

# **From Understanding to Action: Community-Based Options for Improving Safety and Security in Synthetic Biology**

Stephen M. Maurer, Keith V. Lucas & Starr Terrell  
Goldman School of Public Policy  
University of California at Berkeley



**UNIVERSITY OF CALIFORNIA, BERKELEY**  
**RICHARD & RHODA GOLDMAN SCHOOL OF PUBLIC POLICY**

Draft 1.0 April 4, 2006

## Executive Summary

The vast majority of today's biosafety and biosecurity concerns predate synthetic biology and would be substantially the same even if this new field did not exist. Nevertheless synthetic biologists have an obligation to make sure that their work does not amplify earlier risks or create new ones. That discussion has been ongoing in various formal and informal venues since 2000. Today, synthetic biologists share a deep understanding of the biosafety/biosecurity problem and – in some cases – emerging consensus about what can and should be done to manage it. Many options can be implemented through community self-governance without outside intervention.

Understanding alone is not sufficient. The challenge now is action. Synthetic Biology 2.0 provides a natural forum for community self-governance. Because time is limited, however, members must come prepared. This document provides a self-contained review of previous discussions (Section I), discusses design principles for possible interventions (Section II), identifies instances where synthetic biology could potentially change earlier biosecurity/biosafety risks (Section III), and summarizes possible interventions that the community should consider at Synthetic Biology 2.0 (Section IV). Possible actions include:

***A.1 Insist That All Commercial Gene Synthesis Houses Adopt Current Best Practice Screening Procedures.*** While most gene synthesis companies screen orders for dangerous sequences, a few do not. This gives both community members and outsiders access to feedstocks for both wild-type and genetically-engineered bioweapons. Community members should stop doing business with any gene synthesis company that fails to implement current best-practice screening methods by January 1, 2007.

***A.2 Create and Endorse New Watch-Lists To Improve Industry Screening Programs.*** Improved watch-lists and software tools can make industry screening more accurate and efficient. Members should prepare the necessary lists and tools in time for Synthetic Biology 3.0.

***B.1. Create a Confidential Hotline For Biosafety and Biosecurity Issues.*** All experimenters contemplating “experiments of concern” should obtain independent expert advice before proceeding. The community should make such advice freely available to all experimenters, including non-members (*e.g.* hackers) who cannot otherwise obtain such advice from formal university, company, or NIH safety committees.

***B.2. Affirm Members' Ethical Obligation to Investigate and Report Dangerous Behavior.*** Members have an obligation to investigate and, if necessary, report dangerous behavior. Members should affirm this obligation by formal resolution at Synthetic Biology 2.0.

***C. Create a Community-Wide Clearinghouse for Identifying and Tracking Potential Biosecurity Issues.*** Members who notice potential biosecurity issues have an obligation to share them with the broader community. A central clearinghouse will help the community to identify, track, and if necessary respond to the biosafety/biosecurity implications of a changing technology.

***D. Endorse Biosecurity/Biosafety R&D Priorities.*** New technologies can potentially reduce current biosafety/biosecurity risks even further. Members should identify, endorse, and urge funding agencies to invest in priority technologies such as safe chasses and bar codes.

This document is part of a sustained effort by The Berkeley SynBio Policy Group to help members learn about security issues and facilitate community self-governance at Synthetic Biology 2.0. In coming weeks, we will host Town Hall Meetings at Berkeley (April 11) and MIT (April 21) to further discuss what the community can do to improve biosafety/biosecurity. Both Town Halls will be webcast to members around the world.

We expect to change this document continually between now and May to reflect ongoing community discussion and debate. This is a living document.

## Berkeley SynBio Policy Group.

The Berkeley SynBio Policy Group is a joint undertaking of Lawrence Berkeley Laboratory's Keasling Lab and UC Berkeley's Goldman School of Public Policy. The Group's goal is to study and facilitate community action on issues of concern to the worldwide synthetic biology community. The Group is funded by The MacArthur Foundation and the Carnegie Corporation.

## I. Introduction

### A. Making Self-Governance Work.\*

Community self-governance provides a realistic and potentially powerful complement or alternative to regulation, legislation, treaties, and other interventions by outside entities. Experience with Asilomar<sup>1</sup> and the Bermuda Protocols shows that biological research communities can and do adhere to voluntary standards. While self-governance tends to be less stringent than legislation and cannot change existing laws or institutions, it also offers significant advantages. First, self-governance is the right thing to do. In the words of the Fink Report, biologists need to “take responsibility” for “preventing potential misuses of their work.”<sup>2</sup> Second, almost always faster than other methods. Second, it derives from consent and is therefore frequently more elegant than externally imposed solutions.<sup>3</sup> Finally, it is inherently international. This can be a crucial advantage in a world where science and commerce routinely span national boundaries.

**The Discussion So Far.** Over the past six years, synthetic biologists have devoted enormous effort to thinking about biosecurity/biosafety issues. In that time, the problem has become well-understood and many proposals – some widely admired – have emerged.

The First International Conference on Synthetic Biology 1.0 began to formalize this process in July, 2004. It hosted “moderated discussions to help begin to explore ... current and future biological risk”<sup>4</sup> and a community-wide attempt “to be proactive about precautionary measures.”<sup>5</sup> More recently, groups funded by the Sloan Foundation<sup>6</sup> and the Federation of American Scientists<sup>7</sup> have deepened and extended these discussions. This activity has fostered a widespread expectation that “the future is now”<sup>8</sup> and that Synthetic Biology 2.0 will make “significant progress” toward a “code of ethics and standards.”<sup>9</sup>

**The Berkeley SynBio Policy Group: Reducing Frictions.** Average members of the synthetic biology community have relatively little time to prepare and think about biosafety/biosecurity issues. Day 3 of the Conference will offer only limited time to learn this material.<sup>10</sup> For this reason, success will depend on members’ ability to think about and discuss these issues in advance. The Berkeley SynBio Policy Group’s goal seeks to promote this discussion and ensure that members have basic information at their fingertips. Steps in this process include:

*This Document.* This document provides a snapshot of current biosecurity/biosafety risks and possible interventions for managing them. The

---

\* The authors wish to thank the MacArthur Foundation for funding this project, The Carnegie Corporation for additional support, Jay Keasling and Drew Endy for useful suggestions, and the nearly two dozen community members who participated in interviews for this project. Any errors are ours alone.

goal is to provide a concise, easy-to-use references that members can consult in support of an informed, rational discussion and vote at Synthetic Biology 2.0. We expect to update this document repeatedly to reflect ongoing community input between now and Synthetic Biology 2.0.

***Interview Program.*** The Berkeley SynBio Policy Group has conducted extensive interviews to learn what members believe, want, and are prepared to vote for. The current document reflects more than twenty of generous and input from twenty-one leading academic scientists, four industry representatives, and six European members.\*

***Coordination With Other Institutions and Working Groups.*** The Berkeley SynBio Policy Group has received extensive input from US Senate Staff, NIH's National Science Advisory Board for Biosecurity ("NSABB") and the Federation of American Scientists. The Sloan Foundation's MIT/Venter Institute/CSIS study group (herinafter "Sloan group")<sup>11</sup> has been particularly generous in supplying ideas for possible interventions.

***Town Halls.*** The Berkeley SynBio Policy Group will hold Town Hall meetings at UC Berkeley (April 11) and MIT (April 21) to discuss the various proposals outlined in this document and to elicit further suggestions from members. An additional, European-focused Town Hall is currently under discussion. Each Town Hall will feature a full discussion followed by a non-binding advisory ("straw poll") vote.

**Synthetic Biology 2.0: A Unique Opportunity.** Members have publicly announced that they expect Synthetic Biology 2.0 to produce "significant progress" toward a "code of ethics and standards."<sup>12</sup> Members participating in Day 3 deliberations will be able to call numerous nationally recognized experts, including representatives of the Sloan group and NSABB.

## B. How to Use This Document.

This document is designed to help members make a rational and informed vote at Synthetic Biology 2.0. Section II ("Doing Policy") summarizes general principles for evaluating policy interventions in the biosecurity/biosafety arena. Section III reviews the traditional biosecurity/biosafety problem, focusing on the comparative handful of points where synthetic biology could have a significant impact. Finally, Section IV ("Possible Interventions") provides a menu of self-regulation interventions that the community should consider adopting at Synthetic Biology 2.0. For ease of reference, we have color-coded these interventions as follows:

---

\*Some categories overlap. A full list of interviewees can be found at Appendix A.

**Emerging Consensus Proposals.** Our interviews have identified a core group of intervention proposals that (a) appear technically feasible, and b) already enjoy widespread support among members. These interventions form an obvious “short list” for discussion at Synthetic Biology 2.0. We highlight them in what follows.

**Resolutions.** Each Emerging Consensus Proposal ends with the draft text of a resolution that members could adopt at Synthetic Biology 2.0. A complete set of draft resolutions appears at Appendix B.

**Other Proposals.** Some novel proposals are unlikely to be refined and debated in time for Synthetic Biology 2.0. We nevertheless include them in the interest of completeness and in the hope that promising ideas will eventually be refined for discussion at Synthetic Biology 3.0 and later conferences.

As previously noted, this is a living document. We expect it to change repeatedly as a result of community input from the Town Halls and other discussions leading up to Synthetic Biology 2.0. Members are urged to contact the authors with comments and questions.

## II. Doing Policy

Policymakers must address problems logically and consistently. The following principles provide a useful starting point for thinking about biosecurity/biosafety interventions.

### A. Cost-Benefit.

Useful interventions should place minimal burdens on synthetic biology’s ability to deliver value for society.

**General Benefits.** Synthetic biology has already made making existing biotechnology programs dramatically more efficient. The value of these benefits almost certainly runs into the tens of billions of dollars.<sup>13</sup> In the long-term, synthetic biology stands to generate still larger gains by creating products that cannot be achieved by traditional methods.<sup>14</sup> Examples include drug delivery systems that detect and target tumors<sup>15</sup> and the development of standardized parts that let companies tailor organisms to the needs of individual users.<sup>16</sup> Any intervention that threatens these developments is likely to be counterproductive.

**Biodefense Benefits.** Synthetic biology promises powerful new tools for biodefense, most notably in the area of accelerated vaccine development. In the words of one member, the biodefense problem is defined by the fact that there

“are more good guys than bad guys.” For this reason, regulations that handicap all researchers indiscriminately are almost always be bad for society.<sup>17</sup>

The expected benefits of synthetic biology are large. Proposed interventions must avoid stifling research.

