Commentary on Ray Zilinskas' Presentation
on the Security Implications of Synthetic Biology
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My first observation would be that this presentation needs to be repeated on a regular basis for policymakers, the media, and the public. Thank you, Ray, for a first-rate overview of the promise and perils, as your *New Atlantis* article with Jonathan Tucker put it, of the fast moving field of synthetic biology. The more outreach that is done to explain these matters, the better. Policymakers and the public need to appreciate that synthetic biology holds the promise of doing many wonderful and as yet even un-definable things to change medicine, energy, environmental remediation, agriculture, and industry, but the perils part of synthetic biology also need to be recognized and addressed with thoughtful, meaningful guidelines for safe and appropriate conduct of synthetic biology research.

To the extent that policymakers and the public are aware that this technology could be misused, their concerns will be exacerbated by knowing that:

- some viruses can now be synthesized (e.g., poliovirus, 1918 influenza), and within two to five years it should be possible to synthesize all viruses;
- synthesis of bacteria will be feasible within five to ten years;
- within ten to fifteen years, "superbugs" could be created, marrying the most virulent and contagious properties of multiple microorganisms into entirely new ultra-dangerous pathogens; and,
- gene foundries and other companies, including businesses in Iran and China, are making and selling at remarkably inexpensive prices (e.g., $2 per base pair) the strands of DNA and recombinant DNA needed to synthesize pathogens.

To arrive at the proper formula for governing this field of science, both the promise and the peril need to be explained and kept in perspective.

Given the nascent state of this discipline, there is a unique opportunity to set guidelines that range from ethical expectations to legally binding conduct requirements for those practicing this area of biotechnology. Like their predecessors, the early genetic engineers who met in Asilomar, synthetic biologists are to be applauded for taking the initiative to start a dialogue about governance. Ideally, practitioners will frame their own guidelines because far too few policymakers and even regulatory bureaucrats grasp the intricate technical details of synthetic biology sufficiently to craft meaningful and reasonable guidelines and regulations. Thankfully, the practitioners of synthetic biology have seized the initiative. Should they relinquish it, synthetic biologists could face regulations driven by fear and misunderstanding and public skepticism about, if not downright rejection of, the fruits of their labor.

Among several constructive recommendations that Ray has made is one that would address concerns about the safety of synthetically generated organisms being

released into the environment. Public safety concerns should be alleviated by the microcosm and mesocosm testing of synthetic organisms that Ray suggests. The difficulty here will be establishing the length of the testing period sufficient to merit public confidence in the safety of the tested organisms. The Goldilocks test, articulating the length of the testing period that is suitable for public and environmental safety while also being fair to inventors who wish to market their product, will be substantial. Perhaps more so in Europe than in the United States, pre-existing public concerns about the use of genetically modified organisms may complicate efforts to establish reasonable testing standards for synthetic organisms. Microcosm and mesocosm testing, however, is a reasonable and appropriate way to govern this risk.

Another commendable proposal that Ray has made would require gene foundries to screen orders for pathogenic DNA sequences. This recommendation seems to be reasonably effective from the standpoint of thwarting misbehavior and also reasonably feasible to implement without an undue burden to the industry. I am encouraged that the participants at Synthetic Bio 2.0 in May 2006 agreed to proceed with the development and sharing of software to facilitate such screening and that a policy statement was made encouraging individuals to avoid gene synthesis companies that do not institute screening.

However, I would hope that both consumers and producers of these materials could take stronger steps. For their part, U.S. gene synthesis companies should convene to discuss this matter and agree to common rules for screening of orders. For example, similar to the Australia Group's no-undercut policy, companies could agree to share information on orders that they decline with other cooperating suppliers, alerting them to the possibility that this customer may also approach them. The reasons for the declined order, if not obvious by the nature of the material requested, can be briefly stated and all companies participating would also agree to not to sell those particular materials to that particular customer, although other unobjectionable materials might be sold to that customer. This unofficial screening cooperative would demonstrate the budding industry's intention to operate responsibly with both public and scientific interests in mind. Companies from Europe, Asia, and elsewhere should be encouraged to join as rapidly as possible. To guide consumers to shop responsibly, a website could be established to list the companies that have screening in place and to explain the procedures and the reasons they have been instituted. Industry collaboration on screening and other governance policies can be viewed as pro-active and self-interested and is likely to be well received by a public worried about foul play in synthetic biology.

