States was well on its way to achieving large-scale production at War's end.⁷² Policymakers could have done little to stop these developments.

Case 6: Other Pathogens. Anthrax apart, potential weapons pathogens are much too delicate to survive in the open. During the 1940s, government R&D programs learned how to spread pathogens as microscopic droplets of special protective liquids called "formulation." However, these wet agents were relatively ineffective. For this reason, modern biological weapons uniformly depend on freeze-drying⁷³ organisms into a powder. No policymaker could have anticipated that freeze-drying would make organisms hardier when academic scientists invented the technique in the 1890s. At least in principle, however, they should have been able to recognize the threat after scientists discovered that freeze-dried pathogens could be revived in 1909.⁷⁴ At this point, determined policymakers could have defunded academic efforts to scale up the technology to the point where it could be used to make weapons. Instead, successive researchers continued to improve the process until it reached industrial scales in the mid-1930s.⁷⁵ At this point, policymakers could do little to stop governments from further developing the technology. Government R&D programs duly perfected bulk freeze-drying for blood plasma during World War II and extended the technology to make biological weapons in the 1950s.⁷⁶

Case 7: Genetically Engineered Threats. Biologists' discovery that organisms frequently exchange DNA opened the door to deliberate genetic engineering experiments in the 1960s. No policymaker could

⁷² HARRIS & PAXMAN, *supra* at note 66.

⁷³ I am indebted to my former research assistant, Tania Dutta, for uncovering the history of freeze-drying.

⁷⁴ See Homer F. Swift, *Preservation of Stock Cultures of Bacteria by Freezing and Drying*, 33 J. EXPERIMENTAL MED. 69 (1921) (reviewing early literature on freeze-drying of bacteria and viruses). This early work also discovered various subsidiary tricks for keeping freeze-dried organisms alive (e.g., adding milk or sugar) that were later used by the United States and others to manufacture biological weapons in the 1950s. Bernard W. Hammer, *A Note on the Vacuum Desiccation of Bacteria*, 24 J. MED. RESEARCH 527, 527 (1911) (describing liquid solutions containing milk sugar, milk powder, and starch).

⁷⁵ Earl W. Flosdorf & Stuart Mudd, *Procedure and Apparatus for Preservation in "Lyophile" Form of Serum and Other Biological Substances*, 29 J. IMMUNOLOGY 389, 392 (1935) (reporting development of large-scale freeze-drying equipment and asserting that "[t]here is little doubt that [freeze-drying technology] can readily be adapted to full industrial scale operation").

⁷⁶ See R.I.N. Greves, *Centrifugal Vacuum Freezing: Its Application to the Drying of Biological Materials from the Frozen State*, 153 NATURE 485, 485-87 (1944) (discussing wartime freeze-drying developments and noting "great advances" in large-scale freeze-drying of blood products during World War II); *Instant Coffee*, WIKIPEDIA, http://en.wikipedia.org/wiki/Instant_coffee (last visited Apr. 10, 2011).

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have foreseen or prevented this development. Policymakers could, however, have stopped the massive commercial R&D programs that expanded the technology thereafter. Absent this groundwork, the Soviet Union would have found it difficult, or impossible, to pursue genetically engineered weapons in the 1970s and 1980s.

Surveying our case studies, it is clear that our hypothetical regulators would have had little or no chance of blocking the development of contagious disease (Case 4) and anthrax weapons (Case 5). On the other hand, ruthless intervention to defund academic research would have stood an excellent chance of blocking the development of atomic (Case 1), radiological (Case 2) and most pathogen weapons (Case 6). Similarly, international agreements to limit commercial R&D would almost certainly have stopped the development of chemical weapons (Case 3). Finally, combinations of ruthless defunding and limits on commercial research could plausibly have prevented the development of genetically engineered weapons (Case 7).

The key word, of course, is “ruthless.” Historically, real attempts to stop WMD have usually focused on treaties to suppress government R&D programs after the basic science has been established so that only engineering problems remain. While occasionally effective, such treaties are necessarily hard to verify and invite cheating.⁷⁷ More recently, government officials and academics have debated the feasibility of stopping individual “experiments of concern” from going forward.⁷⁸ Our examples suggest that this is unlikely to be more than a stopgap. In the long arc of academic science, individual experiments will almost always be so obvious—and the costs of performing them so modest—that some scientist, somewhere, is bound to try them. For this reason, suppression is unlikely to work for long.⁷⁹

The case would be very different if policymakers were willing to suppress commercial and academic research agendas over a period of decades. After all, experiments showing that freeze-dried organisms can be revived, or that uranium can be made to support chain reactions,

⁷⁷ The point is amply documented by the history of chemical weapons treaties, in which many countries originally developed new weapons defensively to study possible threats and design countermeasures. See, e.g., HARRIS & PAXMAN, *supra* note 66, at 43–44, 48–49.

⁷⁸ See *infra* Part V (discussing the experiments of concern problem).

⁷⁹ Spencer R. Weart, *Scientists with a Secret*, PHYSICS TODAY, Feb. 1976, at 23–30. Temporary suppression may sometimes be a useful goal. During the early days of World War II, U.S. physicists organized an unofficial conspiracy to keep atomic physics research secret. The effort ultimately helped block Nazi efforts to build a nuclear reactor. This result was only useful, however, because the Allied war effort guaranteed that Nazi Germany would build a bomb within five years, or not at all. Temporary suppression was also a more feasible goal because it meant that the conspiracy’s organizers could promise authors that their work would eventually be published.

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were not really serendipitous. Decades of academic or commercial effort were required to reach the point where these experiments could be proposed. Still other breakthrough experiments were unremarkable installments in brute force campaigns to find better insecticides or document radioactive decays across the periodic table. The larger point is that even the clever experiments would usually have been unthinkable had they not been part of much larger and longstanding research agendas.

There are obvious political reasons why such steps have never been taken. Nonetheless, such bans might also have been poor policy. After all, WMD have killed relatively few people⁸⁰ so far while their underlying technologies have delivered significant civilian benefits.⁸¹ Even nuclear energy may yet turn out to be a good thing if it solves the world's energy and greenhouse problems.⁸² Still, the fact remains that these questions could have been asked and action could have been taken. Biosecurity policy is possible.

C. *Is Synthetic Biology Special?*

It is always, of course, possible to argue that synthetic biology is qualitatively different from earlier dual-use technologies. In this case,

⁸⁰ This does not, of course, mean that the risks were worth running *ex ante*. Most obviously, there were many near-misses that could have led to nuclear war. See PETER VINCENT PRY, *WAR SCARE: RUSSIA AND AMERICA ON THE NUCLEAR BRINK* (1999); SCOTT D. SAGAN, *THE LIMITS OF SAFETY: ORGANIZATIONS, ACCIDENTS, AND NUCLEAR WEAPONS* (1993). Any attempt to quantify these risks is necessarily subjective. However, it is worth noting that Soviet Premier Khrushchev privately warned his Politburo that the chances of a nuclear war erupting over Berlin in 1961 were about five percent. FREDERICK KEMPE, *BERLIN 1961* 205 (2011). Given the number of people who would die in such an exchange, even this five percent probability would have given policymakers a persuasive case for suppressing nuclear energy.

⁸¹ For example, the ability to freeze-dry organisms made it possible for biologists to trade organisms by mail. This allowed scientists around the world to conduct experiments on the same model organisms, which vastly accelerated research. See, e.g., SCOTT STERN, *BIOLOGICAL RESOURCE CENTERS: KNOWLEDGE HUBS FOR THE LIFE SCIENCES* 20–22 (2004). The discovery of nerve gases is similarly linked to the discovery of DDT, which has saved millions of lives since World War II. See, e.g., Amir Attaran et al., *Balancing Risks on the Backs of the Poor*, 6 *NATURE MED.* 729, 729–31 (2000).

⁸² In a strange way, the recent nuclear accident in Fukujima, Japan actually strengthens the case for nuclear power. Back in the 1950s, it would have been reasonable to say that mankind had very little information about how common and/or destructive nuclear accidents would be. Today we have much better data about how often accidents occur and, especially, their potential downside. Pro-nuclear activists are almost certainly correct when they say that nuclear power has killed far fewer people than, say, the 100,000 workers who died mining coal during the twentieth century. William Tucker, *Why I Still Support Nuclear Power, Even After Fukushima*, *WALL ST. J.*, Apr. 23, 2011, <http://online.wsj.com/article/SB10001424052748704396904576226820013417298.html>.

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arguments that today's WMD technologies could have been controlled might not matter. That said, the existing evidence seems to fit the historical pattern. Synthetic biology's first decade produced two clear experiments of concern—synthetic polio and then 1918 influenza—both of which were clearly predictable and even routine by the time they were performed.⁸³ As in our WMD examples, these results could only have been stopped by blocking the relevant academic research agendas decades ago.⁸⁴

V. PREVENTING WMD BREAKTHROUGHS: THE "EXPERIMENTS OF CONCERN" PROBLEM

Part IV argued that society can plausibly control existing WMD technologies and sometimes even steer R&D away from dangerous topics. However, we have said little about how such interventions might be designed in the case of synthetic biology. This section reviews efforts to steer synthetic biology R&D away from paths that would make weapons more powerful and easier to acquire. In practice, this debate has focused almost entirely on identifying and regulating so-called "experiments of concern." This section will consider efforts to discourage and/or censor such experiments. Parts VI and VII will detail the parallel debates over how best to control synthetic biology technologies that already exist.

A. *Censoring Results*

Probably the most obvious way to control synthetic biology R&D is to suppress dangerous results if and when they are discovered. Shortly after 9/11, the Department of Homeland Security ("DHS") and the White House announced that they were developing regulations to control the "discussion and publication" of non-classified research that could nevertheless affect national security.⁸⁵ Alarmed, the American Society

⁸³ The decade's most controversial molecular biology experiment outside synthetic biology was almost certainly the demonstration that mousepox could be made more virulent.

⁸⁴ That said, blocking the experiments might still have delayed the demonstration and dissemination of these technologies for a few years. While it has become fashionable to talk of the fight against terrorism as "The Long War," there is no obvious reason why Al-Qaeda could not collapse or at least become drastically less capable within the next decade. In that case, suppressing artificial virus technology for even a few years could still be a useful investment.

⁸⁵ For further details, see, e.g., Steinbruner & Harris, *supra* note 34, at 5.

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for Microbiology ("ASM") asked the U.S. National Academy of Sciences ("NAS") to explore voluntary alternatives.⁸⁶

The result was a high-profile national workshop in August 2002.⁸⁷ Attendees were evenly divided between security professionals from the public and private sectors and academics including research scientists, journal editors, and scientific society officials. The group spent most of its time debating a proposal that would have restricted publication for six types of research that could be used to turn Select Agents into practical weapons.⁸⁸ However, this proposal failed in the face of opposition from universities, journals, and scientists.⁸⁹ Unable to reach

⁸⁶ *Id.*

⁸⁷ Raymond A. Zilinskas & Jonathan B. Tucker, *Limiting the Contribution of the Open Scientific Literature to the Biological Weapons Threat*, J. HOMELAND SECURITY, Dec. 3, 2002, <http://www.homelandsecurity.org/newjournal/articles/tucker.html>. The Workshop on Guidelines for the Publication of Scientific Research Potentially Related to Biological and Toxin Warfare was held on August 12, 2002 in Washington, D.C. *Id.* at n.1.

⁸⁸ *Id.* Participants at the workshop discussed categories that included research designed to:

Enhance pathogen infectivity, pathogenicity, antibiotic resistance, or resistance to host immunological defenses.

Improve the ability of a microbial pathogen to remain viable and virulent during prolonged storage and/or after release into the environment.

Facilitate the dissemination of biological agents as a fine-particle aerosol.

Facilitate the dissemination of a biological agent by contamination of food or water sources.

Create a novel pathogen or one with characteristics that have been altered to evade current detection methods or host immune defenses.

Assemble oligonucleotides to synthesize the genome of a pathogenic microorganism.

Id. (numbering omitted).

⁸⁹ *Id.* Academic scientists reportedly made the following arguments:

- The proposal appears to establish a system for national censorship in which scientific journals would be the guardians of the censored material. . . .
- Research universities and scientific journals would not agree to the proposed mechanism. . . .
- The proposed review process ignores the fact that the intellectual knowledge generated under grants (as opposed to contracts) is the property of the investigator[s] and that many research projects involve students and foreign nationals. . . .
- Scientists may be unwilling to take on the responsibility of reviewing a potentially "sensitive" paper
- Scientific journals are not set up to deal with the segregation of sensitive data or to provide for secure means of review and publication. . . .

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agreement, the group threw the question back into the academic research community's lap by calling on "bioscientists and their professional organizations [to] take the lead in informing security experts how best to meet the threats of biological warfare and terrorism" in a way that would not unduly harm the scientific enterprise.⁹⁰

Government officials renewed the pressure to act at a second NAS meeting in January 2003 in which they called on the scientific community, and especially journal editors, to "devise a better process" for handling unclassified research.⁹¹ This time, the statement was accompanied by an explicit threat that scientists needed to "come up with a process before the public demands the government do it for them."⁹²

Journal editors responded to this pressure by announcing "that they hoped to release a joint statement shortly."⁹³ The resulting Journal Editors Group Statement was duly published on February 21, 2003.⁹⁴ The twenty-nine signatories included sixteen past or present editors of leading science journals including *JAMA*, *New England Journal of Medicine*, *Nature*, and *Science*.⁹⁵ Two professional society publishers,⁹⁶

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- Once a document has been designated "Restricted," it must be tracked and its security monitored. . . .
 - . . . The proposed system would impose high legal and professional risks on journals, with minimal benefits.