## B. Comparative Principle.

Current biosecurity/biosafety risks predate synthetic biology by many years.<sup>18</sup> These risks would be substantially the same if synthetic biology had never been invented. This does not mean that synthetic biology irrelevant or that members can responsibly ignore biosafety/biosecurity concerns in their work. It does, however, suggest that policy should be done “at the margin,” *i.e.*, by focusing on how synthetic biology *changes* preexisting risks for better or for worse. Section III follows this prescription by focusing on areas where synthetic biology (a) potentially introduces qualitatively new pathways for accidents, or (b) potentially makes bioweapons cheaper, easier, or more effective than earlier technologies.

## C. Flexibility.

It is only natural to want permanent, guaranteed solutions to policy problems. Unfortunately, this goal is seldom realistic, particularly in the biosafety/biosecurity arena. In keeping with our comparative principle, members should be prepared to consider even incomplete interventions that reduce risk.

This observation leads to three corollaries:

***Relationship to Existing or Future Law.*** Self-regulation will not necessarily displace traditional interventions based on regulation, legislation, and treaties. Community action should be implemented in ways that yield to more formal methods where regulation/legislation/treaties already exist or are subsequently introduced.

***Complete Solutions are Illusory.*** It is seldom, if ever possible to achieve complete security against a determined adversary. However, this may not be necessary. A complex terrorist conspiracy must daily negotiate a long chain of security hurdles. The fact that *individual* hurdles can be circumvented with high probability may not matter if the *cumulative* chance of failure is large.<sup>19</sup>

***Permanent Solutions are Illusory.*** Few, if any, security policy solutions are permanent. The best that policymakers can hope to do is to set a baseline policy and then update it in light of new developments. This suggests that members

should establish permanent institutions to follow developments and update policy on a regular basis.<sup>20</sup>

The Romans observed long ago observed that “The better is the enemy of the good.” In what follows we assume that even interventions with modest payoffs may be desirable provided that the cost is low.

### III. How Does Synthetic Biology Affect Traditional Biosecurity/Biosafety Concerns?

The bioweapons/biosafety problem is only tangentially related to synthetic biology. This document is designed to help members see synthetic biology in a broader context. In keeping with our comparative principle, the focus throughout is on identifying instances where synthetic biology could potentially change pre-existing biosafety/biosecurity risks.

#### A. Biosecurity.

Biosecurity concerns range from assassination and psychological intimidation<sup>21</sup> to WMD at the nuclear weapons scale. Following most authors, we focus here on mass casualty scenarios. This benchmark case makes sense for at least three reasons. First, bioweapons offer few advantages over cheaper and more familiar technologies (*e.g.* high explosive) at scales comparable to the World Trade Center attacks (2,752 deaths<sup>22</sup>). According to our comparative principle, synthetic biologists can do little to reduce the danger of such attacks in any case. Second, no small scale attack is likely to erase synthetic biology’s expected net value to society. Our cost benefit principle suggests that we should focus on mass casualties.<sup>23</sup> Finally, the interventions described in Section IV, *infra*, are broad enough to mitigate biosecurity risks across the board. Our focus on mass casualties is only illustrative.

The non-occurrence of significant biological terrorist attacks over the past fifty years<sup>24</sup> strongly implies that a WMD-scale bioweapons capability requires substantial investment.\* Historically, even the smallest weapons programs required massive facilities and thousands of personnel.<sup>25</sup> Significantly, advances in biology have done little to reduce these costs. This lesson is underscored by Soviet experience in the 1980s and early 1990s, in which genetic engineering did little or nothing to cut total program

---

\*This does not, of course, imply that bioweapons are comparably expensive to other forms of WMD. “In comparison to nuclear and chemical weapons (CW) programs, individuals’ intellectual capabilities play a far greater role in determining the success or failure of a program than the physical resources to which they may have access.” UNSCOM, “Iran Survey Group Final Report,” available at [http://www.globalsecurity.org/wmd/library/report/2004/isg-final-report/isg-final-report\\_vol3\\_bw-01.htm](http://www.globalsecurity.org/wmd/library/report/2004/isg-final-report/isg-final-report_vol3_bw-01.htm).

costs.<sup>26</sup> Iraqi and South African bioweapons programs of the late 1980s similarly document the continued need for resources and manpower.<sup>27</sup>

Of course, the experience of state-sponsored programs only provides a starting point. Today, the main focus is terrorism. This section asks whether and to what extent synthetic biology erodes old cost- and knowledge-based barriers to acquiring bioweapons.\*

**Identifying Candidate Organisms.** Early bioweapons programs devoted enormous effort to demonstrating that candidate diseases could, in fact, be “weaponized.”<sup>28</sup> The identity of these diseases is now public knowledge. Iraq’s decision to pursue “classical weapons” previously developed by the US shows that there is a powerful incentive to pursue weapons that are already known to work.<sup>29</sup>

Genetic engineering is disadvantageous along this dimension. Synthetic biology does little or nothing to change this result.

**Obtaining Feedstocks.** Obtaining genetic material for a potential bioweapon from Nature is difficult.<sup>30</sup> For this reason, weapons makers have usually started with feedstocks obtained from research laboratories and type collections.<sup>31</sup> Despite recent reforms, control of these materials remains highly imperfect. The problem is aggravated by inconsistent international standards that undercut country-by-country regulation.<sup>32</sup>

Synthetic biology introduces a new channel for potentially obtaining access to dangerous sequences and, ultimately, organisms. Recent experiments recreating the polio<sup>33</sup> and 1918 influenza<sup>34</sup> viruses show that this route is viable but also non-trivial. **Proposals A.1 through A.4** seek to fill this gap by promoting and strengthening industry screening practices so that dangerous sequences are not shipped to unknown or untrustworthy purchasers.

**Large Scale Manufacturing.** The manufacturing requirements for a bioweapons attack are non-trivial, particularly on the scale of a conventional terrorist bombmaking plot. The earliest and still-simplest bioweapon is a concentrated liquid or “wet agent.” British military calculations from World War II suggest that an anthrax attack would require about five tons of wet agent per square kilometer.<sup>35</sup> Postwar advances involving aerosol sprays and contagious diseases suggest that this figure can probably be cut to 1000 pounds per square kilometer.<sup>36</sup> Comparing this figure against population densities for Manhattan<sup>37</sup> suggests that terrorists would still need to manufacture about 200 pounds of agent in order to kill 5000 people.† Japanese experience with very simple manufacturing

---

\*The benchmark should also be adjusted to the extent that terrorists can potentially jettison normal military requirements that (a) the proposed bioweapon exhibit dependable, well-understood effects and (b) reliable countermeasures for friendly forces operating the area.

† This very rough estimate ignores the fact that much of the target population would be sheltered in doors. World War II-era planners routinely assumed that one-fourth of the bomb load in a bioweapons attack would be high explosive.

facilities in the 1930s suggests that this would require 100 fermentation tanks and 300 workers.<sup>38</sup>

Modern bioweapons programs typically process wet agents further to make so-called “biopowders.” Reports of a Cold War-era Soviet anthrax accident<sup>39</sup> and American bioweapons tests<sup>40</sup> suggest that an attack on 5,000 people would require one to ten kilograms of material. While small in absolute terms, this would still require a thousand-fold increase over the 2-3 grams used in the 2001 anthrax attacks.<sup>41</sup> Iraqi experience during the 1980s suggests that extending bench- to pilot-scale production is non-trivial.<sup>42</sup>

Technologically, the key to more efficient wet agent production is high fermentation densities. Automated fermentation<sup>43</sup> and biotech manufacturing techniques<sup>44</sup> would be central to this effort. Improved biopowder production would require additional expertise in spray drying, milling, and other material processing technologies. Synthetic biology would add little or nothing to these efforts.

**Safety.** Most bioweapons manufacturing programs repeatedly infect workers. Japanese experience during World War II suggests that low tech programs can expect casualties of about one percent per year.<sup>45</sup> In practice, rates for a terrorist conspiracy could well be higher. The long history of terrorist bomb factory accidents since the 1870s suggests that accidents would impose substantial burdens on both morale and security.<sup>46</sup>

Conventional containment and manufacturing technologies are the key to achieving reasonable safety levels. Synthetic biology is largely irrelevant to this enterprise. Genetic engineering could, however, become relevant if terrorists sought to create “binary weapons” that could be safely handled prior to use.<sup>47</sup>

**Hardiness.** Wet agents have a short shelf life ranging from weeks to months.<sup>48</sup> This limits the value of stockpiling and makes manufacturing problems more acute. Once released, most bioweapons degrade quickly in the presence of sunlight,<sup>49</sup> oxidation,<sup>50</sup> air pollution,<sup>51</sup> high wind,<sup>52</sup> and humidity.<sup>53</sup> This further limits the casualties that can be inflicted in practice.

Traditional technologies for hardening bioweapons involve adding chemical stabilizers to wet agents or microencapsulating biopowders within a protective coating.<sup>54</sup> In theory, genetic engineering could also enhance environmental resistance.<sup>55</sup> In practice, however, genetically engineered organisms are usually less hardy than natural ones.<sup>56</sup> This may change as scientists learn to manipulate more factors simultaneously.<sup>57</sup>

**Virulence and Antibiotic Resistance.** Antibiotic resistance complicates public health defense and is therefore desirable in a bioweapon.<sup>58</sup> Genetic engineering could similarly modify organisms to evade standard identification, detection, and diagnostic methods<sup>59</sup> and produce agents that are more communicable, lethal, or have a longer latency or higher mortality.<sup>60</sup> Russian scientists are known to have used genetic engineering to

create vaccine-resistant bioweapons<sup>61</sup> and more virulent versions of anthrax and Marberg<sup>62</sup> during the 1980s.

Synthetic biology potentially makes these genetic engineering manipulations more accessible. **Proposals A.1** and **A.2** make it harder for terrorists to obtain gene sequences needed to build drug resistant bioweapons. Similarly, **Proposal B.1** addresses “experiments of concern” that could potentially push synthetic biology in directions that made it more useful to terrorists.

**Delivery Systems.** Aerosols tend to be inefficient delivery systems since (a) large droplets are seldom inhaled, and (b) very small droplets are unstable to evaporation. For the most part, terrorists seeking to improve efficiency would turn to industrial technologies for making uniform aerosols. Genetic engineering could, however, help make some wet agents easier to aerosolize.<sup>63</sup>

The formula and production methods for making biopowders is classified. While originally expensive to develop, the biopowder formula is reportedly simple.<sup>64</sup> Terrorists who do not already know the secret would presumably turn to such material handling technologies as spray drying, milling, and other methods.<sup>65</sup> Extensive testing would also be needed to ensure that agents remained effective. Synthetic biology adds little to these technologies.