For their part, consumers should not just be "encouraged to avoid" but to pledge not to patronize companies that fail to screen orders. The objective is to create an economic disincentive for non-screening companies through the collective action of responsible consumers, ideally compelling such companies to establish screening and join the industrial screening cooperative. Such steps can be taken in advance of regulatory requirements to screen orders. Screening of orders is one of several good governance concepts that have been introduced for consideration, including many that

were presented in the draft report called *Synthetic Genomics: Options for Governance*, which is the product of collaboration between MIT, the Venter Institute, and CSIS.

Along those lines, proactive oversight of dual-use research is certainly in order, and the National Science Advisory Board for Biosecurity is working to fashion guidance. Ideally, the guidelines that the NSABB produces should be adopted internationally, or harmonized with the guidelines established by other countries that are taking a proactive approach to governance. As beneficial as the NSABB process is, one has to concede that this process is moving rather slowly. Rather than wait for the NSABB horse to appear, I wonder if a constructive cart might be placed in front of it to move jumpstart governance and also to compensate for the fact that the NSABB is an entity with domestic reach only.

For example, the formation of a professional society could serve multiple useful purposes, particularly with regard to the articulation of professional standards. As noted, some practitioners have already initiated the governance discussion and are introducing concepts for consideration. A professional society, say, the International Society of Synthetic Genomics, could become an instant focal point to drive that discussion to agreement among the leading practitioners of an initial set of standards (e.g., code of ethics, purchase and sales policies, publication guidelines, biosafety standards for synthetic biology research). Although a professional society has limited, if any capacity to enforce such standards, at least the bar will have been set for those who wish to be legitimate practitioners, members in good standing of the synthetic biology community. Given the complexities and risks of this field, the more rapidly professional standards are articulated, the better it will be for current practitioners and those just starting in the field. The society's professional standards should be incorporated into the synthetic biology courses at universities and colleges.

Through its webpage, conferences, and journal, the society could be the standard bearer for responsible conduct and a hub for those entering the field. As scientists use these channels to keep informed about developments in the field, awareness will be raised about responsible conduct. Acknowledging the rapid spread of this technology globally and taking the initiative to involve practitioners around the world, from the outset the society should be international, rather than American only.

By setting professional standards, the society can help define reasonable government regulations, where necessary. In their respective countries, members of the society can be appointed to reach out to legislators and regulators to explain their craft and their approach to governance, much as Ray has done here today. Finally, gene synthesis companies and manufacturers of relevant equipment are natural corporate partners for the activities of this professional society, whether to offset funds for conference activities or to help maintain the society's webpage. Partner companies, of course, would be observing responsible standards of conduct.

Once professional standards have been set for the core practitioners of synthetic biology, the society should reach out to the other disciplines (e.g., computer science, engineering) that are also engaged in synthetic biology. This outreach can be

accomplished through key personnel in these other disciplines as well as through their professional societies. No matter what their core discipline, all practitioners of synthetic biology should observe good governance guidelines. Other disciplines can be encouraged to embrace the society's standards or the society can work with other disciplines to adjust them, as necessary.

One of the toughest parts of this equation will be how to extend governance to biohackers or garagistas, as they have been called. Whether intentionally or not, these individuals could create and propagate organisms that pose dangers to humans or the environment. Efforts should be made to solicit the input of hackers about governance issues, to bring them to the table. Perhaps that can be done by sponsoring a few workshops where hackers could interact with the leading practitioners in the field. During such sessions, standards of responsible conduct should be emphasized and perhaps, as professional relationships form, a few hackers can be persuaded to serve as champions for responsible conduct within the subcommunity of biohackers. Also, consideration should be given to establishing a hotline for biohackers. Through the society's website or via telephone, hackers should be able to consult designated experts that can help them make responsible decisions should their activities take them into questionable or dangerous territory.