Id. Most participants were, however, willing to concede "that under rare circumstances, the open communication of unclassified research could pose such a high risk of substantial harm as to warrant controlling the distribution of that information." *Id.*

⁹⁰ *Id.* (emphasis added).

⁹¹ Erica Check, *US Officials Urge Biologists to Vet Publications for Bioterror Risk*, 421 *NATURE* 197, 197 (2003).

⁹² *Id.*

⁹³ *Id.*

⁹⁴ Journal Editors & Authors Group, *Statement on Scientific Publication and Security*, 299 *SCIENCE* 1149 (2003).

⁹⁵ See *Journal Editors and Authors Group, SCL*, <http://www.sciencemag.org/content/299/5610/1149/rel-suppl/46c0b496b5237cd0/suppl/DC1> (last visited Apr. 10, 2011) (listing among the signatories Ronald Atlas, *Critical Reviews in Microbiology*; Philip Campbell, *Nature*; Nicholas R. Cozzarelli, *PNAS*; Greg Curfman, *New England Journal of Medicine*; Lynn Enquist, *Journal of Virology*; Annette Flanagan, *Journal of the American Medical Association*; Gordon Hammes, *Biochemistry*; Donald Kennedy, *Science*; Emilie Marcus, *Neuron*; Alison O'Brien, *Infection and Immunity*; Andrew Onderdonk, *Journal of Clinical Microbiology*; Beatrice Renault, *Nature Medicine*; Robert Rich, *Journal of Immunology*; Thomas Shenk, *Journal of Virology*; Herbert Tabor, *Journal of Biological Chemistry*; and Keith Yamamoto, *Molecular Biology of the Cell*).

⁹⁶ *Id.* (Samuel Kaplan, Chair, American Society for Microbiology Publications Board; and Mary Scanlan, Director of Publishing Operations, American Chemical Society).

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three U.S. government agencies,⁹⁷ two security intellectuals,⁹⁸ five academic biologists,⁹⁹ and a free speech activist¹⁰⁰ also signed the document. Reflecting what appears to have been mainstream opinion at both NAS workshops, the group acknowledged that information should sometimes be suppressed. Crucially, however, it left the actual decision to individual editors:

We recognize that on occasion an editor may conclude that the potential harm of publication outweighs the potential societal benefits. Under such circumstances, the paper should be modified, or not be published. Scientific information is also communicated by other means: seminars, meetings, electronic posting, etc. Journals and scientific societies can play an important role in encouraging investigators to communicate results of research in ways that maximize public benefits and minimize risks of misuse.¹⁰¹

The obvious problem with this statement was that it asked each editor to reach her own individual judgment about the balance of harms. This necessarily implied a weakest-link dynamic in which the community could only suppress papers if every single editor agreed. As of 2003, however, it was still possible to think that editors would eventually close this loophole by negotiating detailed procedures and standards for deciding when papers should be suppressed.¹⁰² Fatally, this was not done.¹⁰³

⁹⁷ *Id.* (Elizabeth George, National Nuclear Security Administration/Department of Energy; Rachel Levinson, Office of Science and Technology Policy; and Harold Varmus and Henry Metzger, National Institutes of Health).

⁹⁸ *Id.* (David Heyman, Center for Strategic and International Studies; and Thomas Inglesby, *Biosecurity and Bioterrorism*).

⁹⁹ *Id.* (Gerald Fink, MIT; Stephen S. Morse, Columbia University; Steven Salzberg, Institute for Genomic Research; Ariella Rosengard, University of Pennsylvania; and Eckard Wimmer, Stony Brook).

¹⁰⁰ *Id.* (Judith Krug, Office for Intellectual Freedom, American Libraries Association).

¹⁰¹ *Id.*

¹⁰² The most obvious solution would be to create an advice panel containing some suitable mix of security experts and academic scientists. This would automatically ensure quality and consistency across decisions. Some biologists called for an international committee to guide scientists whose work produced unexpectedly dangerous results even before 9/11. See generally Steinbruner & Harris, *supra* note 34.

¹⁰³ Academic scientists did, however, press for general rules defining data that should not be classified. See e.g., COMM. ON GENOMICS DATABASES FOR BIOTERRORISM, NAT'L RESEARCH COUNCIL OF THE NAT'L ACADS., SEEKING SECURITY: PATHOGENS, OPEN ACCESS, AND GENOME DATABASES 25-27 (2004) [hereinafter SEEKING SECURITY] (discussing open-access policies for genome databases).

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The crisis came in 2005 after *Science* editor-in-chief Donald Kennedy published an extraordinary editorial defending his journal's decision to publish a synthetic biology paper whose authors had successfully resurrected the 1918 influenza virus.¹⁰⁴ The first part of Kennedy's defense—that *Science* had only reached its decision after consulting with the heads of the Centers for Disease Control, the U.S. National Institute of Allergy and Infectious Disease, and NIH's Office of Biotechnology Activities—was unexceptional.¹⁰⁵ The problem, Kennedy went on to explain, was that the head of NIH had not been satisfied and asked *Science* to contact the NSABB as well. Because *Science* had complied, one might have expected Kennedy to congratulate himself on taking this extra step. Instead, he loudly claimed that his "convictions" would have led him to publish the paper even if NSABB had wanted it suppressed.¹⁰⁶ In effect, Kennedy had publicly announced that he would publish what he liked—and dared critics to criticize him. No one did.

Three years after 9/11, it was clear that neither the public nor the Bush Administration cared enough to press the issue. Instead, each editor was now free to do whatever she thought best—a result which more or less guaranteed that every experiment would be published by some journal somewhere. As Professor Selgelid remarked, the editors' extended flirtation with self-censorship had ended in an "unacceptable" result.¹⁰⁷

B. Discouraging "Experiments of Concern"

The obvious alternative to censorship is to review controversial experiments before they start. Unlike censorship, this strategy can do little to suppress unexpected results. At the same time, it has the practical advantage that a blocked experiment produces no results, and is therefore far easier to suppress. Pre-experiment review also avoids

¹⁰⁴ Donald Kennedy, *Better Never Than Late*, 310 SCI. 195, 195 (2005).

¹⁰⁵ A careful reader might, however, have worried that none of the reviewers had any obvious weapons experience. As Malcolm Dando and colleagues have repeatedly documented, biological weapons are a distinct and complex academic sub-discipline. The fact that someone is a famous biologist (and in this case a Washington insider) does not necessarily mean that he or she is capable of spotting, let alone deciding, complex dual-use issues.

¹⁰⁶ Kennedy, *supra* note 104, at 195 ("So would I, given our own convictions, the timing, and what we had learned from our consultations with Gerberding, Fauci, and others, have published the paper even if the NSABB had voted otherwise? Absolutely—unless they had it classified.").

¹⁰⁷ Michael J. Selgelid, *A Tale of Two Studies: Ethics, Bioterrorism, and the Censorship of Science*, HASTINGS CENTER REP., May-June 2007, at 35, 41.

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asking experimenters to discard months and perhaps even years of work.

By 2003, academics had recommended various review schemes that could be implemented through voluntary self-governance¹⁰⁸ or government regulation.¹⁰⁹ These scattered proposals received a powerful boost in 2004 when the Fink Committee called on NIH to expand its existing review procedures to include what it termed “experiments of concern,” i.e., research that could make biological weapons cheaper or more effective.¹¹⁰ In general, this recommendation was warmly received by the synthetic biology establishment, who hoped to obtain increased government funding and needed a convincing but uncomplicated answer to biosecurity concerns.¹¹¹ Promising an additional review layer was an easy way to do this.

Fatally, the Fink Committee failed to say what this new review system would look like. Instead, it asked the federal government to convene an advisory committee to fill this gap.¹¹² Ultimately, this new

¹⁰⁸ Gigi Kwik et al., *Biosecurity: Responsible Stewardship of Bioscience in an Age of Catastrophic Terrorism*, 1 *BIOSECURITY & BIOTERRORISM: BIODEFENSE STRATEGY, PRAC., & SCI.* 27 (2003).

¹⁰⁹ See JOHN STEINBRUNER ET AL., CTR. FOR INT’L & SEC. STUDIES AT MD., *CONTROLLING DANGEROUS PATHOGENS: A PROTOTYPE PROTECTIVE OVERSIGHT SYSTEM* (2003), available at http://www.cissm.umd.edu/papers/files/pathogens_project_monograph.pdf (envisioning a worldwide system).

¹¹⁰ SEEKING SECURITY, *supra* note 103, at 17–18. The “experiments of concern” definition combined the six “weaponization” criteria developed at the National Academies’ August 2002 Workshop with a somewhat recursive seventh category covering experiments that “[e]nable the weaponization of a biological agent or toxin.” *Id.* at 18. The call was immediately echoed by a Royal Society Report in the United Kingdom. THE ROYAL SOC’Y & WELLCOME TRUST, *DO NO HARM: REDUCING THE POTENTIAL FOR THE MISUSE OF LIFE SCIENCE RESEARCH 1* (2004), available at http://www.wellcome.ac.uk/stellent/groups/corporatesite/@policy_communications/documents/web_document/wtx023408.pdf (“Research institutions and funding agencies need to consider how to build on existing processes for reviewing research projects to ensure that risks of misuse are assessed in an appropriate and timely manner.”).

¹¹¹ The connection between money and review was particularly evident in the high-profile Gesteland Committee, then about to recommend that the U.S. Department of Energy massively increase its synthetic biology research budget. Embracing the Fink Committee’s proposed review system allowed the Committee to treat security as if the problem had already been solved. See DEP’T OF ENERGY BIOLOGICAL & ENVTL. RESEARCH ADVISORY COMM., DEP’T OF ENERGY, *SYNTHETIC GENOMES: TECHNOLOGIES AND IMPACT 8* (2004) [hereinafter BERAC], available at <http://www.science.doe.gov/ober/berac/SynBio.pdf> (last visited March 20, 2011) (“Acknowledging the potential for misuse of synthetic genome technology before adequate defenses can be mounted, [and arguing that] it would be prudent for scientists to work together with experts in national security to explore and develop practical strategies to prevent . . . its misuse, as recommended by the [Fink] Committee.”).

¹¹² NAT’L SCI. ADVISORY BD. FOR BIOSECURITY, *PROPOSED FRAMEWORK FOR THE OVERSIGHT OF DUAL USE LIFE SCIENCES RESEARCH: STRATEGIES FOR MINIMIZING THE POTENTIAL MISUSE*

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National Science Advisory Board for Biosecurity (“NSABB”) did little more than repeat the Fink Committee’s call for government action without adding useful specifics.¹¹³ This left the ball squarely in HHS’s court. Five years later, HHS still has no procedure for reviewing biosecurity issues. The agency has, however, promised to revisit the review issue as part of a broader initiative to create a “culture of responsibility” for dual-use technologies.¹¹⁴

In the meantime, many biologists saw no point in waiting and took action. Since the Fink report, roughly one-third of all U.S. research universities have modified their safety reviews to include at least some security issues.¹¹⁵ By far the most ambitious example was a multi-university collaboration called the Southeast Regional Center of Excellence for Emerging Infections and Biodefense (“SERCEB”).¹¹⁶ It operated a mandatory review system for member scientists from 2004 to 2009. As of 2007, SERCEB had reviewed twenty-seven research proposals, of which ten were found to include significant research of concern.¹¹⁷ These risks were managed through various strategies including training, physical security, experimental design, and limited published descriptions of sensitive methods.¹¹⁸ Interestingly, SERCEB never halted or significantly delayed a project.¹¹⁹ Indeed, its leadership reports that it became steadily more likely to avoid this outcome as time passed.¹²⁰

OF RESEARCH INFORMATION (2007) [hereinafter NSABB], available at http://oba.od.nih.gov/biosecurity/pdf/Framework%20for%20transmittal%200807_Sept07.pdf.

¹¹³ See *id.* at 10. NSABB suggested that experimenters who failed to seek review might be subject to unspecified “penalties.” Alternatively, compliance could “perhaps” be made “a term and condition of funding” or else a factor to be considered in grant applications. *Id.*

¹¹⁴ Public Consultation on Personnel Reliability and Culture of Responsibility Issues, 75 Fed. Reg. 76,997 (Dec. 10, 2010).

¹¹⁵ E-mail from Robert Cook-Deegan, Ctr. for Genome Ethics, Law & Policy, Duke University, to author (March 1, 2011, 12:18 EST) [hereinafter Cook-Deegan E-mail] (on file with author).

¹¹⁶ SERCEB’s main member institutions included Duke, Emory, Vanderbilt, the University of North Carolina, the University of Florida, and the University of Alabama at Birmingham. *Id.*

¹¹⁷ We will see that this rate is roughly 1,000 times higher than biology as a whole. See *infra* text accompanying note 123. The discrepancy is almost certainly explained by SERCEB’s unusual focus on infectious diseases and biodefense research.

¹¹⁸ E. Megan Davidson et al., *Practical Experiences in Dual Use Review*, 316 SCIENCE 1432, 1433 (2007).

¹¹⁹ *Id.* at 1433. This continued to be true until the end of the program. See Cook-Deegan E-mail, *supra* note 115.