**Infectious Diseases.** In principle, terrorists could obviate the need for elaborate production and delivery systems by turning to infectious diseases. During the Cold War, the Soviets concluded that the United States was such a distant “deep target” that an epidemic would never reach Russia.<sup>66</sup> It is reasonable to think that terrorists could reach a similar judgment. That said, infectious bioweapons face their own development barriers. These include:

**Public Health Defenses.** Wild-type versions of anthrax, botulism, brucellosis, cholera, and plague disease already strike the US, though typically in numbers fewer than ten cases per year.<sup>67</sup> Innate characteristics of the organisms (*e.g.*, transmission from human to human and the public health and sanitation system would similarly limit the spread of organisms used as bioweapons. These barriers can be substantial. During the 1970s, European public health authorities reportedly quarantined tens of thousands and vaccinated hundreds of thousands to prevent smallpox from spreading.<sup>68</sup>

**Stability.** Natural diseases<sup>69</sup> and classical bioweapons<sup>70</sup> both tend to become steadily less virulent over time as they adapt to human hosts. While it is reasonable to think that a genetically engineered organism would similarly lose its engineered traits to evolution, the extent and timing of this phenomenon is not known. The fact that bioremediation companies routinely choose naturally-occurring organisms over artificial ones suggests that genetically-engineered stability poses significant challenges.<sup>71</sup> On the other hand, genetically engineered

organisms released into nutrient-rich environments (*e.g.* jungle streams) are known to be stable.<sup>72</sup> It is not clear where genetically engineered human pathogens fall along this continuum.

**Predictive Power.** Current epidemiologic models have limited ability to predict how well new infectious organism would spread if released into a complex biological system. One reason for this is that epidemic dynamics seem to be sensitive to the characteristics of small numbers of infected humans. Furthermore, many of these characteristics are either unknown or poorly understood.<sup>73</sup> The resulting lack of predictive power means that using synthetic biology to create a radically new organism would be an unreliable way to start epidemics. Instead, terrorists would probably find it more efficient to (a) use naturally occurring organisms that are already known to cause epidemics, or (b) modify these wild-type organisms in relatively modest ways (*e.g.* drug resistance) using traditional genetic engineering mechanisms.

We have already remarked how synthetic biology could potentially complicate public health defenses and make genetically modified organisms more stable. **Proposal B.1** addresses experiments of concern which could potentially make it easier to produce drug resistant organisms.

## B. Biosafety.

Members interviewed for this project noted that there has never been a documented accident in which a genetically engineered organism escaped from a laboratory and caused harm.<sup>74</sup> The intuition behind this observation is that most genetically engineered organisms (and all synthetic biology experiments to date) can only survive in elaborately artificial environments.<sup>75</sup> In principle, synthetic biologists should be able to design traits that reduce organisms' survival chances even further. **Proposal D.1** urges funding agencies to invest in these technologies.

At the same time, the fact that current biosafety risks are low does not mean that there is no room for improvement. The recent experiment of Jackson *et al.*<sup>76</sup> in which researchers trying to boost an immune system managed to turn it off instead shows how experiments can lead to unexpected results. Furthermore, even simple accidents – for example, noticing that it is possible to stick a needle through protective gloves – can provide “instructive examples” that make researchers think differently about safety.<sup>77</sup> Both examples suggest that better reporting and sharing of information are a good way to promote biosafety. **Proposal C.2** would create a community-wide clearinghouse for reporting and sharing safety-related information.

## C. Policy Implications.

No member interviewed for this project believes that today's synthetic biology significantly changes earlier biosecurity/biosafety risks. The foregoing analysis confirms this intuition. This does not, however, mean that interventions to reduce risks are useless. To the contrary: The fact that biosecurity/biosafety problems are manageable suggests that even modest interventions can make a difference. Furthermore, synthetic biology is changing rapidly. There is no guarantee that a similar analysis five years from now would reach the same conclusion. **Proposals C.1** and **C.2** would provide institutional mechanisms for identifying and if necessary responding to new biosafety/biosecurity developments as they emerge.

## IV. Possible Interventions

This section reviews four broad classes of self-regulation that members can adopt to reduce the already small biosafety/biosecurity risks posed by synthetic biology. **Part A** suggests steps that community can take to reduce the chance that commercial synthesis companies will supply dangerous genetic sequences to terrorists outside the community. **Part B** suggests new channels that would allow experimenters to obtain advice about potential "experiments of concern" and report dangerous or unsafe behavior. **Part C** proposes community-wide institutional mechanisms for tracking, publicizing, and if necessary responding to emerging biosecurity/biosafety issues over time. Finally, **Part D** urges funding agencies to fund promising technologies for enhancing biosafety and biosecurity.

### A. Supporting and Extending Responsible Industry Screening Practices

As explained in Section III, the rise of commercial biosynthesis and oligo companies creates a potential new channel for terrorists seeking to obtain feedstocks for wild-type or genetically engineered bioweapons. Current industry screening practices are (a) non-uniform within gene synthesis companies, (b) generate too many false positives for high volume oligo companies to use, (c) do not include large numbers of potentially dangerous sequences, and (d) may not be able to detect dangerous sequences that have been split into multiple orders. We found strong support among industry and academic members for steps to address the first three items. The significance of the last item remains controversial.

## A.1 Insist That All Commercial Gene Synthesis Houses Adopt Current Best-Practice Screening Procedures.

Community members overwhelmingly believe that industry should screen orders whenever it is feasible to do so.\*

**Non-Uniform Screening Practices.** In November, 2005 the journal *New Scientist* asked twelve gene synthesis companies whether they routinely screened orders for sequences that terrorists could turn into weapons. Only five said “yes.” The remainder answered that they did so “usually” (1 firm), “not routinely” (3 firms) or not at all (3 firms).<sup>78</sup> While it is possible that some of these firms have since adopted screening, at least one large Chinese firm reportedly still does not screen.<sup>79</sup> The continued existence of non-screener puts responsible companies at a competitive disadvantage and creates economic incentives to cut corners on security.<sup>80</sup>

**Intervention.** Industry members contacted for this project uniformly agreed that a community-wide pledge not to do business with companies that fail to adopt screening is worth doing and would likely persuade more companies to screen.<sup>81</sup> Apart from its ethical value, there is reason to think that a pledge would effect real world improvements in industry practice:

***Feasibility for Industry.*** Firms that adopt screening sacrifice little output or profits *provided that all firms do it*. A pledge would help to enforce this coordination. Current “best practice” screening is also straightforward to implement. The required software can be purchased commercially<sup>82</sup> or else built in-house using only modest expertise.<sup>83</sup> Companies that fail to screen can be readily detected.<sup>84</sup>

***Feasibility for Community.*** Synthetic biologists account for no more than a few percent of current commercial gene synthesis purchases. However, this figure could easily reach fifty percent within five years.<sup>85</sup> For this reason, a community-wide pledge is likely to exert useful economic pressure on non-conforming firms. A pledge would also have moral value. Large pharmaceutical and biotechnology companies would feel pressure to follow suit. These entities account for roughly two-thirds of today’s market.

***Costs.*** The fact that most gene synthesis companies already screen suggests that costs would not rise for most community members. In a few cases, however, researchers who currently patronize non-screening companies could see costs rise. This could make research harder for underfunded scientists.<sup>86</sup>

---

\*Of the \_\_ community members consulted for this project, only one (\_\_%) argued that the case for screening was unproven. This member remarked that he, too, would endorse screening if it became “clear” that screening “could reduce [the risk of] harm in a specific way.”

**A First Step.** Persuading industry to adopt current “best practice” screening policies is not a panacea. For reasons discussed in below, current screening practices have significant defects. That said, universal screening would be an improvement. It is also a necessary first step toward any future progress.

**Resolved:** Gene synthesis companies have an ethical responsibility to screen orders consistent with “best practices” within the industry, including but not limited to the routine use of automated searches (equivalent to current Blackwatch release or higher) and hand examination of all suspect sequences by qualified scientists. Companies that practice such screening should publicly certify the fact by January 1, 2007. Thereafter, community members pledge not to place orders with any company that fails to comply with this resolution.

## A.2 Create and Endorse New Watch-Lists to Improve Industry Screening.

In keeping with a recent National Research Council Report<sup>87</sup>, our project found universal agreement<sup>88</sup> that current watch-lists are inadequate. These defects include:

***Incompleteness.*** Current lists focus almost exclusively on select agents and toxins. Many other potentially dangerous sequences are not included.<sup>89</sup>

***Overbreadth.*** Current organism-level lists generate a large number of false positives which must be examined by hand. This makes screening impractical for oligo houses that fill up to one thousand orders per day.\* The number of false positives will also become a problem for gene synthesis companies as their businesses grow.<sup>90</sup>

Better software and more specific sequence lists can potentially fix these defects. Such tools would (a) make existing gene synthesis screening more accurate and sustainable, and (b) allow oligo companies to start their own screening programs.<sup>91</sup> In an ideal world, government would take the lead in providing such a list. For now, however, no such project exists.

Members uniformly agreed that members should create the software and watch-lists needed to make current screening practices more effective. Ideally, the new tools would be available for members to review and endorse at Synthetic Biology 3.0. The proposed initiative would make current gene synthesis screening more effective and encourage oligo companies to adopt their own screening programs. It would also lay the groundwork for an eventual government-approved list.

---

\* Recent experiments in recreating polio and 1918 influenza both used oligos.

**Resolved:** Better screening software and machine-readable, detailed sequence watch-lists are urgently needed to improve screening. A community-wide initiative is currently underway to create these tools on or before December, 2006. Members will have an opportunity to review and endorse these products when they meet for Synthetic Biology 3.0

### A.3 Endorsing Surveillance Across Multiple Orders

In principle, terrorists can evade screening by sending multiple requests for individually innocuous sequences to a single supplier or by placing orders with multiple suppliers simultaneously. They could then re-assemble the sequences into a dangerous organism.<sup>92</sup> In practice, this strategy is highly non-trivial. Splitting orders so that they successfully evade screening would require a skilled bioinformaticist.<sup>93</sup> Furthermore, reassembling the desired genome from multiple orders would be difficult. Current state-of-the-art methods for assembling 5kbp genomes (*e.g.* polio, 1918 influenza) fall well short of 200kbp that characterize most bioweapons.

In principle, screening could be improved by forwarding orders to a centralized screening facility.<sup>94</sup> However, biotechnology and pharmaceutical companies might stop purchasing services from outside suppliers if this meant compromising the confidentiality of their orders. Instead, they would demand gene synthesis kits that allowed them to perform synthesis in-house. The proliferation of such kits would pose a significant danger in its own right.<sup>95</sup>

### A.4 Using Genetic “Signatures” or “Bar Codes” to Detect and/or Identify the Source of Organisms.

Several members suggested that DNA sequences could be inserted for multiple purposes including:

***Facilitating Detection.*** Sequences could be optimized so that organisms containing selected bar codes could be readily identified using PCR.<sup>96</sup>

***Facilitating Deterrence.*** Demonstrating that DNA used to make a bioweapon can be traced to a particular company or transaction could deter some terrorists.