¹²⁰ Davidson et al., *supra* note 118, at 1432. On at least two occasions, SERCEB reviewers adopted this position in cases where the researchers themselves would have recommended suppressing publication and destroying their research materials. See E. Megan Davidson et al., *Supporting Online Material for Practical Experiences in Dual-Use Review*, SCI. AAAS (June 8,

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Since 2007, the NIH has similarly required thousands of intramural scientists to report any experiments of concern to a special Dual Use Screening Committee. To date, the Committee has responded to several inquiries. No "experiments or reporting of . . . results have required modification based on dual use concerns."¹²¹ Finally, a group at the Goldman School of Public Policy at Berkeley has operated an online advice portal since April 2009. It has received no inquiries to date.¹²²

While disappointing, these results are not very surprising. They do, however, teach two important lessons. First, experiments of concern are very, very rare. Indeed, it has been estimated that experiments of concern account for just 0.03% of all molecular biology experiments.¹²³ This suggests that even very aggressive systems may not generate large numbers of reviews. Second, rank-and-file community members did not wait for government action. Instead, they established their own voluntary review systems. Section VIII will describe other instances in which synthetic biologists have moved faster and more decisively than regulators.

2007), <http://www.sciencemag.org/content/suppl/2007/06/05/316.5830.1432.DC1/Davidson-SOM.pdf>. There are several possible reasons for this divergence. First, SERCEB leaders have had more time for study and reflection than individual researchers. In this case, allowing the experiments to proceed was simply the best outcome. Second, SERCEB's leaders may have valued scientific freedom more than the average community member. This is plausible because researchers with strong views often self-select into leadership roles. Finally, SERCEB leaders may have been protecting the community from an externalities problem. Public controversy is expensive; therefore, investigators may sometimes suppress results even when publication is appropriate. In this view, SERCEB's strong defense of publication gave researchers the political cover they needed to make the right decision.

¹²¹ E-mail from Henry Metzger, Scientist Emeritus, Nat'l Inst. of Arthritis & Musculoskeletal & Skin Diseases, Nat'l Insts. of Health, to author (Mar. 9, 2011, 10:08 EST) [hereinafter Metzger E-mail] (on file with author).

¹²² Barry Bergman, *Goldman School Portal Takes the Worry Out of 'Experiments of Concern'*, THE BERKELEYAN, April 2, 2009, http://www.berkeley.edu/news/berkeleyan/2009/04/02_concern.shtml. Peter Aldhous, *Are Fears Over Bioterrorism Stifling Scientific Research?*, NEW SCIENTIST (Feb. 5, 2009), <http://www.newscientist.com/article/dn16539-are-fears-over-bioterrorism-stifling-scientific-research.html>. The facility will shut down in June 2011. Erika Check Hayden, *'Experiments of Concern' to Be Vetted On Line: Expert Panel to Offer Advice on Science with Bioterror Applications*, 457 NATURE 643, 643 (2009).

¹²³ Jeffrey Brainard, *Advisory Panel Proposes That Scientists Monitor Their Own Security-Related Research*, CHRON. HIGHER EDUC., April 20, 2007; see also STEINBRUNER ET AL., *supra* note 109, at 45 (arguing that experiments of concern account for well under one percent of all experiments).

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VI. CONTROLLING EXISTING TECHNOLOGY (A): CODES OF CONDUCT,
EDUCATION, AND TECHNICAL MEASURES

Most observers agree that existing synthetic biology technologies pose risks that justify at least modest control efforts. This Part reviews various measures, including codes of conduct, educational initiatives, and technology solutions that synthetic biologists have debated over the past decade. Efforts to control access to artificial DNA are discussed separately in Part VII.

A. *Codes of Conduct*

Professional societies have adopted several codes of conduct since the 1980s, which prohibit biologists from developing weapons. These efforts arguably intensified after 9/11.¹²⁴ By 2005, the World Medical Association, British Royal Society, Red Cross, UN General Assembly, UN Security Council, UK House of Commons Foreign Affairs Committee, Wellcome Trust, and sixty-eight national academies of science were calling on researchers to draft still more codes.¹²⁵ These calls were seconded in the United States by the National Research Council's high-profile Fink (2004)¹²⁶ and Relman (2006)¹²⁷ reports.

Against this background, synthetic biologists began discussing their own code as early 2003.¹²⁸ By 2005, many community members agreed that a code would be useful, although these discussions remained "fragmentary."¹²⁹ Furthermore, there were widespread expectations that SB2.0 would make "significant progress" on the issue when it met in 2006.¹³⁰ While these hopes turned out to be premature,¹³¹ community members and outside scholars have continued to call for a code ever since.¹³²

¹²⁴ See Brian Rappert, *Responsibility in the Life Sciences: Assessing the Role of Professional Codes*, 2 BIOSECURITY & BIOTERRORISM: BIODEFENSE STRATEGY, PRAC., & SCI. 164, 164-74 (2004) (discussing a detailed history of these efforts).

¹²⁵ *Id.*; see also INTERACADEMY PANEL ON INT'L ISSUES, IAP STATEMENT ON BIOSECURITY 2 (2005) (listing the organizations that endorse the call for researchers to draft more codes).

¹²⁶ FINK REPORT, *supra* note 38.

¹²⁷ COMM. ON ADVANCES IN TECH. & THE PREVENTION OF THEIR APPLICATION TO NEXT GENERATION BIOWAREFARE THREATS, NAT'L RESEARCH COUNCIL, GLOBALIZATION, BIOSECURITY, AND THE FUTURE OF THE LIFE SCIENCES (2006) [hereinafter RELMAN REPORT].

¹²⁸ See, e.g., Endy, *supra* note 28, at 5 ("As one obvious example, biological engineering training could include professional development programs and codes of ethics. . . .").

¹²⁹ Church, *supra* note 43, at 423.

¹³⁰ *Id.*

¹³¹ See *infra* Part VIII.A.

¹³² See e.g., EUROPEAN GRP. ON ETHICS IN SCI. & NEW TECHS. TO THE EUROPEAN COMM'N, OPINION NO. 25: ETHICS OF SYNTHETIC BIOLOGY (Nov. 17, 2009), available at

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Why, then, is there still no synthetic biology code? Professor Rappert argues that the problem is political. Calls for codes usually reflect a fragile alliance between researchers who care about security, and those who mainly want to preempt government action.¹³³ These groups almost always disagree as soon as the code project moves from generalities to specific “content or plans for promulgation.”¹³⁴ Rappert’s observation also explains why the written codes “are less consequential and compliance-oriented and more circular than they might appear at first glance.”¹³⁵

In 2004, the Fink Committee tried to sidestep this dynamic by asking the federal government to create an entirely new body – the NSABB – to make the hard choices that codes demand. However, the NSABB refused to grasp the nettle. Instead, it only produced what it called a “resource” that “scientific societies, professional associations, and research institutions” could use to write codes of their own.¹³⁶ While NSABB suggests that some of its “considerations” can be adopted verbatim, these are bland indeed.¹³⁷

In the meantime, the National Research Council’s Relman Committee in 2006 proposed a second way around the problem: create online forums where members can report problems, share best practices, and eventually write codes together.¹³⁸ Though the Committee did not say so, the tactic makes political sense because such forums will disproportionately attract scientists who sincerely care about reform. Forums also make practical sense. Synthetic biology is so new that researchers may not know enough to identify threats or design sensible

http://ec.europa.eu/european_group_ethics/docs/opinion25_en.pdf; RINIE VAN EST ET AL., RATHENAU INST., CONSTRUCTING A WORLD OF LIFE: THE WORLD OF SYNTHETIC BIOLOGY (2007).

¹³³ Rappert, *Responsibility*, *supra* note 124.

¹³⁴ *Id.* at 164.

¹³⁵ Brian Rappert, *Codes of Conduct and Biological Weapons: An In-Process Assessment*, 5 *BIOSECURITY & BIOTERRORISM: BIODEFENSE STRATEGY, PRAC., & SCI.* 145, 150 (2007).

¹³⁶ NSABB, *supra* note 112, at 28–29. The document also stressed proper communication, thereby implying that the security problem had as much to do with public perception as any actual threat. *Id.*

¹³⁷ The document urges researchers, *inter alia*, to “[c]onsider[]” whether their work could be misused, “[s]triv[e]” to design research that avoids dual-use concerns, “[w]eigh[] carefully” the benefits of the research against harms that could occur, and observe safe and ethical behaviors. *Id.* at 48. Similarly, it urges funding agencies to make sure that “appropriate systems are in place” to review experiments of concern and “[e]nsur[e] that both researchers and reviewers are knowledgeable of, and adhere to, all ethical, institutional, and legal requirements.” *Id.* at 48–49. The document does nothing to define these and similarly ambiguous terms. Nor does it explain how this framework would be applied to any specific example.

¹³⁸ RELMAN REPORT, *supra* note 127.

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solutions. Forums are a natural way to collect this information. Sadly, the Relman Committee's proposal was never implemented.¹³⁹

B. *How Useful Would It Be?*

Before leaving the subject, one should ask what purpose codes could serve. Here, the naïve view—that a rule against making biological weapons will suppress terrorism—is almost certainly wrong. Terrorists, after all, have extreme and very strong beliefs. Even if we admit that codes might influence the average person, their effect on terrorists is almost certainly negligible.

A more sensible justification is that most people, and Americans in particular, are reluctant to investigate and tell authorities about suspicious activities. Publicly affirming the value of whistleblowers could plausibly increase scientists' willingness to step forward. In principle, code adoption could also encourage scientists working in covert state weapons programs to defect.¹⁴⁰ As former Soviet weapons scientist Ken Alibek has stressed, it is hard to work for a biological weapons program when the world clearly despises such methods.

Beyond these limited examples, it is hard to know what purpose a biosecurity code would serve. Some activities, notably biosafety, lend themselves to the explicit, step-by-step instructions that codes provide. But few biosecurity tasks are like this.¹⁴¹ Instead, threats come in many different and often subtle forms. Here, a code's main function may be to remind researchers that they are not competent to judge biosecurity risk and should turn to outside experts when issues arise.¹⁴²

C. *Education*

Codes of conduct are only effective when researchers are able to recognize problematic experiments. However, empirical studies show

¹³⁹ The Sloan Foundation studied but ultimately rejected the forum idea based on survey evidence that synthetic biologists would not participate absent "the threat of government regulation or some other external pressure on the scientific community." Pearson, *supra* note 32, at 6.

¹⁴⁰ Codes will not, of course, encourage many scientists to defect. This may not matter, however, for covert state weapons programs that employ dozens and even hundreds of scientists, only one of whom must defect to reveal the secret.

¹⁴¹ One important exception, as we will see, is screening DNA orders for possible threat sequences. See *infra* Part VII (describing screening methods). This activity, however, is much too specialized to include in a community-wide synthetic biology code.

¹⁴² Such codes only make sense if the advice is actually obtainable. However, many researchers may have trouble locating qualified biosecurity experts. The Berkeley project has established its online advice portal to help fill this gap. See *supra* note 122 and accompanying text.

that life scientists know very little about dual-use issues.¹⁴³ The National Research Council's Fink and Relman Committees have both called for improved, and perhaps mandatory, biosecurity education to fill this gap.

In the meantime, some biologists moved forward with voluntary initiatives. For example, SERCEB had administered a dual-use training module to more than 450 scientists by 2007.¹⁴⁴ Similarly, NIH has repeatedly reminded its intramural researchers of dual-use issues, most recently in its Research Ethics Case Discussion exercise for 2009–2010.¹⁴⁵ Other groups that have developed education modules include the Federation of American Scientists, Bradford University, and the Center for Arms Control and Non-Proliferation.¹⁴⁶

Despite this, government has yet to say how much, if any, security education synthetic biologists should receive. In 2010, NSABB published a report chiding the U.S. federal government for its failure to implement an "oversight paradigm."¹⁴⁷ The report also called on government to develop "[o]utreach and education strategies" aimed at "raising awareness of the dual use issue among synthetic biology's diverse practitioners, especially among those that have not been participants in recent discussions on this topic."¹⁴⁸ HHS is currently considering regulations to implement some or all of these recommendations, although it is still not clear what will emerge.

D. Technical Measures

Given synthetic biology's strong focus on engineering, it was more or less inevitable that members would suggest technical measures to

¹⁴³ BRIAN RAPPERT, *BIOTECHNOLOGY, SECURITY AND THE SEARCH FOR LIMITS: AN INQUIRY INTO RESEARCH AND METHODS* (2007). SERCEB's in-house program for reporting and reviewing experiments of concern similarly found that "few investigators were aware of the dual-use dilemma," that "many investigators were unaware of dual-use issues in their own research," and that "sensitivity to dual-use concerns is highly subjective." Davidson et al., *supra* note 118, at 1432–33.

¹⁴⁴ Davidson et al., *supra* note 118, at 1433.

¹⁴⁵ Metzger E-mail, *supra* note 121.

¹⁴⁶ See *Biosecurity Education Portal*, FED'N AM. SCIENTISTS, <http://www.fas.org/programs/bio/educationportal.html> (last visited March 23, 2011).

¹⁴⁷ NAT'L SCI. ADVISORY BOARD FOR BIOSECURITY, *ADDRESSING BIOSECURITY CONCERNS RELATED TO SYNTHETIC BIOLOGY* iii (2010) [hereinafter NSABB, *ADDRESSING BIOSECURITY*], available at [http://oba.od.nih.gov/biosecurity/pdf/NSABB%20SynBio%20DRAFT%20Report-FINAL%20\(2\)_6-7-10.pdf](http://oba.od.nih.gov/biosecurity/pdf/NSABB%20SynBio%20DRAFT%20Report-FINAL%20(2)_6-7-10.pdf).