***Facilitating Authorship and Responsibility.*** Signatures potentially offer a variety of benefits beyond security. These include fostering a feeling of responsibility and authorship,<sup>97</sup> and potentially facilitating the enforcement of intellectual property rights.<sup>98</sup>

**Feasibility.** Several members interviewed for this project felt that bar codes were technologically feasible today.<sup>99</sup> However most felt that additional technical obstacles had yet to be resolved. These include:

***Incremental Value Compared to Natural Markers.*** The fact that existing pathogens already provide forensic clues potentially diminishes the value of bar codes.<sup>100</sup> Experience in the 2001 anthrax attacks – in which identification of the Ames strain provided only ambiguous evidence of origin<sup>101</sup> – suggests considerable room for improvement.

***Stability and Countermeasures.*** Despite preliminary experiments, bar coding technologies have yet to be demonstrated. In particular, it is not clear whether bar codes would be stable against mutation.<sup>102</sup> Many members believe bar codes could be readily detected and removed.<sup>103</sup>

***Making Science Harder.*** Bar codes would inevitably interfere with experiments involving short DNA sequences.<sup>104</sup> Experience in the explosive “taggants” debate suggests that this will likely be the most durable objection.\*

Three-quarters of the members we interviewed believe that genetic bar codes were either immediately useful or deserved further study.

## A.5 Other Proposals: Licensing Biologists

Some members argued that screening should be limited to confirming that orders were being placed by responsible biologists.<sup>105</sup> In fact, commercial companies already do this.<sup>106</sup> Even if it were desirable, it is unclear whether the community could persuade companies to stop current screening practices in favor of examining purchasers’ credentials.

---

\* The 25 year-old debate over the use of “taggants” in explosives is instructive. On the one hand, there is widespread consensus that such measures can be defeated by sophisticated terrorists, are subject to countermeasures, and are limited to commercially-produced materials. On the other hand, there is near-unanimity that taggants remain useful in “facilitating the investigation of almost all significant criminal bombings in which commercial explosives were used.” In essence, the deciding factor is how much taggants interfere with the normal functioning of explosive, fertilizer, and ammunition. *See e.g.* Office of Technology Assessment, *Taggants in Explosives* (1980) at p. 9; US Treasury, Interim Progress Report on Marking, Rendering Inert, and Licensing of Explosive Materials” (1997); and US National Academy of Sciences, “Marking, Rendering Inert, and Licensing of Explosive Materials: Interim Report” (1997).

## B. Developing Norms and Practices for An Emerging Community.

The accompanying paper by Laurie Zoloth argues that individuals have an ethical obligation to (a) obtain advice from independent experts before conducting experiments of concern, or (b) to report dangerous behavior by others.<sup>107</sup> Without such obligations, the pace of experiments is always dictated by the community's most adventurous members so that community opinion become meaningless.<sup>108</sup> This section describes various institutional options for increasing consultation and communication within the community.

### B.1 Make Advice About Experiments of Concern Freely Available to Both Members and Non-Members.

Most members who were asked agreed that individuals should seek independent expert advice before conducting “experiments of concern” that would push synthetic biology that could potentially push synthetic biology in directions that made it more useful to terrorists.<sup>109</sup> Many members already have both formal resources (*e.g.* safety committees) and personal contacts who fulfill these functions. However, the Fink<sup>110</sup> and Wellcome Trust<sup>111</sup> Reports both express doubt that these bodies have sufficient biosecurity expertise to screen experiments of concern. For this reason, most members agreed that it would be useful to have a body they could consult. Such a body would also provide essential guidance to non-members (including, potentially, future biohackers) who lack access to normal university and NIH resources.

**Design Issues.** Despite widespread support, most members emphasized that an ethics advisory committee would have to be very carefully designed. Design issues include:

***Defining “Experiments of Concern.”*** While there is still no “official” or “consensus” definition embracing all possible “experiments of concern,” members agreed that the Fink Report definitions were well known and would provide a useful starting point.<sup>112</sup> Our flexibility principle suggests that the community should to adopt those definitions even if it later needs to amend them.

***Academic Competition.*** Several members interviewed for this project expressed concern that independent experts could take advantage their position to steal ideas for proposed experiments.<sup>113</sup> These concerns can be mitigated by (a) directing inquiries to identified individuals and (b) documenting all inquiries.

***Mitigating Bureaucracy.*** Several members noted that informal consultation would be counterproductive if they led to an additional layer of bureaucracy. This

danger would, however, be minimized if the consultative body made clear decisions and documented its reasoning.<sup>114</sup>

**Building a Model Institution.** In the US, many state and county bar associations operate Ethics Hotlines for attorneys who need advice. Callers' identities are invariably kept confidential; additionally, many lines accept anonymous inquiries.<sup>115</sup> Some hotlines also produce and publish short opinions explaining their decisions.<sup>116</sup> This practice reduces arbitrariness, sharpens existing ethics principles, and provides guidance to the broader community. UC Berkeley is in the process of extending this model to synthetic biology. Its Bioethics Advisory Committee ("BEAC") will provide biosafety/biosecurity advice to synthetic biologists at UC Berkeley and Lawrence Berkeley National Laboratory.

The BEAC will respond to inquiries from any experimenter, whether or not s/he is part of the UC system. Institutions at other universities are urged to follow suit.

**Resolved:** Experimenters considering an "experiment of concern" within the meaning of the Fink Report should obtain expert independent advice before proceeding. The community has an ethical obligation to make such advice freely available, particularly to non-members who lack access to university- or company-funded safety committees.

## B.2 Endorse Members' Ethical Obligation to Investigate and Report Dangerous Behavior.

All members interviewed for this project agreed that scientists have an ethical obligation to report dangerous or inappropriate behavior. In some cases, members believe that safety committees and other appropriate official channels already exist to do this.<sup>117</sup> However, other members feel that existing bodies have insufficient biosecurity expertise and that an alternative body could better fill this need.<sup>118</sup>

**Resolved:** Members have an ethical obligation to investigate and, if necessary, report behavior that they believe poses a significant danger to human life and property. Members may satisfy this obligation through existing channels, by calling authorities, or by contacting community bodies established for this purpose.

## B.3 Other Proposals for Developing Norms and Practices.

Our interviews disclosed various novel proposals that have not yet been widely discussed within the community. These include:

***Buddy System.*** Laurie Zoloth has suggested a provocative extension of normal academic mentoring in which PhD. advisors hold periodic reunions to track former students and identify troubling behavior. Members were divided over the suggestion.<sup>119</sup>

***Include Ethical Statements in Grant Proposals.*** One member pointed out that a resolution calling on members to include ethical analysis in each grant application would encourage applicants to compete along ethical as well as scientific dimensions.<sup>120</sup>

***Education.*** Two members argued that early education of young scientists and undergraduates about ethics and responsible design practices would improve biosafety/biosecurity.<sup>121</sup> However, another member noted that education would have only limited value against malicious individuals.<sup>122</sup>

***Promote International Cooperation.*** Members believe that scientists in different countries should pursue closer cooperation on biosecurity matters.<sup>123</sup>

## C. Maintain an Ongoing Institutional Commitment to Biosecurity and Biosafety.

This document provides a snapshot of a rapidly changing technology. The picture five years from now could well be different. For this reason, the community needs to monitor and potentially respond to future biosecurity/biosafety threats as they emerge. This will require new institutions to ensure, in the words of a recent National Research Council report, that “regular and deliberate reassessments of advances in science and technology and identification of those advances with the greatest potential for changing the nature of the threat spectrum.”<sup>124</sup>

### C.1 Create A Community-Wide Clearinghouse for Identifying and Tracking Emerging Biosafety and Biosecurity Issues.

Communities in potentially dangerous industries frequently share information about risks to accelerate community learning and reduce the chance of accidents. The practice is particularly well developed in aviation, where the US Federal Aviation Authority’s “Aviation Safety Reporting System”<sup>125</sup> receives and compiles data from 30,000 voluntary reports each year. The FAA uses this information to identify emerging safety hazards and issue advisories.

Most members interviewed for this project agreed that an on-line clearinghouse or working group should be established to share information about potential accidents<sup>126</sup> and

biosecurity threats.<sup>127</sup> Although members expressed skepticism about how much information such a site would yield, they nevertheless concluded that such a site was a sensible investment given (a) its low expected cost<sup>128</sup> and (b) the chance that it might yield substantially more information than anticipated.<sup>129</sup>

**Design Issues.** Several members mentioned design issues that should be considered in designing a site:

***Breadth.*** One members cautioned that a site could create the false impression that synthetic biology is inherently more dangerous than other forms of genetic engineering or microbiology. This impression could, however, be negated if the site was deliberately broadened to include potential accidents involving genetic engineering or even microbiology as a whole.<sup>130</sup>

***Attribution, Confidentiality or Anonymity?*** Several members remarked that an anonymous site could become a focal point for naïve, irresponsible or hoax statements that the public would then attribute to the community. This argues against classic **anonymous** sites like the US Navy’s “Anymouse”<sup>131</sup> program.\* On the other hand, an **attribution** site that publicly disclosed contributors’ identities would likely deter participation. **Confidential sites** like the FAA’s ASRS System (*supra*) provide a potentially appealing compromise.

***Partial Overlap.*** Some members noted that information reported to the site would potentially duplicate that sent to university safety committees,<sup>132</sup> although a community-wide would presumably help to span institutional barriers. Other members worried that the most useful information was already published in academic journals.<sup>133</sup> The extent to which the site would develop additional but still useful information is an empirical question.

**Web Page and Working Group.** The Synthetic Biology conference series provides a natural focal point for reporting, analyzing, and sharing new biosafety/biosecurity developments. Members operating the site could deliver talks updating the community at each successive Synthetic Biology conference.

**Resolved:** Members have an ethical obligation to share facts, experiences, and conjectures that increase community awareness of, and ability to manage, biosafety and biosecurity risks. Community members are encouraged to establish confidential clearinghouses to collect, analyze, and disseminate this information.

---

\* Community opinion appears evenly divided. Five of the nine members asked about anonymity thought that an anonymous site was appropriate.