¹⁴⁸ *Id.* at 13. The reference "diverse practitioners" provides a broad hint that some groups—for example, mainstream biologists—may need less education than others. This foreshadows the Presidential Commission on Bioethics' more recent claim that synthetic biology's "culture of responsibility" is already adequate and that future initiatives should focus on extending it to other groups. See *infra* Part IX.C (describing the Commission's synthetic biology report).

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reduce risk. These have taken various forms. Probably the best-known idea has been to insert hidden (“steganographic”) messages, also known as watermarks, into gene sequences. This data would bolster deterrence by helping authorities trace DNA used in attacks back to its source. The idea has been current since 2002¹⁴⁹ and was widely discussed at SB1.0¹⁵⁰ and in the weeks preceding SB2.0.¹⁵¹ So far, however, it has yet to be implemented in practical experiments.

A second popular idea is to modify the “chassis” organisms that synthetic biologists use to host their designs so that they could not survive in the wild, were programmed to self-destruct after a fixed time, or included artificial genes that could not function in naturally occurring organisms.¹⁵² The Venter Institute took a first step in this direction by deliberately engineering its *Mycoplasma mycoides* bacterium so that the organism cannot cause disease in humans or survive outside the laboratory.¹⁵³

Finally, some synthetic biologists believe that customers will eventually be able to make genes on tabletop machines. In principle, these devices could be programmed so that they refused to make problematic sequences.¹⁵⁴

E. Conclusion

Despite extensive discussion, synthetic biologists have done relatively little to implement codes of conduct. They have, however, developed important voluntary review and education programs. HHS may eventually make some form of review and education mandatory.

VII. CONTROLLING EXISTING TECHNOLOGY (B): DENYING SYNTHETIC DNA TO TERRORISTS

The proposals so far would apply to almost any branch of microbiology. One issue, however, is specific to synthetic biology. We

¹⁴⁹ See Andrew D. Ellington, Intelligence Countermeasures for Biological Threats *passim* (2002) (unpublished manuscript) (on file with author) (discussing the use of “genetic taggants” within the context of biological terrorism).

¹⁵⁰ Carlson, *supra* note 42.

¹⁵¹ Stephen M. Maurer et al., *From Understanding to Action: Community-Based Options for Improving Safety and Security in Synthetic Biology* (Goldman Sch. of Pub. Policy, Working Paper Draft 1.1, 2006), available at <http://gspp.berkeley.edu/iths/UC%20White%20Paper.pdf>.

¹⁵² Church, *supra* note 43, at 423; Pennisi, *supra* note 45, at 769.

¹⁵³ Steinbruner & Harris, *supra* note 34.

¹⁵⁴ SCI. POLICY CTR., THE ROYAL SOC’Y, NEW APPROACHES TO BIOLOGICAL RISK ASSESSMENT 9 (2009).

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have seen that the synthetic biology revolution was built on cheap commercial sources of DNA. Denying this resource to would-be terrorists has become synthetic biology's most-discussed priority.¹⁵⁵

A. *Licensing*

The most obvious way to control synthetic DNA is to license the equipment and reagents that make it. Synthetic biologists discussed this option widely in the wake of 9/11,¹⁵⁶ and many scholars still endorse it today.¹⁵⁷ At the same time, implementation would require congressional action. This makes licensing politically unlikely, at least in the short term.

B. *Screening Technologies*

We have already seen that most commercial gene-makers began screening customer orders shortly after 9/11. However, these programs were developed in isolation and tend to be inconsistent. The basic issue is how much effort companies should invest before deciding that a particular order is legitimate. In practice, there are three choices: (1) human screening, (2) predefined threat lists, and (3) advanced software.

Despite differences in detail, most of today's gene-makers follow the first strategy—human screening. The process begins by having a computer compare the customer's order against the U.S. government's exhaustive Genbank database to find the nearest matches among reported genes. At this point, human experts examine each match's known function as reported in Genbank annotations or the underlying literature. These functions turn out to be problematic about one percent

¹⁵⁵ The Department of Energy's Gesteland Report had already noted in 2004 that synthetic biologists faced the special problem of "monitoring DNA sequences shipped from DNA synthesis facilities capable of producing large segments of DNA." BERAC, *supra* note 111, at 8.

¹⁵⁶ Carlson, *supra* note 42 ("Not for the first time in this circle did I hear suggestions of licensing for scientists and of strict controls on the distribution of technology and reagents."); *see also* Maurer et al., *From Understanding to Action*, *supra* note 151, at 18 (documenting prevalence of licensing idea among synthetic biologists in the 2005- 2006 time frame).

¹⁵⁷ *See, e.g.*, EUROPEAN GRP., *supra* note 132 (arguing that departments or research groups that use synthetic biology to perform biodefense experiments should be licensed and listed in a central registry); GARFINKEL ET AL., *supra* note 45 (describing options for registering synthesis machines and owners and people who purchase reagents); George Church, A Synthetic Bio-Hazard Non-Proliferation Proposal (Aug. 6, 2004) (unpublished manuscript), available at http://arep.med.harvard.edu/SBP/Church_Biohazard04c.doc (discussing licensing scheme for reagents and instruments).

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of the time. In such cases, companies must conduct further investigations to make sure that the sequence is being purchased for legitimate research. Companies typically do this by checking the customer's identity, asking about the proposed experiment, and, if necessary, consulting the authorities.¹⁵⁸

The current alternative to human screening relies on predefined lists. Instead of relying on employees to conduct research and make threat judgments after orders are received, companies could simply identify every Genbank threat in advance. Once this list existed, human experts could be safely replaced by computers. The problem, for now, is that existing threat lists are still painfully incomplete. This suggests that human screening will continue to outperform list-based systems for at least a decade.¹⁵⁹

Lastly, existing screening methods are based on comparing requested DNA against similar sequences with known functions. Some day scientists may be able to detect threats by inspecting the requested sequence itself. For now, this remains a distant goal.¹⁶⁰ That said, some researchers are writing advanced software to partially solve the problem. It is still not clear how well this will work.¹⁶¹

While human screening works best today, other methods could eventually overtake it. The real difference is economic. While human screening costs little on average, experts can and do spend up to two hours in individual cases. These costs are significant in an industry where the typical gene sells for about \$10,000. Automated solutions based on software or predefined lists would cut this cost nearly to zero.

C. Screening Goals

Over time, the debate over screening has come to include four sometimes incompatible goals. The first, and by far the most obvious, is security—i.e., protecting human and animal life from terrorism. This goal predominates in all public discussions and supplies the political pressure for regulation. Over time, however, various subsidiary considerations have crept in. The first involves companies' understandable desire to know when they have complied with U.S. law.

¹⁵⁸ See Maurer et al., *supra* note 1 (describing current industry screening practices).

¹⁵⁹ E-mail from Tom Slezak, Lawrence Livermore Nat'l Lab., to author (Mar. 1, 2011, 12:42 PST) (on file with author).

¹⁶⁰ COMM. ON SCIENTIFIC MILESTONES FOR THE DEV. OF A GENE SEQUENCE-BASED CLASSIFICATION SYS. FOR THE OVERSIGHT OF SELECT AGENTS, NAT'L RESEARCH COUNCIL, SEQUENCE-BASED CLASSIFICATION OF SELECT AGENTS: A BRIGHTER LINE (2010) [hereinafter SEQUENCE-BASED CLASSIFICATION].

¹⁶¹ See Maurer et al., *supra* note 1, at 24–25.

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While Congress's Select Agent statute clearly applies to DNA, it has never been clear which sequences are covered. Companies and regulators want to eliminate this ambiguity.¹⁶²

Relatedly, companies also prefer screening systems in which threat judgments are replicable. This goal is poorly served by human screeners who can and sometimes do draw different threat judgments from the same data. Some gene-makers have objected to this on the ground that threat judgments should be "consistent" from one company to the next.¹⁶³ The downside, of course, is that consistency is not accuracy. Indeed, a system could have a 100% error rate and still be consistent, provided it made the same mistakes every time.

Finally, companies would like to automate screening as much as possible. Large gene-makers, in particular, have invested heavily in automation that allows them to make DNA faster and cheaper than their competitors. Automated screening would enhance this advantage by eliminating the cost and delay associated with manual screening.

On balance, it seems clear that screening's original core purpose—biosecurity—favors solutions based on human screening. On the other hand, statutory compliance, consistency, and competitive considerations all favor automated screening. Government, industry, and academics have spent much of the past decade trying to balance these considerations.

D. (Mis-)Framing the Debate

This tradeoff between human and automated screening methods is surely fundamental. Strangely, however, most synthetic biology reports give human screening short shrift or overlook it entirely. Part of the problem has to do with how threats are defined. Historically, biosecurity professionals have almost always sided with the Relman Committee's judgment that policymakers need to be aware of non-Select Agent threats, including other naturally occurring pathogens and even synthetic organisms.¹⁶⁴ Furthermore, most synthetic biology studies have similarly embraced this position.¹⁶⁵ But this presents a problem.

¹⁶² See, e.g., Hans Bügl et al., *DNA Synthesis and Biological Security*, 25 NATURE BIOTECHNOLOGY 627, 628 (2007).

¹⁶³ See, e.g., Claes Gustafsson Presentation Slides, FBI "Building Bridges" Conference, San Francisco, Cal. (Aug. 4–5, 2009) (on file with the author). Gustafsson is DNA2.0's Vice President for Marketing.

¹⁶⁴ RELMAN REPORT, *supra* note 127; see also Eileen R. Choffnes et al., *A Brave New World in the Life Sciences: The Breadth of Biological Threats Is Much Broader Than Commonly Thought and Will Continue to Expand*, BULL. ATOMIC SCIENTISTS, Sept.–Oct. 2006, at 26–33 (arguing that the biosecurity threat is much broader than Select Agent organisms).

¹⁶⁵ See, e.g., Campos, *supra* note 1; SEQUENCE-BASED CLASSIFICATION, *supra* note 160.

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The reason is that broad threats imply extensive countermeasures. However, scholars have yet to develop any agreed or even intellectually coherent method for deciding which countermeasures are cost-effective.¹⁶⁶ This has tempted some analysts to simplify the problem by pruning the threat definition. Within synthetic biology, the Sloan Report seems to have been the first to pursue this tack:

Over the next five years, the key concern is for synthesis of a small number of highly pathogenic viruses that are otherwise difficult to obtain. Ten years from now, it may be easier to synthesize almost any pathogenic virus than to obtain it through other means. Eventually, the synthesis of bacterial pathogens may become possible as well.¹⁶⁷

The danger, of course, is that this approach makes the problem *too* manageable. After all, a threat that can be reduced to “a small number of [known] viruses” implies that predefined lists are feasible.¹⁶⁸ If so, the main strength of human solutions—flexibility in the face of unforeseen threats—vanishes.

Is this truncation legitimate? Here, everything hinges on the Report’s judgment that viruses are the only “key concern.”¹⁶⁹ Because the authors do not explain this choice, their reasoning is necessarily speculative. On the one hand, one can plausibly argue that “a small number of highly pathogenic viruses” really do pose a greater threat than other concerns.¹⁷⁰ On the other hand, this hardly justifies ignoring other, assertedly lesser threats. Security scholars have spent the past two decades warning against genetically engineered threats that range from inserting a single gene (e.g., to confer vaccine resistance on existing weapons) to massively reengineering entire genomes (e.g., to confer virulence on normally benign organisms). Synthetic DNA makes all of these experiments enormously easier and may put them within the reach of terrorists. In principle, this risk might be excludable on cost-benefit grounds. Such a judgment would, however, invite a much more detailed

¹⁶⁶ See, e.g., Thomas Edmunds & Richard Wheeler, *Setting Priorities: Assessing Threats and Identifying Cost-Effective Responses to WMD Terrorism*, in *WMD TERRORISM: SCIENCE AND POLICY CHOICES* 191–210 (Stephen M. Maurer ed., 2009).

¹⁶⁷ GARFINKEL ET AL., *supra* note 45, at 13.

¹⁶⁸ *Id.*

¹⁶⁹ *Id.*

¹⁷⁰ *Id.* Smallpox, uniquely among existing biological weapons, could plausibly inflict hundreds of thousands of casualties. See, e.g., Rutherford & Maurer, *supra* note 6, at 122–27.

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and probably inconclusive debate. On closer examination, then, the Sloan Report's truncation is not very satisfying.¹⁷¹

Alas, truncation is not the only problem. In most cases, the literature fails to mention human screening at all.¹⁷² Indeed, some scholars do not seem to realize that human screening is even an option.¹⁷³ In hindsight, there are probably three reasons for this. First, automated solutions are technological. This makes them fun to think and write about. By comparison, human screening methods are prosaic and make for uninteresting reading. Second, most studies conventionally assume that concrete action will take place five or ten years into the future. This encourages scholars to stress what automated systems might do in the future¹⁷⁴ instead of asking what human screening can actually do today. Finally, we have seen some synthetic biologists argue that human screening is unaffordable. Although this argument is doubtful, no one seems to have performed a careful analysis before 2009.¹⁷⁵

E. Conclusion

The synthetic biology community has invested enormous time and effort in studying the screening problem. Despite this, most of the

¹⁷¹ This is not really surprising, because any detailed justification would have to invoke the same kinds of cost-benefit calculus that the Report's "key concept" rhetoric is supposed to avoid.