## C.2 Other Ideas for Developing Community Norms and Practices.

Various other proposals made during the course of our interviews remain preliminary. These include:

**Conferences.** Members approve of recent biosecurity workshops and want to see them continue.<sup>134</sup> Greater information sharing between universities is also desirable.<sup>135</sup>

**Developing Formal Standards for Synthetic Biology.** Most members think that existing recombinant DNA rules adequately cover synthetic biology.<sup>136</sup> However, a few members wondered whether it would be better to develop standards specific to synthetic biology.<sup>137</sup>

**Codes of Ethics.** Two recent National Research Council reports have recommended that biological research communities develop and adopt codes of ethics.<sup>138</sup>

**NIH Advisory Body.** One member suggested that the community could form an advisory group to help NIH review proposals to create novel organisms and recommend additional safeguards as necessary.<sup>139</sup>

**Professional Society.** In the near term, institutions like the proposed biosafety/biosecurity reporting site can be housed within the Synthetic Biology conference series. In the longer term, the community may want to start a professional society. A professional society would, *inter alia*, help members exercise greater self-governance on a variety of issues relating from security to intellectual property rights and communicating with the public.

## D. Invest in New, Safety- and Security-Enhancing Technologies.

Technology promises to make biosecurity/biosafety more effective. Members are uniquely qualified to prioritize technologies and should consider recommending promising ideas to funding agencies.

### D.1 Endorse Biosecurity/Biosafety R&D Priorities.

Members interviewed for this project responded favorably to two possibilities, bar codes and inherently safe organisms. Other promising categories may emerge during Town Halls and Synthetic Biology 2.0.

**Bar Codes.** As previously explained, bar codes provide a promising technology for detecting organisms and deterring improper use of commercial gene sequences.

**Resolved:** Funding agencies should invest in research to explore the use of “bar code” technology to detect and trace the origins of genetically modified organisms.

**Inherently Safe Organisms.** In principle, current biosafety risks can be reduced still further by performing experiments in host organisms that have been deliberately engineered to minimize the chances for survival and propagation outside the laboratory. However, current examples of such technologies – *e.g.* using organisms that are oxotrophic or depend on materials like tetracycline not found in the wild – are primitive and offer only limited protection.<sup>140</sup>

Members overwhelmingly agreed that research into these techniques should be actively funded and pursued<sup>141</sup> and no one opposed such research. Promising research directions include, but should not be limited to, organisms that can readily be killed using simple chemicals (*e.g.* salt or common antibiotics), organisms that depend on specialized nutrients or environments not found in Nature, co-dependent organisms that would likely become separated from one another in the wild, and organisms that cannot reproduce more than a pre-set number of times. Properly designed organisms should also be stable against evolutionary pressures that might otherwise delete these engineered safety features.<sup>142</sup> Some members expressed doubt that the community will ever produce a completely safe organism. That said, even an imperfect technology could be worthwhile if it improved safety.<sup>143</sup>

Inherently safe organisms are not a panacea. For example, inherently safe organisms cannot be used for projects in which organisms are released into the wild or for research agendas that do not follow a parts-and-chassis view of synthetic biology.<sup>144</sup> Nevertheless, it might make sense for a future conference to call on members to adopt such technologies whenever feasible.

**Resolved:** Funding agencies should invest in research to engineer host organisms for synthetic biology experiments that have little or no chance of surviving, propagating, or interacting with organisms outside the laboratory.

### D.3 Other Ideas.

Various other proposals made during the course of our interviews remain preliminary. These include:

**Prize Incentives.** Instead of endorsing existing technology ideas, the community could potentially call on agencies to offer prizes for new applications.<sup>145</sup> Since

the grant system is already designed to elicit new ideas, the gains from such a strategy would likely be limited.<sup>146</sup> A prize system might nevertheless offer potential advantages to the extent that (a) it offered larger reward than researchers could normally expect from grants, or (b) it extended beyond the relatively small group of researchers who normally compete for synthetic biology support. Everything else being equal, the utility of prizes would depend on how many ideas are likely to be generated from students and other groups outside the normal grant system.

***US Biodefense Policy Review.*** Synthetic biologists could potentially organize a blue ribbon committee to review current US biodefense priorities.<sup>147</sup>

## IV. Conclusion

Six years of almost continuous discussion have given synthetic biologists a solid understanding of biosafety/biosecurity risks and the available possible policy instruments for reducing them. The challenge now is implementation. This document has presented a menu of choices that could potentially improve security at modest cost. Synthetic Biology 2.0 offers a chance to turn this understanding into action.

---

<sup>1</sup> For a brief history of self-regulation following Asilomar, see National Research Council, *Biotechnology Research in an Age of Terrorism: Confronting the Dual Use Dilemma*, (2004), hereinafter “Fink Report” at viii.

<sup>2</sup> *Id.* at viii.

<sup>3</sup> See, e.g., Royal Society and Wellcome Trust: “Do No Harm: Reducing the Potential for the Misuse of Life Science Research (2004) at p. 1 (“Self governance by the scientific community was favoured, rather than new legislation”). The report is available at <http://www.royalsoc.ac.uk/displaypagedoc.asp?id=10360>.

<sup>4</sup> Anon., “First Annual Meeting on Synthetic Biology,” (2004), available at [http://openwetware.org/images/7/79/SB1.0\\_overview.pdf](http://openwetware.org/images/7/79/SB1.0_overview.pdf).

<sup>5</sup> Robert Carlson, “Synthetic Biology 1.0,” *Future Brief* (2005), available at <http://www.futurebrief.com/robertcarlsonbio001.asp>. Discussions covered various proposals including licensing scientists, strict controls on the distribution of technology and reagents, and using artists’ signatures to trace the source of altered DNA. Much of this debate was, however, controversial and the discussion inconclusive. *Id.*

<sup>6</sup> MIT News Office, “Study to Explore Risks, Benefits of Synthetic Genomics” (2005) (announcing 15 month, \$570,000 grant).

<sup>7</sup> Conversation with Mike Stebbins (March 10, 2006).

<sup>8</sup> National Research Council, *Globalization, Biosecurity, and the Future of the Life Sciences* (2006) at p. viii.

<sup>9</sup> George Church, “Let Us Go Forth and Safely Multiply,” *Nature* 438:423 (2005): “A code of ethics and standards should emerge for biological engineering as it has done for other engineering disciplines. The community recognizes this need, but discussions are fragmentary. The next international meeting on synthetic biology (in May 2006 at the University of California, Berkeley) should make significant progress in that direction.”

<sup>10</sup> For updated agenda information, see *Synthetic Biology 2.0*, available at <http://pbd.lbl.gov/sbconf/>.

<sup>11</sup> Conversations with Drew Endy (March 21) and George Church (March 9, 2006).

<sup>12</sup> George Church, “Let Us Go Forth and Safely Multiply,” *Nature* 438:423 (2005): “A code of ethics and standards should emerge for biological engineering as it has done for other engineering disciplines. The

## From Understanding to Action: Community-Based Options for Improving Security and Safety in Synthetic Biology

---

community recognizes this need, but discussions are fragmentary. The next international meeting on synthetic biology (in May 2006 at the University of California, Berkeley) should make significant progress in that direction.”

<sup>13</sup>The ability to order ready-made genes and oligos drastically cuts the cost of traditional genetic engineering projects by freeing skilled laboratory workers for other tasks. This means that more experiments can be done within existing budgets, allowing companies to bring more – and more ambitious – products to market. Adam Arkin (personal communication). The resulting efficiency gains are presumably proportional to the current value of biotechnology products, which is believed to exceed \$50 billion. Biotechnology Industry Association, *Bio 2005-2006 Guide to Biotechnology*, available at <http://www.bio.org/speeches/pubs/er/BiotechGuide.pdf#search=’bio%202005%20%202006%20guide’>

<sup>14</sup> For detailed list of possible benefits, see Ray Gesteland, *Synthetic Genomes: Policies and Impacts* (2004) and NRC, “Globalization, Biosecurity, and the Future of the Life Sciences,” (2006) at pp. 121-123.

<sup>15</sup> See, e.g., Bernadette Tansey, “Science Tweaks Nature’s Toolbox,” *San Francisco Chronicle* (August 20 2005) available at <http://www.sfgate.com/cgi-bin/article.cgi?f=/c/a/2005/08/20/BUG4LEAGRT1.DTL&sn=001&sc=1000>.

<sup>16</sup> D. Endy, “Foundations for Engineering Biology,” *Nature* **438**:449 (2005)

<sup>17</sup> Conversation with John Mulligan (Feb. 24, 2006).

<sup>18</sup> Today’s biosafety debate has changed relatively little since the Asilomar conference of 1975. See generally, Philip McClean, *Historical Events in the rDNA Debate*, <http://www.ndsu.nodak.edu/instruct/mcclean/plsc431/debate/debate3.htm> Similarly, modern biosecurity policy reflects a range of technologies developed between World War II. See, e.g., Jeanne Guillemin, *Biological Weapons: From the Invention of State-Sponsored Programs to Contemporary Bioterrorism* (Columbia Univ. Press: 2005) and Robert Harris and Jeremy Paxman, *A Higher Form of Killing: The Secret History of Chemical and Biological Warfare* (Random House: 2002). Genetically engineered bioweapons were massively explored by Soviet workers during the 1980s. See e.g., Guillemin, *supra*, and Ken Alibek, and Stephen Handelman *Biohazard* (Random House: 1999).

<sup>19</sup> See generally, S. Maurer, “What’s So Hard About Terrorism?” available at [http://www.cs.washington.edu/education/courses/csep590/05au/lectures/slides/Maurer\\_Sept7.ppt#56](http://www.cs.washington.edu/education/courses/csep590/05au/lectures/slides/Maurer_Sept7.ppt#56); Accord, National Research Council, *Globalization, Biosecurity, and the Future of the Life Sciences*, (2006) at pp. 190, 196 (greater biosecurity awareness among scientists would “change the risk calculus of potential offenders”).

<sup>20</sup> Accord, National Research Council, *Globalization, Biosecurity, and the Future of the Life Sciences* (2006) at p. viii (scientists “need to survey the threat horizon continually”).

<sup>21</sup> M. Dando, *The New Biological Weapons: Threat, Proliferation and Control* London: 2001 at p. 1. The psychological effect of bioweapons is probably overstated in any case. Social psychology research shows that human beings place relatively little weight on how (as opposed to when) they die. Furthermore, people tend to fear rare, unfamiliar risks more than familiar ones. See generally, Paul Slovic, *The Perception of Risk* (EarthScan: 2000). Small scale bioweapons may be more frightening *before* they are used.

<sup>22</sup> Phil Hirschhorn, “New York reduces 9/11 death toll by 40,” CNN October 29, 2003, available at <http://www.cnn.com/2003/US/Northeast/10/29/wtc.deaths/>

<sup>23</sup> Government cost-benefit calculations typically value lives saved at \$1-6 million each. Cass Sunstein, “Valuing Life, A Plea for Disaggregation,” 54 *Duke L.J.* 385 (2005). Casualty rates would have to be in the thousands to erase the benefits that conservatively run into the tens of billions.

<sup>24</sup> For a survey, see W. Seth Carus, “Unlawful Acquisition and Use of Biological Agents,” in Joshua Lederberg (ed.), *Biological Weapons: Limiting the Threat* (MIT Press: 2000); see also, Jeffrey Bale and Gary Ackerman, “How Real is the ‘WMD Terrorism’ Threat?” available at <http://www.cs.washington.edu/education/courses/csep590/05au/lectures/>.

<sup>25</sup> The Japanese program employed roughly 6,000 workers. Harris and Paxman, *Higher Form of Killing* at p. 80. The much larger US program employed “several hundred” scientists and research staff and invested billions of dollars from World War II through the late 1960s. J. Guillemin, *Biological Weapons*, Columbia Univ. Press 2005 at p. 109 (spending in the early 1960s totaled \$300 million per year).

<sup>26</sup> The Soviet program reportedly employed a staggering 32,000 scientists and staff working at forty separate facilities with a budget of “several hundred million” per year. Roughly half of the employees

worked to develop diseases; the other half made cures. B. Preston, “The Bioweaponers,” *The New Yorker* (March 9, 1998) at p. 53 (half of the employees made diseases, the other half medicines); Tom Mangold and Jeff Goldberg, *Plague Wars: The Terrifying Reality of Biological Warfare* (1999) at p. 93.

<sup>27</sup> The South African program, which focused primarily on assassinations, employed 200 people with an annual budget of £4-5 million. Mangold and Goldberg, *Plague Wars, supra*, at p. 266. The Iraqi program included at least five separate production facilities and an extensive testing program that reportedly included the use human prisoners. *Id.* at 264, 299.

<sup>28</sup> Fort Detrick’s approximately 1800 scientists and staff principally worked on identifying suitable “weaponizable” diseases task of Fort Detrick’s from 1945 to 1950. Mangold and Goldberg, *Plague Wars, supra*, at p. 32, 34. Japanese program used used hundreds of animals and, eventually, more than 10,000 human subjects. Harris and Paxman, *A Higher Form of Killing* at pp. 80-81.

<sup>29</sup> M. Dando, *The New Biological Weapons, supra* at p. 11

<sup>30</sup> Isolating in wild would be difficult. There are more than seventy different strains of *bacillus anthracis*, but only a small minority are highly virulent. J. Tucker, *Biosecurity: Limiting Terrorist Access to Deadly Pathogens* (United States Institute of Peace, 2004) at p. 15, available at <http://www.usip.org/pubs/peaceworks/pwks52.pdf>.

<sup>31</sup> Individual laboratories house large collections leftover from research on outbreaks and epizootics. The FBI has estimated that there may be as many as 22,000 such laboratories in the US alone. .J. Guillemin, *Biological Weapons*, Columbia Univ. Press 2005.

<sup>32</sup> J. Tucker, *Biosecurity: Limiting Terrorist Access to Deadly Pathogens* (United States Institute of Peace, 2004) at p. 13, available at <http://www.usip.org/pubs/peaceworks/pwks52.pdf>; *Fink Report, supra* n. 1, at pp. 2 (US oversight “will ultimately afford little protection if it is not adopted internationally”) and 86 (“Only an international set of standards will help to minimize the misuse of biotechnology.”); National Research Council, *Globalization, Biosecurity, and the Future of the Life Sciences* (2006) at p. viii (“Science does not stop at our borders”).

<sup>33</sup> J. Cello, A. Paul, and E. Wimmer (2002) Chemical synthesis of poliovirus cDNA: generation of infectious virus in the absence of natural template. *Science* **297**: 1016–1018. Although important as a demonstration, the experiment was “a very laborious and difficult way to accomplish this synthesis.” *Fink Report, supra*, n. 1 at p. 22.

<sup>34</sup> *Science* (T. M. Tumpey *et al.* **310**, 77–80; 2005).

<sup>35</sup> British Joint Staff estimated that that an anthrax attack would require 636 four-pound bomblets per square mile in theory and 8500 bomblets in practice. Mangold and Goldberg, *Plague Wars, supra*, at p. 33; Harris and Paxman, *A Higher Form of Killing, supra*, at pp. 102, 106. Assuming that each bomblet contained ¾ wet agent by weight, the required quantity of agent runs to 12.5 tons or about 4.8 tons per kilometer. Attacks using aerosols could be somewhat more efficient. Nevertheless, the fact that postwar exercises invariably used warships suggests that tons of material were used. Mangold and Goldberg, *Plague Wars, supra*, at p. 35, 37.

<sup>36</sup> Sprayers reportedly have a 26% efficiency compared to 15 percent for bomblets. M. Dando, *The New Biological Weapons: Threat, Proliferation, and Control*. Lynne Rienner: London (2001). Postwar estimates reportedly found that required bombloads could be reduced by an order of magnitude if more contagious diseases were substituted for anthrax. Harris and Paxman, *A Higher Form of Killing, supra* at p. 135.

<sup>37</sup> Population density for large US cities typically runs from 5,800 people per km<sup>2</sup> to a high of 26,400 in midtown Manhattan. S. Glasstone and P.J. Dolan, *The Effects of Nuclear Weapons* (US Government Printing Office 1977) at p. 544. The authors remark that densities for midtown Manhattan would be “much higher” during the workday.

<sup>38</sup> Mangold and Goldberg, *Plague Wars, supra*, at pp. 18-19, 2. The Unit could reportedly produce 660 pounds of plague, 1400 pounds of anthrax, 2000 pounds of typhoid, or 2200 pounds of cholera as required. Harris and Paxman, *A Higher Form of Killing, supra* at p. 78. The facility used 900 tanks, each of which could produce 40 grams of bacteria every few days. Russian investigators estimated that it could produce eight tons of bacteria per month. *Id.*

<sup>39</sup> The Soviet accident occurred in Sverdlovsk when a 24-inch filter exploded releasing an estimated 1 to 3.5 kilograms of anthrax from a rooftop site. Casualty estimates range from 64 to 600 people. Vaccine

was subsequently administered to tens of thousands of residents. Mangold and Goldberg, *Plague Wars, supra*, at pp. 69, 404, 406.

<sup>40</sup> In 1968 the US program reportedly conducted tests demonstrating that a single aircraft dispersing three grams of powder per meter could deliver an LD-50 dose over a 30 km depth. Mangold and Goldberg, *Plague Wars, supra*, at p. 39; J. Guillemin, *Biological Weapons*, Columbia Univ. Press 2005 at p. 111 (test delivered dose over nearly 1,000 square miles); B. Preston, “The Bioweaponers,” *supra* at p. 60; Department of Defense, “Fact Sheet: Project Shipboard Hazard and Defense (SHAD) DTC Test 68-50 (reporting use of staphylococcal enterotoxin over “a 40 to 50 kilometer downwind grid.”), available at [http://www1.va.gov/shad/docs/DTC\\_Test\\_68-50\\_SHAD\\_DoD\\_Fact\\_Sheet.pdf](http://www1.va.gov/shad/docs/DTC_Test_68-50_SHAD_DoD_Fact_Sheet.pdf). Assuming Manhattan-type population densities, the estimate naively suggests that 100 grams of material is sufficient to deliver an LD-50 dose to 5,000 people. This simple calculation assumes an unreasonable geometry in which peak population density occurred along the full length of a 30 kilometer corridor. It also neglects the fact that much of the population would be sheltered indoors.

<sup>41</sup> Paul DeArmond, “The Anthrax Letters: Five Deaths-Five Grams-Five Clues,” *Albion Monitor* (Sebastopol CA.) August 16 2002 available at [www.monitor.net/monitor/0208a/anthrax.html](http://www.monitor.net/monitor/0208a/anthrax.html).

<sup>42</sup> A three year Iraqi program failed to achieve pilot scale production of *Bacillus thuringiensis* in the late 1990s, although the country later went on to produce 40 tons per year. Iraq Survey Group Final Report: Evolution of the Biological Warfare Program, available at [http://www.globalsecurity.org/wmd/library/report/2004/isg-final-report/isg-final-report\\_vol3\\_bw-01.htm](http://www.globalsecurity.org/wmd/library/report/2004/isg-final-report/isg-final-report_vol3_bw-01.htm).

<sup>43</sup> M. Dando, *The New Biological Weapons, supra* at p. 36.

<sup>44</sup> *Id.* at p. 37.

<sup>45</sup> Mangold and Goldberg, *Plague Wars, supra*, at p. 77, 79 (reporting approximately 20 injuries per year from 3000 member workforce).

<sup>46</sup> The most recent example involves the disruption of Al Qaeda’s so-called Bojinka conspiracy in 1995 after a fire broke out in a terrorist bomb factory. CNFF, Terrorism Trial Begins in New York – 3 Men Accused of Plotting to Bomb US Planes,” (May 13, 1996), available at <http://www.cnn.com/US/9605/12/terror.plot/>. For earlier examples, see S. Maurer, “What’s So Hard About Terrorism?” available at [http://www.cs.washington.edu/education/courses/csep590/05au/lectures/slides/Maurer\\_Sept7.ppt#56](http://www.cs.washington.edu/education/courses/csep590/05au/lectures/slides/Maurer_Sept7.ppt#56).

<sup>47</sup> Steven M. Block, “Living Nightmares: Biological Threats Enabled by Molecular Biology” in S. Drell, A. Sofaer & G. Wilson (eds.), *The New Terror: Facing the Threat of Biological and Chemical Weapons* (Stanford: 1999) at p. 47 (citing 1997 JASONS study: “Clearly, some elements of this ‘wish list’ seem rather far away from current state of the art.”). The fact that nation states have yet to develop such weapons suggest that terrorist groups would have a hard time producing them.

<sup>48</sup> Iraq Survey Group Final Report: Evolution of the Biological Warfare Program, available at [http://www.globalsecurity.org/wmd/library/report/2004/isg-final-report/isg-final-report\\_vol3\\_bw-01.htm](http://www.globalsecurity.org/wmd/library/report/2004/isg-final-report/isg-final-report_vol3_bw-01.htm); Mangold and Goldberg, *Plague Wars, supra*, at p. 79 (wet agents based on cholera and dysentery can be stored for weeks; anthrax lasts several months).

<sup>49</sup> B. Preston, “The Bioweaponers,” *supra*, at p. 60 (tularemia lasts “only a few minutes” in sunlight); M. Dando, *The New Biological Weapons, supra* at p. (botulinum toxin degrades in sunlight at a rate of 7.8% per minute).