¹⁷² The author does not know of a single article or report that focuses on the fundamental choice between human screening and automated methods prior to 2008. Human screening was not even mentioned in the exhaustive and widely influential Sloan Report. See generally GARFINKEL ET AL., *supra* note 45. Nor did the author mention human screening in his own report for SB2.0. Maurer et al., *From Understanding to Action*, *supra* note 151. Looking back, the problem may have been that academic security discussions invariably assumed that screening was a theoretical subject. This overlooked the fact that most synthetic gene-makers had operated screening programs for years and knew a great deal about the problem. This only became evident to the author once he began interacting with Markus Schmidt and other industry executives in early 2008. The fact that many prominent gene companies, most notably DNA2.0, were lobbying the government for automated standards deepened the confusion.

¹⁷³ See, e.g., EUROPEAN GRP., *supra* note 132, at 44 ("There have been suggestions that these companies screen all sequences for toxicity or infectivity before processing an order. That implies that databases of toxic or infective DNA sequences are available."); NEW & EMERGING SCI. & TECH., EUROPEAN COMM'N, SYNTHETIC BIOLOGY: APPLYING ENGINEERING TO BIOLOGY 18 (EUR 21796) (2005) [hereinafter NEST-EUROPEAN COMM'N], available at ftp://ftp.cordis.europa.eu/pub/nest/docs/syntheticbiology_b5_eur21796_en.pdf (last visited March 25, 2011) (stating that order screening "will require a genomic databank of potential pathogenic microorganisms and viruses, toxic genes and gene circuits").

¹⁷⁴ The Department of Homeland Security also commissioned Gryphon Scientific's Rocco Petrone to write a report surveying industry screening practices. The document has never been made public.

¹⁷⁵ See Maurer et al., *supra* note 1, at 9-12.

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literature either overlooks or fails to mention the fundamental choice between human screening and automated solutions. This loss of focus has, in turn, encouraged scholars and regulators to devote almost all of their attention to automated solutions that are far less capable than the human screening methods that most gene-makers already use today.

VIII. TAKING ACTION

By early 2006, most synthetic biologists agreed that artificial gene-makers should screen customer orders for potential threat sequences.¹⁷⁶ The question was how to put this instinct into practice. In the end, the community tried three different tracks: government regulation, private industry standards, and academic self-regulation.¹⁷⁷

A. *Academic Self-Governance*

SB1.0 highlighted security issues and fed expectations that SB2.0 would take concrete action.¹⁷⁸ The question remained, however, what academics could meaningfully do to improve security. Here, the obvious “Asilomar” model was to lobby the government for regulation. However, some community members realized that direct action was also possible. As early as 2003, Professor Drew Endy pointed out that academics could refuse to do business with gene synthesis houses unless they “[could] assure us that [they were] not synthesizing known threat agents.”¹⁷⁹ Given the synthetic biology community’s purchasing power and moral authority, this tactic would exert significant pressure on companies to screen. In late 2005, the University of California, Berkeley project began interviewing synthetic biologists to identify still more ideas that could be implemented by a community-wide vote at SB2.0. In

¹⁷⁶ See Maurer et al., *From Understanding to Action*, *supra* note 151, at 14 (reporting that nineteen of the twenty-one synthetic biologists interviewed agreed on the need for screening).

¹⁷⁷ The academic, commercial, and government channels were almost entirely independent. That said, many leading figures participated in more than one track. For example, many academic scientists were associated with startup companies while most large gene-makers participated in both private and government standard setting. The result was that actors who failed to get their way in one channel could and did try to obtain different outcomes elsewhere.

¹⁷⁸ Church, *supra* note 43, at 423. *But see Futures of Artificial Life*, 431 NATURE 613, 613 (2004) (“[T]here is no plan as yet for anything like another Asilomar.”).

¹⁷⁹ Endy, *supra* note 28, at 5. Endy’s group later carried the procedure into practice. See Editorial, *The Peril of Genes for Sale*, NEW SCIENTIST, Nov. 12, 2005, at 5, available at http://www.precaution.org/lib/05/genes_for_sale.051112.htm (reporting that Endy’s MIT lab only does business with companies “that operate transparent procedures for screening gene-synthesis orders for potential bioweapons”).

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the end, the project compiled six resolutions that appeared to be both feasible and popular:

1. *Mandatory Screening.* The community could urge gene synthesis companies to screen according to prevailing best practices. Community members would stop placing orders with any company that failed to comply by year's end.
2. *Improved Screening.* The community could work to develop better screening tools. Members would "review and endorse these products" when they met the following year for SB 3.0.¹⁸⁰
3. *Establishing Norms: Obtaining Advice.* The community could remind members considering experiments of concern of their obligation to obtain "expert independent advice before proceeding." The community would make this advice available to anyone who needed it.¹⁸¹
4. *Establishing Norms: Investigating and Reporting Dangerous Behavior.* The community could remind members that they had "an ethical obligation to investigate and, if necessary, report" dangerous behavior to authorities.¹⁸²
5. *Clearinghouses.* Members could establish a "confidential clearinghouse[]" to collect, analyze, and disseminate" experiences and information about biosecurity risk.¹⁸³
6. *Technical Solutions.* Members could urge funding agencies to explore technologies for (a) inserting data into DNA identifying the maker ("watermarking"), and (b) engineering host organisms that had "little or no chance of surviving" outside the laboratory ("inherently safe chasses").¹⁸⁴

In early 2006, community members discussed these proposals in two town hall meetings webcast from Berkeley, California and Cambridge, Massachusetts.¹⁸⁵ The roughly three-dozen attendees voted to debate the first four resolutions at SB2.0.

This success was short-lived. A few weeks before the conference, organizers convened a telephone meeting that decided against holding the scheduled vote after all.¹⁸⁶ The reasons for this about-face were never announced. Conversations with attendees, however, suggest that the

¹⁸⁰ Maurer et al., *From Understanding to Action*, *supra* note 151, app. A at 4.

¹⁸¹ *Id.*

¹⁸² *Id.*

¹⁸³ *Id.* app. A at 5

¹⁸⁴ *Id.*

¹⁸⁵ *Id.* at 3.

¹⁸⁶ Apart from the two organizers, none of the attendees were synthetic biologists.

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decision was motivated by concerns that SB2.0 had no constitutional procedure for voting, that a vote might split the community, and that a vote might invite public controversy.¹⁸⁷ This decision was later reinforced when thirty-five activist groups wrote to conference leaders demanding that the previously announced vote be canceled.¹⁸⁸

Members of the press attending SB2.0 was quick to note what had happened. For example, *New Scientist* explained that SB2.0 had rejected the proposals because they were “controversial” and “too much for synthetic biologists themselves.”¹⁸⁹ It also suggested that some participants thought that it was too early to act until more research had been done on screening and other options.¹⁹⁰ Similarly, *Science* remarked that SB2.0 “only took baby steps toward self-regulation.”¹⁹¹

Organizers softened this disappointment by offering the press an online Declaration¹⁹² in place of the promised vote. This generally followed the original conference proposals by promising (a) to “support the organization of an open working group,” (b) to coordinate improved and freely available software tools for screening, (c) to encourage companies to adopt “best-practice sequence checking technology,” and (d) to “encourage individuals and organizations to avoid patronizing companies that do not systematically check their DNA synthesis

¹⁸⁷ See Stephen M. Maurer & Laurie Zoloth, *Synthesizing Biosecurity*, BULL. ATOMIC SCIENTISTS, Nov.-Dec. 2007, at 16-18.

¹⁸⁸ *Backgrounder: Open Letter on Synthetic Biology*, ETC GROUP (May 17, 2006), <http://www.etcgroup.org/en/node/11>. There is an urban legend that synthetic biologists dropped their plans for self-regulation because of this e-mail. See, e.g., de Vriend, *supra* note 46, at 65 (“[T]he organizers . . . were sensitive to critical comments of various participants and the NGO letter. This has most likely contributed to the decision not to vote on a common statement on the third day of the conference in May 2006.”). In fact, the decision had already been taken weeks earlier.

¹⁸⁹ Peter Aldhous, *Synthetic Biologists Reject Controversial Guidelines*, NEW SCIENTIST (May 23, 2006), <http://www.newscientist.com/article/dn9211-synthetic-biologists-reject-controversial-guidelines.html>.

¹⁹⁰ *Id.* The article gives a useful cross section of what attendees were thinking: But in the end, the proposal proved too much for synthetic biologists themselves. Some argued that it is too early to boycott gene synthesis firms, as it is not yet clear how best to screen for sequences that might be used to make a bioweapon. Also, they say, there are currently no clear channels through which dangerous experiments could be reported. The meeting declaration, due to be released later this week, will instead pledge to help develop software and other tools to improve companies’ ability to identify orders for potentially dangerous DNA.

Id.

¹⁹¹ Service, *supra* note 25, at 1116.

¹⁹² See *Declaration of the Second International Meeting on Synthetic Biology*, SYNTHETICBIOLOGY.ORG (2006), <http://syntheticbiology.org/SB2Declaration.html>.

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orders.”¹⁹³ Ironically, the Declaration was never finalized. This, however, has not stopped scholars from citing it as an authoritative statement by the community.¹⁹⁴ More importantly, it seems to have encouraged work on improved screening technologies that might not otherwise have taken place.¹⁹⁵

Despite the Declaration, scholars have quite reasonably seen SB2.0's self-governance initiative as a “failed attempt.”¹⁹⁶ Certainly, synthetic biologists have tried nothing of the sort since. There are at least three reasons for this. First, modern academic communities lack any deep tradition of self-governance.¹⁹⁷ Absent Carnegie support, it is doubtful that SB2.0 would have attempted a vote in the first place. Second, SB2.0 showed members how easily a vote can be derailed. This was bound to deter future organizers. Third, the same activists who opposed governance at SB2.0 were later invited to attend SB3.0 and organize a session at SB4.0.¹⁹⁸ This gave them a much improved platform for blocking community self-governance in the future.

¹⁹³ *Id.* The document also supported further discussions about “challenges to biological security and biological justice.” *Id.*

¹⁹⁴ See, e.g., ANDREW BALMER & PAUL MARTIN, INST. FOR SCI. & SOC'Y, SYNTHETIC BIOLOGY: SOCIAL AND ETHICAL CHALLENGES (2008), available at http://www.synbiosafe.eu/uploads///pdf/synthetic_biology_social_ethical_challenges.pdf; Bügl et al., *supra* note 162, at 627-29 (announcing collaboration to implement the Declaration); Alexander Kelle, *Synthetic Biology and Biosecurity: From Low Levels of Awareness to a Comprehensive Strategy*, 10 EMBO REPS. S23 (2009), available at <http://www.nature.com/embor/journal/v10/n1s/pdf/embor2009119.pdf>.

¹⁹⁵ Kelle, *supra* note 194. The Declaration promised that “an open working group” would improve the “existing software tools for screening DNA sequences.” *Id.* at S25. This was done although no software was ultimately produced. Perhaps more importantly, the Declaration kept the screening issue alive. This indirectly contributed to later industry initiatives. See *infra* Part VIII.B (discussing the development of industry standards).

¹⁹⁶ ERIK PARENS ET AL., WOODROW WILSON INT'L CTR. FOR SCHOLARS, ETHICAL ISSUES IN SYNTHETIC BIOLOGY: AN OVERVIEW OF THE DEBATES 12 (2009), available at <http://www.synbioproject.org/process/assets/files/6334/synbio3.pdf>. But see Service, *supra* note 25, at 1116 (quoting Harvey Rubin as stating that the Declaration was “a good thing to start with”).

¹⁹⁷ Biology's most widely advertised example of self-governance, the Asilomar conference, had taken place more than a quarter century before. Furthermore, most of its self-governance had consisted of petitioning the U.S. government for regulation, although members did agree to a voluntary interim moratorium on experiments. See, e.g., ORG. COMM. FOR THE INT'L CONFERENCE ON RECOMBINANT DNA MOLECULES, SUMMARY STATEMENT OF THE ASILOMAR CONFERENCE ON RECOMBINANT DNA MOLECULES 1, 10 (1975), http://profiles.nlm.nih.gov/qq/B/C/G/D/_/qqbcgd.pdf (recommending safety measures, describing ongoing “pause in certain aspects of research,” and noting efforts by national bodies “[i]n many countries” to formulate codes of practice).

¹⁹⁸ Strangely, the activists came to see their participation at these conferences as an achievement in its own right:

Astonishingly ETC Group and friends are on the agenda too. On Saturday we will be running a panel on the Global Societal Impacts of

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It is hard to know when a process is completely moribund. Certainly, one can imagine academic self-governance reemerging in, for example, some future professional society expressly set up for that purpose. For now, however, no such body is in the works. Indeed, recent claims that a consensus exists within synthetic biology have been careful to avoid anything resembling an open vote.¹⁹⁹

B. Industry Standards

A few weeks after SB2.0, four big gene synthesis companies—Genearth, Codon Devices, Blue Heron, and Codagenomics—announced a new International Consortium for Polynucleotide Synthesis (“ICPS”) whose members would “work together to develop technologies that improve safety and security in synthetic biology.”²⁰⁰ Shortly thereafter, six ICPS members coauthored an article in *Nature Biotechnology* along with four FBI agents, two academics, and two non-ICPS business executives announcing what they called “a process for developing effective governance of DNA synthesis technology.”²⁰¹ What this process consisted of, exactly, was unclear. Indeed, ICPS was careful to say that its two main tasks—developing minimum standards for screening and reporting and conducting future research to improve software to reduce false positives and handle higher volumes—were “unresolved issues.”²⁰² By comparison, the article was very explicit

Synthetic Biology along with some civil society colleagues In some ways its [sic] a far cry from two years ago when civil society was turned away from the same Syn Bio confab meeting in California. On that occasion we had to resort to an open letter to prevent a disastrous self governance proposal going ahead.

Hanging in Hong Kong with the Syn Bio Crowd, ETCETERA BLOG (Oct. 10, 2008), <http://etcblog.org/2008/10/10/hanging-in-hong-kong-with-the-syn-bio-crowd/>.

Ironically, the blogger also complains that “meaningful progress on establishing accountable oversight of Synthetic Biology has stalled and doesn’t look likely to start moving again any time soon.” *Id.* The complaint carefully ignores ETC’s own role in blocking self-regulation at SB2.0.

¹⁹⁹ The trend is particularly apparent in the EU-funded SYNBIOSAFE project, which conducted extensive interviews and an online conference to find out what synthetic biologists think. The group then argued that it had found various “consensus” positions without, however, asking synthetic biologists to endorse them. The supposed consensus was roundly criticized by audience members at SB4.0.

²⁰⁰ *About the ICPS*, INT’L CONSORTIUM FOR POLYNUCLEOTIDE SYNTHESIS, <http://polysynth.info/> (last visited June 20, 2007) (on file with author) (stating that ICPS goals include “work[ing] with governmental organizations to help facilitate the creation of a governance framework and associated safety protocols to foster an appropriate regulatory environment for the synthetic biology industry”).

²⁰¹ Bügl et al., *supra* note 162, at 627. The four FBI agents participated as coauthors in their “individual” capacities. *Id.* at 628.

²⁰² *Id.* at 629.

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about what the authors did not want. In particular, it insisted that any eventual screening regime should impose, at most, a “modest cost and with little or no impact on delivery times.”²⁰³ The authors justified this demand with the familiar argument that regulation would drive gene synthesis overseas.²⁰⁴

These constraints clearly ruled out human screening. Instead, the authors predicted a regime in which “companies would use validated software tools to check synthesis orders against a set of select agents or sequences to help ensure regulatory compliance and flag synthesis orders for further review.”²⁰⁵ Companies would pay for this ICPS-approved software through licensing fees.²⁰⁶ In the end, none of this mattered. In the summer of 2009, ICPS quietly folded without producing any software.

One might have thought that this was the end of the story. In fact, industry was just getting started. In April 2008, the International Association Synthetic Biology (“IASB”), Germany’s leading trade association, hosted a workshop to discuss practical steps that industry could take to improve biosecurity.²⁰⁷ Participants publicly promised to move forward with a slate of specific “work packages” including: (a) a

²⁰³ *Id.* at 628.

²⁰⁴ *Id.* at 628–29. The article also rejected previous suggestions that gene-makers pool customer order data in a central repository. This was said to be “impractical and ineffectual” although no reasons were given. *Id.* at 629.

²⁰⁵ *Id.* at 627 (caption to Figure 1).

²⁰⁶ Significantly, the authors said nothing about how their scheme would impact competition. ICPS’s Membership Agreements strongly suggest that the organization planned to earn substantial license revenues from non-ICPS members. *See, e.g.*, Int’l Consortium for Polynucleotide Synthesis, Director Membership Agreement (Aug. 13, 2007) (on file with author) (recognizing that ICPS holds “all right, title, and interest in and to any and all software and documentation created or developed, and in and to all patentable inventions conceived or first reduced to practice solely by the Consortium, its employees, or consultants”). Strangely, U.S. authors have hardly ever analyzed the antitrust implications of this scheme. For a European perspective, see NEST-EUROPEAN COMM’N, *supra* note 173 (arguing that European database laws should be invoked to override copyright laws that deny access to lists needed to screen) and Anna Deplazes et al., *The Ethics of Synthetic Biology: Outlining the Agenda*, in *SYNTHETIC BIOLOGY*, *supra* note 1, at 5.

²⁰⁷ *See* HUBERT BERNAUER ET AL., INT’L. ASS’N SYNTHETIC BIOLOGY, TECHNICAL SOLUTIONS FOR BIOSECURITY IN SYNTHETIC BIOLOGY (2008), http://www.ia-sb.eu/tasks/sites/synthetic-biology/assets/File/pdf/iasb_report_biosecurity_syntheticbiology.pdf.

Workshop participants included representatives from Eurofins MWG, Sloning, ATG Biosynthetics, Febit, Entelechon GmbH, TESSY, Information Services to Life Science, Geneart, Craic Computing, and Integrated DNA Technologies, Inc. The first seven companies were IASB members. *Id.* at 3. Geneart, Craic, and IDT were ICPS members and initially suggested that ICPS might join in the report. The idea was dropped when ICPS disbanded later that summer.

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Code of Conduct specifying responsible screening practices;²⁰⁸ (b) an online platform that would allow member companies to share threat data (“VIREP”); (c) a white paper discussing current industry practice with respect to screening; and (d) a Technical Biosecurity Group to share information and further develop best practices.²⁰⁹ IASB began work on all but the last of these initiatives within a few months. By early 2009, IASB’s Code initiative had been singled out for praise in the pages of *Nature*²¹⁰ and was being actively tracked by actors ranging from the U.S. State Department to diplomats attending biological weapons talks in Geneva.

By mid-2009, the draft Code was largely complete. That July, IASB announced that it would host a meeting in Cambridge, Massachusetts to finalize the document. So far, so good. In August, however, two big gene-makers, DNA2.0 and Genent, hastily assembled a competing proposal.²¹¹ Unlike IASB’s Code, the new proposal was based on using a predefined list. This made it, as its authors boasted, “fast” and “cheap.”²¹² The question, as with all list-based proposals, was completeness. This judgment, however, could not be made since DNA2.0’s list was, and is, secret.²¹³ In any case, the proposal did not last very long. In September, *Nature* reported that a “standards war” had broken out between IASB and the Genent/DNA2.0 coalition.²¹⁴ DNA2.0 and Genent stopped mentioning their fast and cheap proposal shortly afterward.

They did not, however, abandon the standards war. Instead, they approached three other big U.S. gene-makers to develop a new and, as it turned out, much stronger standard. Over time, these secret discussions led to an agreement and self-styled “Consortium.”²¹⁵ Collectively, this new group claimed to represent about eighty percent of the industry’s

²⁰⁸ IASB’s Code should not be confused with the codes for governing general professional behavior described in Part VI. Instead, it was limited to defining a specific task in detail. It probably would have been more accurate to call IASB’s document a protocol instead. This usage was eventually taken up by a later competing document in November 2009. See *infra* notes 219–21.

²⁰⁹ BERNAUER ET AL., *supra* note 207, at 16–18.

²¹⁰ See Editorial, *Pathways to Security*, 455 NATURE 432, 432 (2008) (praising IASB’s Code initiative as “laudable”).

²¹¹ DNA2.0 Presentation Slides, FBI “Building Bridges Conference,” San Francisco, Cal. (Aug. 4–5, 2009) (on file with the author).

²¹² *Id.*

²¹³ More recently, DNA2.0 has said that a list exists but is secret. May, *supra* note 49.

²¹⁴ Erika Check Hayden, *Keeping Genes Out of Terrorists’ Hands*, NATURENEWS (Aug. 31, 2009), <http://www.nature.com/news/2009/090831/full/461022a.html>.

²¹⁵ DNA2.0 later described the discussions as a “secret pact.” Daniel Grushkin, *Synthetic Bio, Meet “FBio,”* SCIENTIST, May 2010, at 44, available at <http://www.the-scientist.com/article/display/57355/>.

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worldwide installed capacity.²¹⁶ Unlike the IASB, this new alliance was closed to all but the largest gene-makers.²¹⁷ This was done, according to one member, to maintain a big company “perspective about the scale of the gene-synthesis industry, which helps us to decide what are practically implementable decisions.”²¹⁸ Closed membership also meant that Consortium members could make decisions without exposing themselves to criticism from other companies or the public at large.

IASB held its Cambridge meeting as scheduled on November 3, 2009.²¹⁹ Unlike the Consortium, the proceedings were open. Indeed, representatives of the U.S. government, the press, and even two Consortium members, Geneart and Blue Heron, attended.²²⁰ Most of the session was devoted to careful line-by-line revisions of the draft. Members then finalized the document and took it back to their respective companies for ratification. By month’s end, eight companies had signed the document. Significantly, this figure included two Shanghai-based gene-makers that had not previously been involved in the process.²²¹

At first, Consortium members were non-committal and suggested that they, too, might join the IASB standard.²²² Three weeks later, however, they announced a competing “Harmonized Protocol” document. This puzzled many observers because the Protocol—though couched in entirely new language—mirrored the IASB Code point-for-point, most notably in its commitment to human screening.²²³ Creating a

²¹⁶ INT’L GENE SYNTHESIS CONSORTIUM, HARMONIZED SCREENING PROTOCOL: GENE SEQUENCE & CUSTOMER SCREENING TO PROMOTE BIOSECURITY 1, http://www.genesynthesisconsortium.org/Harmonized_Screening_Protocol_files/IGSC%20Harmonized%20Screening%20Protocol.pdf.

²¹⁷ Erika Check Hayden, *Gene-makers Form Security Coalition*, NATURENEWS (Nov. 18 2009), <http://www.nature.com/news/2009/091118/full/news.2009.1095.html>.

²¹⁸ *Id.* (quoting DNA2.0 President Jeremy Minshull).

²¹⁹ Geneart representatives asked IASB to cancel the vote at the last moment, arguing that the big companies were working on a standard that the entire industry could use. This suggestion had essentially no chance of being adopted because Consortium members refused to let IASB members attend, much less vote at their meetings.

²²⁰ Corie Lok, *Gene-makers Put Forward Security Standards*, NATURENEWS (Nov. 4, 2009), <http://www.nature.com/news/2009/091104/full/news.2009.1065.html>.

²²¹ *Code of Conduct for Best Practices in Gene Synthesis*, INT’L ASS’N SYNTHETIC BIOLOGY, <http://www.ia-sb.eu/go/synthetic-biology/activities/press-area/press-information/code-of-conduct-for-best-practices-in-gene-synthesis/> (last visited Apr. 28, 2011). Probably the most important compromise was to limit human screening to matches drawn from bacteria and viruses. This was based on a judgment that current technology could not make weapons from other organisms in any case. The compromise allowed computers to prescreen ninety-nine percent of all orders automatically. The compromise was proposed by the U.S.-based Synthetic Biology Industry Association, which later endorsed the Code.

²²² Lok, *supra* note 220.

²²³ IGSC promised to use “automated screening as a filter to identify pathogen and toxin DNA sequences.” HARMONIZED SCREENING PROTOCOL, *supra* note 216, at 2. All of these

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parallel standard did, however, let Consortium members avoid open meetings and power-sharing with IASB.²²⁴ This was important because Consortium members had explicitly retained the right to change the Protocol in the future.²²⁵

Even so, the Consortium's decision to create a redundant standard was only a detail. Between the Code and Protocol, more than eighty percent of all gene-makers had now endorsed human screening. This, in turn, put even more pressure on the industry's remaining hold-outs to adopt one standard or the other. At this point, it was reasonable to think that the dominoes would continue falling until the entire industry had adopted human screening.

It was not to be. On November 28th, the U.S. government issued draft guidelines for screening. Unlike the two private standards, this official document suggested that a predefined list might be good enough after all. Not surprisingly, commercial gene-makers reacted to this announcement by adopting a wait-and-see attitude. No new companies have joined the Code or Protocol since then.

C. Government Regulation

The U.S. government's draft guidelines had been a long time coming. Five years earlier, the National Research Council's Fink Committee had called for a new body that could advise the federal government on the need for regulation. The Bush Administration duly created the National Scientific Advisory Committee for Synthetic Biology ("NSABB") in 2005. One of the Committee's first projects was to write a report urging the U.S. government to develop a process that private synthetic gene companies could use to screen incoming orders.²²⁶ Strikingly, the report stressed that these standards should address all threat sequences whether or not they were associated with Select Agents.²²⁷ Beyond this, however, the report said almost nothing about

would then be reviewed by "a human expert." *Id.* IASB members had similarly agreed to permit an automated prescreen several weeks earlier. *See supra* note 208 and accompanying text.

²²⁴ The depth of this feeling is reflected in Consortium members' consistent refusal to mention IASB and its Code of Conduct in any article or public talk. This is more than a little strange, because the Consortium Protocol was clearly drafted in response to IASB's Code. Consortium members' silence has caused endless confusion by leading casual observers and some journalists to conflate the Consortium Protocol with the IASB's Code.

²²⁵ HARMONIZED SCREENING PROTOCOL, *supra* note 216, at 4.

²²⁶ *See* NSABB, ADDRESSING BIOSECURITY, *supra* note 147, at 8. Gene-makers who failed to adopt the standards would be barred from doing business with federal grantees or contractors. *Id.* at 11.

²²⁷ *See id.* (providing that federal regulations should apply to all threat pathogens whether "Select Agents or otherwise"). NSABB also called on government agencies to

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what the federal regulations would look like. Worse, it failed to mention the fundamental choice between human screening and automated solutions.²²⁸

In March 2007, the U.S. government convened an interagency Task Force under HHS's leadership to develop formal regulations.²²⁹ In retrospect, this stacked the deck against strong regulation. Indeed, HHS later admitted that any regulation "much more onerous than what providers are currently doing . . . might be of some concern."²³⁰ This position was peculiar, to say the least. After all, the normal assumption is that regulation is necessary because industry has done too little. Here, however, HHS was deliberately treating current industry efforts as a ceiling for regulation. This implied that government regulation could at most harmonize, not raise, the existing level of effort.