<sup>50</sup> J. Bale and G. Ackerman, “Recommendations on the Development and Methodologies and Attributes for Assessing Terrorist Threats of WMD Terrorism” (CNS 2005).

<sup>51</sup> *Id.*

<sup>52</sup> Mangold and Goldberg, *Plague Wars, supra*, at p. 33, 37.

<sup>53</sup> J. Bale and G. Ackerman, Recommendations on the Development and Methodologies and Attributes for Assessing Terrorist Threats of WMD Terrorism (CNS 2005). The effects of humidity are presumably related to how fast aerosol droplets evaporate.

<sup>54</sup> Mangold and Goldberg, *Plague Wars, supra*, at p. 34, 38.

<sup>55</sup> M. Dando, *The New Biological Weapons, supra* at p. 11, 41 (genetic engineering to effect enhanced aerosol and environmental stability).

<sup>56</sup> *Id.* at p. 35. This conclusion is reinforced by experience in bioremediation, in which companies have almost always tried to locate suitable naturally occurring organisms rather than genetically engineer new ones. Conversation with T. Hazen (Feb. 21, 2006).

## From Understanding to Action: Community-Based Options for Improving Security and Safety in Synthetic Biology

---

<sup>57</sup> M. Dando, *The New Biological Weapons*, *supra* at p. 41.

<sup>58</sup> Antibiotic resistance is largely irrelevant for very large WMD attacks, which would require the overnight delivery of impossible quantities of vaccine. B. Preston, “The Bioweaponers,” *supra* at p. 60.

<sup>59</sup> M. Dando, *The New Biological Weapons*, *supra* at p. 41.

<sup>60</sup> Steven M. Block, “Living Nightmares: Biological Threats Enabled by Molecular Biology” in S. Drell, A. Sofaer & G. Wilson (eds.), *The New Terror: Facing the Threat of Biological and Chemical Weapons* (Stanford: 1999) at p. 47 (describing 1997 JASONs study: “Clearly, some elements of this ‘wish list’ seem rather far away from current state of the art”).

<sup>61</sup> Mangold and Goldberg, *Plague Wars*, *supra*, at p. 180 (Soviet program used genetic engineering to create antibiotic resistance in the 1980s); B. Preston, “The Bioweaponers,” *supra* at p. [60-63] (describing how Oblolensk group published a paper on genetically engineered vaccine-resistant anthrax strains in the British journal *Vaccine*.)

<sup>62</sup> B. Preston, “The Bioweaponers,” *supra* at p. 52

<sup>63</sup> Steven M. Block, “Living Nightmares: Biological Threats Enabled by Molecular Biology” in S. Drell, A. Sofaer & G. Wilson (eds.), *The New Terror: Facing the Threat of Biological and Chemical Weapons* (Stanford: 1999) at p. 47 (“Clearly, some elements of this ‘wish list’ seem rather far away from current state of the art”).

<sup>64</sup> B. Preston, “The Bioweaponers,” *supra* at p. 52 (“[H]e told me the formula for the Alibekov anthrax. He uttered just one sentence. The Alibekov formula is simple and the formula is somewhat surprising, not quite what you’d expect. Two unrelated materials are mixed with pure powdered anthrax spores. It took a lot of research and testing to get the trick right and Alibek must have driven his research group hard and skillfully to arrive at it. ‘There are many countries that would like to know how to do this, he said.’”

<sup>65</sup> For the ideal size of bioweapons particles, *see* B. Preston, *supra* at p. 59. Viruses are less likely to be damaged during biopowder production because of their small size. Bacteria are not much smaller than the than the 1 to 5 micron diameter needed to optimize inhalation. *See* <http://www.nanomedicine.com/NMI/10.4.2.5.htm>.

<sup>66</sup> B. Preston, “The Bioweaponers,” *supra*, at p. 52.

<sup>67</sup> *See e.g.*, Centers for Disease Control, “Summary of Notifiable Diseases, United States, 1995” *Morbidity and Mortality Weekly Report*, available at H:\5. Teaching\Intro to Homeland Security\3. WMD\Notifiable Disease Stats, United States, 1995.htm; Centers for Disease Control, “Human Plague – United States 1993 – 94,” *Morbidity and Mortality Weekly Report*, available at <http://www.cdc.gov/mmwr/preview/mmwrhtml/00026077.htm>; Anon., Plague Cases in the USA 1944 – 1993, available at <http://www.imsa.edu/programs/pbln/problems/bernie/bubonicplagueusa.html>.

<sup>68</sup> “In 1970, when a man infected with smallpox appeared in an emergency room in Germany, seventeen cases of smallpox appeared in the hospital on the floors above. Ultimately the German government vaccinated a hundred thousand people to stop the outbreak. Two years later in Yugoslavia, a man with a severe case of smallpox visited several hospitals before dying in an intensive care unit. To stop the resulting outbreak, which forced twenty thousand people into isolation, Yugoslav health authorities had to vaccinate virtually the entire population of the country within three weeks.” B. Preston, “The Bioweaponers,” *The New Yorker* (March 9, 1998) at p.63.

<sup>69</sup> John M. Barry, *The Great Influenza: The Epic Story of the Greatest Plague in History* (Penguin 2005) at pp. 371-73 (mutations made 1918 influenza steadily less lethal as it traveled from the American East to West Coasts and then on to the Midwest.)

<sup>70</sup> M. Dando, *The New Biological Weapons: Threat, Proliferation, and Control*. Lynne Rienner: London (2001) at p. 41.

<sup>71</sup> Conversations with Terry Hazen (Feb. 21, 2006) and Adam Arkin (March 14 2006).

<sup>72</sup> Conversation with Terry Hazen (Feb. 21, 2006).

<sup>73</sup> J.O. Lloyd-Smith, S.J. Schreiber, P.E. Kopp & W.M. Getz, “Superspreading and the effect of individual variation non disease emergence. *Nature* 438:355 (17 Nov. 2005) (noting that skewed infectivity among human hosts makes outbreaks rarer but also more explosive and noting that “other population processes dependent on small numbers of individuals may yield similar insights.”); *see also*, Alison P. Galvani and Robert M. May, “Dimensions of superspreading,” *Nature* 438:293 (17 Nov. 2005) (explaining why

distribution of “superspreaders” within population affects “both the probability that an epidemic will take off and the subsequent course of the epidemic”).

<sup>74</sup> See also, *Fink Report*, *supra* n. 1 at p. 23 (“There have been no reported cases of disease caused by recombinant microorganisms despite the widespread use of gene splicing techniques in academic laboratories and in the production of pharmaceuticals.”)

<sup>75</sup> Conversation with Amy Shutkin (Jan. 31 2006).

<sup>76</sup> Ronald Jackson, “Expression of Mouse Interleukin-4 by a Recombinant Ectromelia Virus suppresses Cytolytic Lymphocyte Responses and Overcomes Genetic Resistance to Mousepox,” *Journal of Virology* 75:1205-10 (2001).

<sup>77</sup> Conversation with George Church (Mar. 9 2006).

<sup>78</sup> *Id.*

<sup>79</sup> Conversation with Marcus Graf (March 14, 2006).

<sup>80</sup> *Id.*

<sup>81</sup> Conversations with John Mulligan (Feb. 24, 2006), Claes Gustaffson (March 6, 2006), Marcus Graf (March 14, 2006), and Marcus Fischer (March 8, 2006).

<sup>82</sup> See Craic Computing LLC, “Products,” available at <http://www.craic.com/products.html>

<sup>83</sup> Interviews with Claes Gustafsson (March 6, 2006) and John Mulligan (Feb. 24, 2006).

<sup>84</sup> Screening practices can be enforced by using a “testing group” to submit sample orders for controlled oligos and reagents. George M. Church, “A Synthetic Biohazard Non-Proliferation Proposal,” (2004). Industry routinely uses similar methods to gather commercial intelligence. Conversation with Marcus Graf (March 14, 2006).

<sup>85</sup> Conversation with John Mulligan (Feb. 24, 2006).

<sup>86</sup> Conversation with Rob Carlson (Feb. 11, 2006).

<sup>87</sup> National Research Council, *Globalization, Biosecurity, and the Future of the Life Sciences*, (2005) at pp. 6 (Recommendation 2: “The Committee recommends adopting a broader perspective on the ‘threat spectrum.’”); 175 (recommending that scientists “[r]ecognize the limitations inherent in any agent-specific threat list and consider instead the intrinsic properties of pathogens and toxins that render them a threat and how such properties have been or could be manipulated by evolving technologies”) and 177 (scientists should “[a]dopt a broadened awareness of threats beyond the classical ‘select agents’ and other pathogenic organisms”).

<sup>88</sup> Conversations with George Church (March 9, 2006), Mike Stebbins (March 10, 2006), John Mulligan (Feb. 24, 2006), Claes Gustaffson (March 6, 2006), Marcus Graf (March 14, 2006), and Marcus Fischer (March 8, 2006).

<sup>89</sup> See e.g., National Research Council, *Globalization, Biosecurity, and the Future of the Life Sciences*, at p. 177 (select agent lists should be extended to include “biologically active molecules, synthetic molecules or life forms”).

<sup>90</sup> Conversation with Marcus Graf (March 14, 2006).

<sup>91</sup> Conversations with George Church (March 9, 2006), Mike Stebbins (March 10, 2006), John Mulligan (Feb. 24, 2006), Claes Gustaffson (March 6, 2006), Marcus Graf (March 14, 2006), and Marcus Fischer (March 8, 2006).

<sup>92</sup> Conversations with. Holman (Feb. 23, 2006), Ron Weiss (Feb. 14, 2006), and Claes Gustafsson (March 6, 2006).

<sup>93</sup> Conversation with Marcus Fischer (March 8, 2006).

<sup>94</sup> Conversation with Chris Voight (March 6, 2006); George M. Church, “A Synthetic Biohazard Non-Proliferation Proposal” ((2004) at p. 1.

<sup>95</sup> Conversation with John Mulligan (Feb. 24, 2006).

<sup>96</sup> Conversation with Drew Endy (March 21 2006) (Sloan group ideas).

<sup>97</sup> Conversations with Tom Knight (March 2, 2006) and Sven Panke (Feb. 6, 2006).

<sup>98</sup> Conversation with Victor De Lorenzo (Feb. 27, 2006).

<sup>99</sup> Conversations with Adam Arkin (Feb. 23), Andrew Ellington (Feb. 14), and Victor de Lorenzo (Feb. 27).

<sup>100</sup> Conversation with David Schaffer (Feb. 9, 2006); Andrew D. Ellington, “Intelligence Countermeasures for Biological Threats (n.d.) at p. 10 (describing use of natural genetic variability to trace the origin of agents.)