The fact that human screening was a practical option should have been obvious, at the latest, when IASB issued its first draft Code of Conduct in September 2008. In practice, however, HHS paid little or no attention to private standards until DNA2.0 and Genent announced their fast and cheap alternative in August 2009.²³¹ Even then, federal officials praised both sides without addressing the fundamental choice between human screening and automated methods.

As already discussed, the great majority of gene synthesis companies embraced human screening standards in November 2009. By then, however, the federal government had invented a very different approach. HHS published this "Best Match" standard on November 27, 2009.²³² It required companies to investigate gene sequences if, and only if, they were closer to genes associated with Select Agents than to any other organism found in Genbank.²³³ The great advantage of Best Match was, of course, that it could be readily automated. At the same time, HHS knew that the Select Agent list did not begin to cover the spectrum

"develop and promote standards and preferred practices for screening orders and interpreting the results, and require that orders be screened by providers." *Id.*

²²⁸ To the contrary, the report seemed to endorse automated solutions by urging the government to develop standards for "determining the sequences for which to screen." *Id.* This was, at the very least, a revealing slip of the pen.

²²⁹ DEP'T OF HEALTH & HUMAN SERVS., SCREENING FRAMEWORK GUIDANCE FOR PROVIDERS OF SYNTHETIC DOUBLE-STRANDED DNA 1 (2010) [hereinafter HHS, SCREENING FRAMEWORK], available at <http://www.phe.gov/Preparedness/legal/guidance/syndna/Documents/syndna-guidance.pdf>.

²³⁰ Wadman, *supra* note 55 (quoting Jessica Tucker).

²³¹ The Task Force was briefed on IASB's activities as early as September 2008.

²³² See Screening Framework Guidance for Synthetic Double-Stranded DNA Providers, 74 Fed. Reg. 62,319, 62,319-27 (Nov. 27, 2009) (discussing the Best Match standard).

²³³ *Id.* at 62,323.

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of possible threats and that Best Match had no chance of detecting them.²³⁴ Only human screeners could do that.

D. Harmonizing Outcomes

HHS did not finalize its Guidelines for nearly a year. During that time, several scholars published articles complaining that Best Match did nothing to detect threats beyond the Select Agent list and was less capable than the private standards that industry had already adopted.²³⁵ Formally, HHS could easily have closed this gap by adding a human screening requirement to Best Match. It did not. HHS did, however, revise the Guidelines in important ways. The original draft had claimed to implement the broad principle that “[p]roviders should know if the nature and identity of the product that they are selling poses a hazard to public health, agriculture, or security.”²³⁶ This implied that companies could meet all of their biosecurity obligations by adopting Best Match. The final Guidelines, by comparison, were limited to the much narrower principle that “[p]roviders should know if the product that they are synthesizing and distributing contains . . . a ‘sequence of concern.’”²³⁷ While HHS admitted that non-Select Agents also posed a biosecurity threat,²³⁸ the final Guidelines said nothing about how to screen for them

²³⁴ The clearest admission is found in the final Guidelines:

The U.S. Government recognizes that there are concerns that synthetic dsDNA sequences not unique to the Select Agents or Toxins or CCL items may also pose a biosecurity concern. . . . However, due to the complexity of determining pathogenicity and because research in this area is ongoing and many such agents are not currently encompassed by regulations in the U.S., generating a comprehensive list of such agents to screen against is not currently feasible and hence is not provided in this *Guidance*.

HHS, SCREENING FRAMEWORK, *supra* note 229, at 9.

²³⁵ See, e.g., Markus Fischer & Stephen M. Maurer, *Harmonizing Biosecurity Oversight for Gene Synthesis*, 28 NATURE BIOTECHNOLOGY 20 (2010); Jonathan B. Tucker, *Double-Edged DNA: Preventing the Misuse of Gene Synthesis*, ISSUES SCI. & TECH., Spring 2010, at 23, available at <http://www.issues.org/26.3/tucker.html>; Malcolm Dando, *Synthetic Biology: Harbinger of an Uncertain Future?*, BULL. ATOMIC SCIENTISTS (Aug. 16, 2010), <http://www.thebulletin.org/web-edition/columnists/malcolm-dando/synthetic-biology-harbinger-of-uncertain-future>.

²³⁶ Screening Framework Guidance for Synthetic Double-Stranded DNA Providers, 74 Fed. Reg. at 62,320.

²³⁷ HHS, SCREENING FRAMEWORK, *supra* note 229, at 3.

²³⁸ *Id.* at 9. HHS admitted in the accompanying FAQs that “it is not possible at this time to provide a robust database that would identify all or even most dangerous sequences.” U.S. Dep’t Health & Human Servs., *Frequently Asked Questions: Screening Framework Guidance for Providers of Synthetic Double-Stranded DNA*, PUB. HEALTH EMERGENCY, <http://www.phe.gov/Preparedness/legal/guidance/syndna/Documents/synbio-faq.pdf> (last visited Apr. 11, 2011) [hereinafter HHS, *Frequently Asked Questions*].

apart from urging industry to address the issue.²³⁹ Each firm would have to decide for itself which, if any, additional steps were needed to operate responsibly.

Why did HHS limit itself to Select Agent threats? Superficially, the answer was that “generating a comprehensive list of [other threats] to screen against is not currently feasible and hence is not provided in this *Guidance*.”²⁴⁰ But this answer only made sense if human screening was somehow undesirable. Here, HHS offered several arguments.²⁴¹ First, it pointed out that human screening involved examining similar gene sequences and that this implied a “cut-off” beyond which matches would not be examined.²⁴² This criterion, HHS argued, “would be arbitrary.”²⁴³ In fact, though, biologists had been using cutoffs for years. It would have been straightforward to incorporate one of these into the Guidelines.

Second, HHS argued that it wanted a standard that was “feasible for small and large providers, as well as international providers.”²⁴⁴ But this argument was also doubtful. After all, most of the industry—including companies of every size—had already agreed to adopt human screening. This plainly implied that human screening was “feasible.”

Finally, HHS argued that Best Match offered “consistency, because a hit for one company should register as a hit for other companies adhering to the guidance.”²⁴⁵ This last argument was probably the most plausible. At the same time, it represented a distinct policy choice. HHS clearly had the power to issue standards that required human discretion.²⁴⁶ By refusing to do so, the agency had elevated a subsidiary goal—that threat judgments should be replicable—over security itself.

²³⁹ See *id.* (remarking that “many providers have already instituted measures to address these concerns” and that “ongoing development of best practices in this area is commendable and encouraged”).

²⁴⁰ HHS, SCREENING FRAMEWORK, *supra* note 229, at 9.

²⁴¹ The FAQs refer to human screening methods as “Top Homology.” HHS, *Frequently Asked Questions*, *supra* note 238.

²⁴² *Id.*

²⁴³ *Id.*

²⁴⁴ *Id.*

²⁴⁵ *Id.*; see also Heidi Ledford, *Gene-Synthesis Rules Favour Convenience*, 467 NATURE 898, 898 (2010) (stating that officials believed that “human screens could lead to inconsistencies between companies,” whereas Best Match would “ensure a consistent baseline that can be uniformly applied across industry” (quoting Theresa Lawrence)).

²⁴⁶ See *Boyce Motor Lines, Inc. v. United States*, 342 U.S. 337, 343 (1952) (affirming regulations incorporating the exercise of human discretion).

E. Conclusion

It would have been both logical and easy for HHS to endorse the human screening standards developed by IASB and the Consortium. The fact that it refused to do so strongly suggests that it had (and presumably still has) little or no appetite for regulation.

IX. THE IMMEDIATE FUTURE

Synthetic biology is now almost a year into its second decade. At least formally, HHS's work is not done. First, it admits that the Guidelines are incomplete. This suggests that they will eventually need to be modified. Second, and more immediately, NSABB has called on the agency to develop review procedures for experiments of concern. HHS is not likely to ignore this commitment. On the other hand, these future regulations—like Best Match itself—could well be anemic. This Section asks how much life is left in synthetic biology's security agenda.

A. The Future of Private Standards

The final HHS Guidelines leave industry responsible for deciding what procedures, if any, should be adopted to guard against threats beyond the Select Agents list. Superficially, at least, the IASB's Code of Conduct and the Consortium's Protocol should remain in force. At the same time, the current situation is unstable. If one or two companies decide to revise or abandon their commitments, price competition could quickly force the rest to follow suit.

As this Article goes to press, the tea leaves are hard to read. On the one hand, DNA2.0 has suggested that it will use a list-based approach, even though, absurdly, its list remains secret.²⁴⁷ On the other, Consortium member IDT has publicly reaffirmed its commitment to human screening, promising that “[t]here’s never a case where we would have a gene go right into production without a human being having looked at both the sequence and the prospective customer.”²⁴⁸ Finally, outside commentators have said that the Guidelines are less a definitive

²⁴⁷ May, *supra* note 49.

²⁴⁸ Michael Eisenstein, *Synthetic DNA Firms Embrace Hazardous Agents Guidance But Remain Wary of Automated ‘Best Match’*, 28 NATURE BIOTECHNOLOGY 1225, 1226 (2010) (quoting Robert Dawson, a director at Integrated DNA Technologies). IASB member Entelechon similarly reaffirmed that employees would continue to examine the “complete lists of hits” and not just those flagged by computers. *Id.* at 1225 (quoting Markus Fischer). Markus Fischer, the director and cofounder of Entelechon, further stated that “[a] fully automated screening system leaves significant biosecurity questions unanswered.” *Id.*

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solution than “something to be improved over time.”²⁴⁹ Such expectations will make it harder for companies that have endorsed the Code or Protocol to change their minds.

B. More Studies Are Needed?

Pressure for reform depends on the public's attention span. This will inevitably fall off if scholars stop writing articles and reports. Ideally, these new publications should also advance the literature. Here, the evidence is mixed. On the one hand, some recent articles do little more than promise to conduct additional research in the future.²⁵⁰ On the other, most authors seem content with the basic threat analysis and response framework that synthetic biologists developed between 2006 and 2008.²⁵¹ This provides at least some hope that new work will build on what has come previously. Urgent topics include (a) deepening our empirical understanding of existing industry screening programs; (b) exploring the fundamental security trade-off between human screening and other methods; and (c) carefully testing the economic assertion that human screening is unsustainable. The problem, for now, is that researchers seem to have moved on to other topics, for example, synthetic biology's impact on “notions of life and the blurring of the line between natural and artificial.”²⁵² Alternatively, many European and

²⁴⁹ *Id.* at 1226 (quoting MITRE researcher James Diggans).

²⁵⁰ BALMER & MARTIN, *supra* note 194, at 5 (“This will require a thorough review of existing controls and regulations, and the development of new measures, particularly relating to biosafety, environmental release and biosecurity.”); Markus Schmidt et al., *A Priority Paper for the Societal and Ethical Aspects of Synthetic Biology*, 3 *SYST. & SYNTHETIC BIOLOGY* 3, 5 (2009), available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2759426/pdf/11693_2009_Article_9034.pdf (advocating “cooperation of DNA synthesis companies” and “further developing and improving the technical means (e.g. software, databases) used to screen for DNA orders,” and noting that “a balance will need to be struck between security gains on one hand and practicability and usefulness on the other”).

²⁵¹ The Center for American Progress has, however, argued that new reports are needed. Denise Caruso, *Synthetic Biology: An Overview and Recommendations for Anticipating and Addressing Emerging Risks*, *SCI. PROGRESS* (Nov. 12, 2008), <http://www.scienceprogress.org/wp-content/uploads/2008/11/syntheticbiology.pdf>. The argument is based on the claim that “[v]irtually all the reports on synthetic biology have come from the synthetic biology community or from a proponent's or an opponent's point of view.” *Id.* at 9. This premise seems debatable, except in the usual sense that all reports, including the Center's, are tinged by their authors' preconceptions. The Center's case would be stronger if it could point to instances in which the existing literature had overlooked specific issues or evidence. Indeed, this is how academic discourse is supposed to work. But the Center report only complains of unspecified “serious logical flaws and omissions of fact.” *Id.*

²⁵² IDEA League Summerschool, *Synthetics: The Ethics of Synthetic Biology* 4 (Aug. 2007), http://www.ethicsandtechnology.eu/images/uploads/Ethics_of_synthetic_biology.pdf.

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also developing world scholars have begun developing self-consciously regional viewpoints about synthetic biology.²⁵³ So far, at least, their insights do not seem much different from American ones.²⁵⁴

C. *The Presidential Commission*

Further action ultimately depends on public impatience. However, recent events suggest a concerted effort to convince the public that biosecurity is a solved problem. In late 2009, President Obama created a new Presidential Commission to evaluate bioethics.²⁵⁵ Not surprisingly, one of the Commission's first orders of business was to address synthetic biology.²⁵⁶ This, however, presented an obvious problem. Unlike earlier panels, the Commission could not simply recommend future action. After all, HHS had already drafted Guidelines. Admitting that this document was incomplete would commit the United States to yet another round of regulation and keep the larger security debate simmering for years.

The Commission worked hard to avoid this result. In September 2010, it held a seventy-five minute hearing on synthetic biology security policy.²⁵⁷ This consisted almost entirely of prepared remarks by the chairman of NSABB's synthetic biology working group and two executives representing Consortium members.²⁵⁸ Readers who have come this far would have found their presentations remarkable. Indeed, none of the speakers so much as mentioned IASB, the tumultuous standards war over human screening, or the fact that one of the represented companies, Geneart, had recently pressed for a fast and cheap automated solution. Not surprisingly, the two industry panelists

For other recent ethics-oriented projects and reports, see EUROPEAN GRP., *supra* note 132, and PARENS ET AL., *supra* note 196.

²⁵³ See Aim, ORG. FOR INT'L DIALOGUE & CONFLICT MGMT., <http://www.idialog.eu/fwf/Aim.html> (last visited Mar. 25, 2011) (reporting new project to investigate synthetic biology risks in Austria and China).

²⁵⁴ Some reports claim that security is a lower priority outside the United States. So far, however, there have been few if any concrete suggestions about how this preference should translate into policy. More fundamentally, we have seen that European gene-makers took the lead in setting private screening standards. This suggests that the usual transatlantic stereotype is badly oversimplified.

²⁵⁵ Exec. Order No. 13,521, 3 C.F.R. 279 (2009), *reprinted as amended in* 42 U.S.C. § 6601 (Supp. III 2010).

²⁵⁶ *Id.*

²⁵⁷ The session was part of a much broader, two-day set of hearings devoted to synthetic biology.

²⁵⁸ 2010 COMMISSION REPORT, *supra* note 13. The event, which was organized by HHS staffers, did not include a single panelist who had criticized the agency's Best Match proposal or endorsed IASB's Code of Conduct.

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also went out of their way to praise HHS's Guidelines without once mentioning Best Match's deficiencies.²⁵⁹

Based on this narrative, the Commission promptly produced a 180-page report.²⁶⁰ Essentially, its goal is to declare victory and go home. "[S]cientists both in and outside government," the Commission argued, have already (a) achieved "a shared culture of responsibility to assure safe conduct of research in the largely uncharted world of genetic engineering,"²⁶¹ and (b) developed "practical mechanisms" to implement security.²⁶² Furthermore, these oversight mechanisms and bodies were "well situated and in the process of reviewing and monitoring the field of synthetic biology as it develop[ed]."²⁶³ "At this time," the Commission concluded, "the risks posed by synthetic biology activities in both settings appear to be appropriately managed."²⁶⁴ Conversely, the Commission sees "no need at this time to create additional agencies or oversight bodies focused specifically on synthetic biology."²⁶⁵

Still, one awkward loose end remained. No one doubted that HHS's Best Match algorithm could only detect threats on the Select Agent list. Yet, NSABB's 2006 report and HHS's Guidelines had both admitted that other threats existed. This implied that synthetic biologists had not solved their biosecurity problem after all. Here, the Commission resorted to the familiar tactic of dialing down the threat. Now, retroactively, it argued that NSABB's 2006 report had been "focused on synthesis of select agents and toxins."²⁶⁶ Furthermore, proposals to control access to non-Select Agent sequences had been "[n]oticeably absent" from NSABB's 2010 report.²⁶⁷ This omission, the Commission

²⁵⁹ The slanted presentation was completely predictable. Consortium members seldom if ever mention IASB or its Code in any public forum, press release, published article, or interview unless compelled to do so. This sometimes requires them to rewrite matters of public record. For example, DNA2.0 executive Claes Gustaffson has argued that the idea of private security code originated in a "secret pact" by Consortium members in August 2009. Grushkin, *supra* note 215. This is plainly inconsistent with IASB's widely publicized efforts to create a standard from April 2008 forward. See *supra* Part I (discussing these efforts).

²⁶⁰ See 2010 COMMISSION REPORT, *supra* note 13.

²⁶¹ *Id.* at 144.

²⁶² *Id.* at 146.

²⁶³ *Id.* at 124.

²⁶⁴ *Id.* at 147. The Commission did recognize that non-biologist academics and, especially hobbyists, "may not be familiar with the standards for ethics and responsible stewardship that are commonplace for those working in biomedical research." *Id.* at 134. It therefore urged government to "educate and inform" these groups. *Id.* Even here, however, the Commission was careful to add that this was "not a call for specific restraints upon the [hobbyist] community at this time." *Id.* at 147.

²⁶⁵ *Id.* at 8.

²⁶⁶ *Id.* at 73.

²⁶⁷ *Id.*

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insisted, appeared to reflect a deliberate policy judgment that non-Select Agent “sequences alone [would] not yield, nor often be sufficient to predict, functions.”²⁶⁸ On its face, this elliptical statement seemed to imply that screening non-Select Agents was impossible. This, however, was clearly a straw man. After all, neither the IASB Code nor the Consortium Protocol had ever called for examining “sequences alone.” Instead, current best practice called for human screeners to compare incoming orders against known sequences whose functions were listed in Genbank. The Commission failed to explain why HHS had rejected this method, nor did it criticize the agency for publishing guidelines that were significantly weaker than the industry’s own standards.

D. Conclusion

Synthetic biology’s first decade was marked by interminable debates coupled with promises of future action. The Commission broke sharply with this pattern by arguing that existing steps had already solved the problem.

X. THE ROAD BACK

At this point, many readers will conclude that the U.S. federal government has no appetite for biosecurity. However, we have seen that rank-and-file synthetic biologists have often pursued reforms without waiting for official action. This Part asks what community members can still do to bring synthetic biology’s security agenda back from the brink.

A. Screening

Industry’s commitment to the Code and Protocol remains fragile. The trick will be to bring prompt, public criticism to bear on any company that downgrades its standards.

The standard that prevails will, in turn, determine the future of screening. Automated systems based on lists are, by definition, static. Because the whole point is to avoid human screening, companies have little opportunity or incentive to find new threats. This suggests that lists will evolve slowly, if at all. By comparison, human screening forces companies to examine each and every order that comes in the door. This is expensive and creates powerful incentives for gene-makers to save and reuse screeners’ work.²⁶⁹ This should lead to increasingly complete

²⁶⁸ *Id.*

²⁶⁹ Strong databases mean that screeners only need to examine a particular Genbank sequence once. The resulting savings are substantial. Indeed, companies currently

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threat lists over time. Moreover, these savings will be even larger if companies agree to pool their data. IASB and the University of California, Berkeley project recently created pilot scale software ("VIREP") to help gene-makers do this. Here, the ultimate goal is to produce a joint-threat database in much the same way that companies currently work together to write Apache and other open source software programs.²⁷⁰

Even if human screening survives, there will still be much to do. As long as the Consortium's meetings and membership are closed, no one can be sure how rigorously the Protocol is being implemented. Worse, gene-makers have an obvious incentive to decide close questions in favor of filling orders. VIREP-style sharing limits this tendency by ensuring that every threat judgment is open to scrutiny and, if necessary, criticism. More generally, the existence of a parallel Code and Protocol can only promote mischief. The synthetic biology community should demand that IASB and the Consortium merge their standards. Thereafter, any amendments to the merged standard should be (a) voted on by all active gene-makers regardless of size, and (b) conducted in meetings open to both public and press.

B. Experiments of Concern and Education

Given NSABB's recommendation, HHS is overwhelmingly likely to develop a review system for experiments of concern. The only real question is whether the new regulations will do any good. Here, the main uncertainties are (a) whether scientists contemplating experiments of concern will actually request reviews, and (b) whether the new review bodies will be more than a rubber stamp. With respect to the first question, much will depend on journal editors. If editors reliably refuse to publish experiments performed without advance review, few if any authors will skirt the system. Deterrence will only work, however, if editors withhold forgiveness. For this reason, the system's ultimate integrity will depend on whether government officials and academic leaders are willing to criticize editors who publish un-reviewed work.

The second question is more searching. No amount of detailed regulation can keep friendly review bodies from rubber-stamping

estimate that they have seen up to five percent of all sequences before. Maurer et al., *supra* note 1, at 24.

²⁷⁰ The business case for sharing threat data is identical to the logic behind Apache and other open source collaborations. Because companies do not compete for customers on the basis of who has the best threat database, they have no reason to hoard data. At the same time, shared data cuts each company's costs.

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results.²⁷¹ Ultimately, the quality of review will have to rest on the reviewers' own professionalism. This can, however, be bolstered by insisting that reviewers write detailed opinions explaining why each experiment should or should not go forward. Furthermore, these opinions should be available for public inspection, either immediately or following some brief interval.²⁷² With luck, exposing opinions to critics will do more than keep reviewers honest. It will also lead to new and better policies. Public opinions will allow scholars to collect, criticize, and (with luck) harmonize reviewers' instincts.

C. *Broader Lessons: U.S. Government Policy*

The most striking lesson from synthetic biology's first decade is that traditional government regulation is not the only way to accomplish security. Indeed, in a world of shrinking American power it may not even be the most effective way. We have seen that the commercial and arguably also the academic communities are capable of self-governance. Indeed, their standards, contrary to expectations,²⁷³ are often more stringent than the government's.²⁷⁴

The Best Match debacle is, in large measure, the story of what happens when government ignores private standards. Reform must begin, therefore, by making sure that officials pay more attention next time.²⁷⁵ The federal government can do this by developing formal guidelines to help agencies decide what to do and say when commercial

²⁷¹ This will be especially true if, as it seems likely, most experiments of concern turn out to be harmless.

²⁷² The claim is sometimes made that publishing reviews will disclose valuable research ideas to the researchers' competitors. But this will not matter if competitors know that the researcher has an insurmountable head start. Embargoing reviews for one year should almost always be sufficient.

²⁷³ The editors of *Nature* had confidently predicted that private standards would inevitably be weaker than public ones. *Pathways to Security*, *supra* note 210, at 432.

²⁷⁴ This observation raises interesting political economy questions. Political theory suggests that government agencies tend to be strongly influenced by narrow and often extreme interests. This probably explains why HHS chose a more lenient standard than the industry itself. Standards wars, on the other hand, are rough and tumble affairs that produce winning standards almost at random. On average, at least, one would expect these views to be relatively mainstream. Stephen M. Maurer, *Beyond Treaties and Regulation: Using Market Forces to Control Dual Use Technologies* 12 (Univ. of Cal., Berkeley, Goldman Sch. of Pub. Policy, Working Paper No. GSPP10-010, 2010), available at http://papers.ssrn.com/sol3/papers.cfm?abstract_id=1705630.

²⁷⁵ Official indifference has been a recurring obstacle for private entrepreneurs trying to organize for a public purpose. For additional examples, see Stephen M. Maurer, *Five Easy Pieces: Case Studies of Entrepreneurs Who Organized Private Communities for a Public Purpose* (Univ. of Cal., Berkeley, Goldman Sch. of Pub. Policy, Working Paper No. GSPP10-011, 2010), available at http://papers.ssrn.com/sol3/papers.cfm?abstract_id=1713329.

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or academic standards overlap their mission.²⁷⁶ This kind of guidance would admittedly have to address deep issues. When are private standards economically feasible or likely to be more effective than formal regulation or treaty? When should government encourage existing private standards initiatives or instigate new ones?²⁷⁷ When should the government intervene in private standards wars by, for example, praising one side or the other?²⁷⁸ And how should the government shape its own regulations so that they build on, rather than ignore or dismantle, what the private sector has done?

At the same time, it is probably more important to ask these questions than answer them. Just recognizing that government has an obligation to engage with commercial and academic standards will be an enormous step forward.

XI. CONCLUSION: EXPECTING MORE

This Article has described the first ten years of synthetic biology's security agenda, its collapse in 2009–2010, and the prospects for reviving it. Many readers will find this picture discouraging. They shouldn't. Most law review articles, after all, end by proposing schemes that have no chance at all of being implemented. By comparison, the idea that the federal government will one day enact, say, human screening seems eminently feasible.

For the past decade, synthetic biology scholars have almost always assumed that the time for taking action was five or ten years distant. Things are different now that government has tried to act and failed. Of course, we can still hope that future government regulations will work better. But that seems unreasonable. HHS's stubborn defense of its

²⁷⁶ Convening a National Research Council committee would be a good first step.

²⁷⁷ This will inevitably include addressing activists' claims that self-governance allows scientists "to act as judge and jury." Service, *supra* note 25, at 1116 (quoting activist Sue Mayer). This argument is far from self-evident, because it assumes a false choice between self-governance and traditional government regulation. In fact, self-governance "does not preclude other forms of governance, any more than the possession of conscience makes redundant the strictures of law." *Policing Ourselves*, 441 NATURE 383, 383 (2006). More precisely, the activists' argument requires the additional assumption that self-regulation changes outcomes by creating "a public image of scientific responsibility . . . that delay[s] . . . appropriate government regulation." *Synthetic Biology – Global Societal Review Urgent!*, ETCGROUP 3–4, http://www.etcgroup.org/upload/publication/11/01/synbiolet_bckgroundfinal.pdf (last visited Apr. 11, 2011). Even then, it is hard to see why communities should not have the same right to make ethical judgments that individuals do.

²⁷⁸ Similar government jawboning of private companies is already familiar when it comes to the domestic economy. For a classic account, see GRANT MCCONNELL, STEEL AND THE PRESIDENCY, 1962 (1963).

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hapless-but-cheap Best Match standard is no accident. “[E]ven a dog,” as Justice Holmes tells us, “distinguishes between being stumbled over and being kicked.”²⁷⁹

Synthetic biology’s security agenda has reached a critical moment. On the one hand, the Presidential Commission has told the country that synthetic biology has a functioning “culture of responsibility,” is adequately managing its risks, and does not need to revisit Best Match. On the other, very little of this can be squared with mainstream scholars’ persistent warnings that biological warfare threats are real and deserve to be taken seriously. The question now is whether anyone will notice.

Much depends on the scholars themselves. If they speak out, synthetic biology’s security agenda may yet come back stronger than ever.

²⁷⁹ OLIVER WENDELL HOLMES, JR., *THE COMMON LAW* 2 (ABA Classics 2009) (1881).