<sup>101</sup> According to Andrew Ellington, “The potential utility of organismal sequence taggants was recently demonstrated by the apparent difficulties in determining the provenance of the B anthracis strains used in the bioterrorism attacks on Senators and others. While the strain was eventually traced back to the dead Texas cow from which it had originally been obtained, the problem was that this particular strain had apparently been transferred from USAMRIID to a number of military and other contractors and collaborators. While it is possible that some genetic variance may eventually be found to be associated with each of these transfers, attempting to delineate the different strains based upon random mutations that may (or may not) have arisen will be extremely difficult. This situation can be contrasted with a scenario in which each organism, upon transfer, was embedded with some manner of sequence taggant. IN this instance, the ‘bar code’ that identified the sender and receiver would accompany the organism throughout its history, and would make attribution of the organism trivial.” Andrew D. Ellington, “Intelligence Countermeasures for Biological Threats (n.d.) at p. 13; *See also*, Paul DeArmond, “The Anthrax Letters: Five Deaths-Five Grams-Five Clues,” *Albion Monitor* (Sebastapol CA.) August 16 2002 available at [www.monitor.net/monitor/0208a/anthrax.html](http://www.monitor.net/monitor/0208a/anthrax.html).

<sup>102</sup> Conversations with Adam Arkin (Feb. 23, 2006) and Dan Fletcher (Feb. 3 1006).

<sup>103</sup> *See, e.g.*, Robert Carlson, “Synthetic Biology 1.0,” *Future Brief* (2005), available at <http://www.futurebrief.com/robertcarlsonbio001.asp>. and conversations with Adam Arkin (Bef. 23, 2006), Tom Knight (March 2 2006) and Jörg Stelling (Feb. 21, 2006).

<sup>104</sup> Conversation with Andrew Ellington (Feb. 14, 2006).

<sup>105</sup> George Church, “A Synthetic Biohazard Non-Proliferation Proposal (2004); *see also*, conversations with Adam Arkin (Feb. 23, 2006) (screening for approved grantees) and Sven Panke (Feb. 6 2006) (screening for accredited purchasers)

<sup>106</sup> Conversations with John Mulligan (Feb. 24, 2006), Marcus Fischer (March 8, 2006) and Marcus Graf (March 14, 2006).

<sup>107</sup> *See also*, National Research Council, *Globalization, Biosecurity, and the Future of the Life Sciences* (2006), p. 9 (suggesting that scientists “report[] ... activity to national authorities when it appears potentially malevolent in intent”).

<sup>108</sup> The argument is reminiscent of Kurt Vonnegut’s Tralfalmadorians, who knew that the universe would end when one of their test pilots experimented with the wrong fuel. Kurt Vonnegut, *Slaughterhouse Five* (Dell: 1969).

<sup>109</sup> The “experiments of concern” framework was originally developed by the Fink Report. For a full discussion of the categories *see*, *Fink Report, supra* n. 1 at pp. 88 – 90. *See also*, National Research Council, *Globalization, Biosecurity, and the Future of the Life Sciences* (2006), p. 54 (describing possible experiments of concern).

<sup>110</sup> According to the Fink Report, “[M]embers of the [Institutional Biosafety Committees] will require substantial education in the potential risks associated with advanced biotechnology research in order to [evaluate experiments of concern] competently. Many IBCs may need to add expertise in immunology, virology, pathology, and epidemiology to undertake this new responsibility.” Fink Report, *supra*. at 90. The report also noted that Institutional Biosafety Committees do not currently have formal jurisdiction over “experiments of concern.” *Id.* at 91. The Report also recommends that the entire “Institutional Biological Safety committee/Recombinant DNA Advisory Committee process [be] augmented to include the assessment of the potential for misuse as a criterion for approval or denial of proposed experiments.” *Id.* pp. 86-87.

<sup>111</sup> “It was agreed that existing regulatory processes did not assess whether experiments should be undertaken. Many of the current systems, such as those for dangerous pathogens, genetically modified organisms and animal experiments, address whether an experiment can be conducted safely, rather than whether the experiment should be conducted at all based on a consideration of the potential misuse of the research. For example, an experiment to reconstruct the 1918 influenza virus would be permitted providing it was conducted in a category 4 laboratory to ensure the required level of containment. However, there would not be any discussion of whether it would be wise to undertake the experiment.” Royal Society and Wellcome Trust: “Do No Harm,” *supra* n. 3 at p. 4.

<sup>112</sup> Conversation with Roger Brent (Nov. 16, 2005).

<sup>113</sup> Conversations with Luis Serrano (Feb. 16, 2006) and Ron Weiss (Feb. 14, 2006).

## From Understanding to Action: Community-Based Options for Improving Security and Safety in Synthetic Biology

---

<sup>114</sup> Conversation with George Church (March 9, 2006).

<sup>115</sup> See, e.g., The California Bar Association Ethics Hotline homepage, available at [http://www.calbar.ca.gov/state/calbar/calbar\\_generic.jsp?cid=10131&id=1118](http://www.calbar.ca.gov/state/calbar/calbar_generic.jsp?cid=10131&id=1118).

<sup>116</sup> See, e.g., The Los Angeles Country Bar hotline opinions posted at <http://www.lacba.org/showpage.cfm?pageid=427>.

<sup>117</sup> Conversations with [SUPPLY]

<sup>118</sup> Conversation with Carlos Bustamonte (Feb. 3, 2006).

<sup>119</sup> Conversations with George Church (March 9, 2006) and Drew Endy (March 21 2006).

<sup>120</sup> Conversation with Tim Han (Jan. 31, 2006)

<sup>121</sup> Conversation with Christina Smolke (Feb. 2, 2006); see also Fink Report, *supra* n. 1 at p. 87 (recommending that professional societies update ethical codes to include biosecurity); National Research Council, *Globalization, Biosecurity, and the Future of the Life Sciences* (2006) at pp. 8 (recommending ethical codes as mechanism to “facilitate the recognition of potentially malevolent behavior (i.e., experiments aimed at purposefully developing potential weapons of biological origin) or potentially inappropriate experiments that might unwittingly promote the creation of a more dangerous infectious agent.”), 188 (recommending explicit national and international codes of conduct and ethics for life scientists”), 190 (“Nor will codes of ethics likely deter anyone who is firmly committed to applying biotechnology for malevolent purposes, such as ... a dedicated member of a terrorist group.”) and 198 (“In considering such codes, the Committee concluded that their primary effect would be to create an enabling environment that would facilitate the recognition of potentially malevolent behavior (i.e., experiments aimed at purposefully developing potential weapons of biological origin), or potentially inappropriate experiments that might unwittingly promote the creation of a more dangerous infectious agent.”).

<sup>122</sup> [SUPPLY]; see also, Wellcome Trust, *Do No Harm*,” *supra* n. 3, at p 1 (“Some skepticism was expressed about the value of codes of conduct”).

<sup>123</sup> Conversation with Drew Endy (March 21 2006) (Sloan group ideas); see also, *Fink Report, supra* n.1 at p. 10 (proposing international forum on biosecurity).

<sup>124</sup> National Research Council, *Globalization, Biosecurity, and the Future of the Life Sciences*, at pp. 177-78.

<sup>125</sup> The ASRS maintains a confidential, voluntary incident reporting system and a database of reported incidents. The purpose is to identify system or latent errors, as well as overt hazards, and to alert the industry about these errors. The ASRS receives more than 30,000 reports annually and issues alerts to the industry on a regular and as needed basis. Most aviation experts agree that these efforts have resulted in an ever-increasing level of civilian airline safety.” <http://www.aorn.org/journal/2002/aprrc.htm> and [http://asrs.arc.nasa.gov/main\\_nf.htm](http://asrs.arc.nasa.gov/main_nf.htm).

<sup>126</sup> Conversations with Ron Weiss (Feb. 14, 2006), Pam Silver (Jan. 28, 2006), and Tom Knight (March 2, 2006).

<sup>127</sup> Conversation with George Church (March 9, 2006).

<sup>128</sup> [SUPPLY]

<sup>129</sup> [SUPPLY]

<sup>130</sup> Conversation with George Church (March 9, 2006).

<sup>131</sup> For a short description of the Anymouse program, see ALMAR 010/03, available at <http://www.usmc.mil/almars/almar2000.nsf/45be3083aa37f0d48525685a004b4bcc/c8dd75f302b9f06f85256cbe005129d4?OpenDocument>. Sample reports can be found in D. Nelson and D. Parsons, *Danger: Life and Death Story's from the US Navy's Approach Magazine*, Osceola WI, 1991.

<sup>132</sup> Conversation with Drew Endy (March 21 2006).

<sup>133</sup> Conversations with Sven Panke (Feb. 5, 2006) and Adam Arkin (Feb. 23, 2006).

<sup>134</sup> Conversation with Carlos Bustamonte (Feb. 3, 2006); see also, Fink Report, n.1 at p. 3 (calling for regular meetings and symposia)..

<sup>135</sup> Conversation with David Schaffer (Feb. 9, 2006).

<sup>136</sup> Conversation with Chris Voigt (March 6, 2006).

<sup>137</sup> Conversations with Dan Fletcher (Feb. 3, 2006), Ron Weiss (Feb. 14, 2006) and Kris Prather (Feb. 14, 2006).

## From Understanding to Action: Community-Based Options for Improving Security and Safety in Synthetic Biology

---

<sup>138</sup> Fink Report, *supra* n. 1 at p. 88; National Research Council, *Globalization, Biosecurity, and the Future of the Life Sciences* (2006) at p. 188.

<sup>139</sup> Conversation with Dan Fletcher (Feb. 3, 2006).

<sup>140</sup> Conversation with Chris Voigt (March 6, 2006), Victor de Lorenzo (Feb. 27, 2006), George Church (March 9, 2006), and Luis Serrano (Feb. 16, 2006).

<sup>141</sup> **[SUPPLY]**.

<sup>142</sup> Conversation with Adam Arkin (Feb. 23, 2006), Tom Knight (March 2, 2006), and George Church (March 9, 2006)

<sup>143</sup> Conversations with Ron Weiss (Feb. 14, 2006), Jörg Stelling (Feb. 21, 2006), and Victor de Lorenzo (Feb. 27, 2006).

<sup>144</sup> Conversation with Andrew Ellington (Feb. 14, 2006).

<sup>145</sup> Conversation with Drew Endy (March 21, 2006) (Sloan group ideas).

<sup>146</sup> For a modern description of grants, *see* S. Scotchmer, *Innovation and Incentives* (MIT Press: 2005).

<sup>147</sup> Conversation with Drew Endy (March 21, 2006) (Sloan group ideas).