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Synthetic Biology

On Aug. 4-5, 2009, the Federal Bureau of Investigation convened its inaugural Synthetic Biology Conference entitled ''Building Bridges Around Building Genomes.'' The goal of the conference was to address the challenges in communication and cross-agency education posed by the dual-use potential of discoveries by the developing synthetic biology industry. This article presents an overview of the conference and its discussion of the role of the FBI as it seeks to address real-world challenges in enforcement and public protection and the need to preserve positive academic and research goals.

Building Bridges—The FBI, Academia, Industry and the Challenges of Synbio

BY J. MARK WAXMAN, ESQ.

I. The Technology and the Dual-Use Potential

The positive goals of synthetic biology (''synbio'') are well chronicled. Through a marriage of engineering and biology, synbio brings the promise of new tools, systems, constructs and devices that can benefit the public in fields such as medicine, pharmaceuticals, environmental preservation, energy, and ''biomaterials.'' At the same time, the potential to develop new and potentially very threatening biological constructs also exists.

From a technological standpoint, at the core of concerns is the ability to build a base or ''minimal'' genome from scratch. While it is possible that someone has already accomplished this, it is clear that within the not too distant future, this accomplishment—''build to suit'' in a reasonably short time frame—will be quite achievable, and from a variety of producers. If this is the case, then the capacity to make an ever-expanding number and type of viruses also increases, and the dual-use challenge materially increases.

This dual-use potential leads to a need to address and, as Gerald Epstein, a conference participant,

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pointed out, ameliorate the risk by addressing a series of biological risk challenges relating to:

- infectious disease,
- biotechnology,
- deliberate misuse,
- international issues, and
- governance.

All of this must be considered as commercial DNA synthesis ''foundries'' proliferate around the world, making this a truly worldwide issue.

The ultimate challenge, of course, is to establish mechanisms that allow an assessment of just what synbio uses or tools actually pose a real security risk. In the past, the likelihood of such a real security risk was low—naturally occurring substances were more accessible: witness the events involving the toxic nerve agent Sarin in 1995 in Japan and more recently in the United States with anthrax. In the future, this may not be the case.

This in turn leads to the international governance challenge, which requires consideration of the following facts:

- There is no international ''governance'' entity.
- There are no required international standards with respect to shipping synbio products—provided they are not already identified as select agents under U.S. government regulations.
- There is no central registry of dangerous constructs.
- There is no central registry of customers placing orders that should invite scrutiny.
- There are widely diverse views of the potential capacities, risks, and solutions.

II. The FBI Perspective

The FBI recognizes clearly the dual-use problem. Its perspective on the problem stems from its important role in bioterrorism prevention. As Jeff Muller, assistant section chief of the Weapons of Mass Destruction Directorate (WMD), pointed out, this leads to FBI responsibility to identify, detect, deter, and disrupt bioterrorism. To be successful in this effort, the FBI must build its bioterrorism threat detection, identification, and reporting capabilities. And for that to occur, ongoing cooperation and positive interaction with academia and industry is essential.

Muller also pointed out that the biological, and in turn, synbio, threat is very real. FBI investigations since the terrorist attacks of Sept. 11, 2001, include multiple examples of individuals attempting to acquire, threatening to use, or having used abrin, anthrax, botulinum toxin, ricin, tetrodotoxin, and various other biological materials. Evidence of international terrorist interest is tangible. Known terrorist groups are actively trying to recruit technical experts to test unconventional biological weapons, and some have acknowledged placing orders to centers such as the U.K. National Center for Type Cultures. It is not unreasonable to suspect that in the future gene synthesis companies will be targeted as a possible route to obtain starter material for a terrorist, terrorist group, lone offender, or countries with whom trade in such materials or devices is either prohibited or highly suspect and discouraged.

To address this new, potentially very dangerous, and rapidly evolving environment, the FBI has significantly increased its efforts, education, and presence. It emerges in sophisticated interagency and interdisciplinary threat assessment, working closer than ever before with Public Health and Centers for Disease Control and Prevention (CDC) staff. As the FBI conference demonstrates, another important element is an outreach strategy seeking to bridge the gap with the research community.

In part, this is an outreach, education, and awareness effort. In part it is one seeking notification and guidance from the research community. In the aggregate, however, it is the FBI reaching out to the broad spectrum of life sciences interests to ensure all those involved understand that, notwithstanding understandable antipathy, there is common ground in furthering the public safety and welfare.

III. The Policy Response

Given the involved communities, there is a need for a collaborative policy response. Larry Kerr, senior biology adviser to the National Counterproliferation Center, framed the goals to be achieved:

- enhance biosecurity;
- foster laboratory safety;
- protect the environment, the people, and natural ecosystems; and
- maintain rapid progress in synbio research.

The difficulty is how to do this. There are gaps in the regulatory environment outside of select agents; the science is evolving; law enforcement is feeling its way under a statutory and regulatory environment that may lack flexibility; industry and academia are not looking for additional layers of complex registration, licensing, and intrusive oversight; and the problems are international.

Fortunately, the templates for action are coming into view. The National Science Advisory Board for Biosecurity (NSABB) has articulated governmental policy options and recommendations:

- develop and disseminate harmonized guidance;
- develop standards and practices;
- promote customer, sequence, and software screening;
- amend the current laws and regulations (in particular the select agent statute, 18 U.S.C. § 175) as appropriate;
- convene experts; and
- consider international implications and faster international collaboration.

Industry and academia also have generated positive ruling options to address not just the dual-use problem, but more generally the concern that the general public (and their elected representatives) may have with respect to synbio development. As representatives of companies such as Gary Burns of AstraZeneca and John Mulligan of BlueHeron pointed out at the conference, industry can be quite responsible through formal company codes of conduct or simply by exercising sound judgment and an open cooperative interaction with the FBI. Thus internally adopted policies for the security of pathogens may play an important role—even in the absence of detailed regulatory requirements.

Industry trade associations such as the Industry Association of Synthetic Biology (IASB) and the newly created Synthetic Biology Industry Association have put industry codes of conduct high on their agendas. Cord Stahler of the German company febit addressed the is-

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sues from the IASB perspective, starting from the baseline belief that ''prevention is possible.'' For IASB, the biosafety challenge is not fundamentally different from traditional genetic engineering. There are, however, new dimensions in efficiency and scale that post an enhanced risk. The first tier response should be one of self-regulation, with an industry-adopted ''best practices'' or code-of-conduct approach. A second element would be creation of a virulence information repository (VIREP)—a central database on virulence factors and genes of concern.

Industry consideration of the areas to address as a part of the industry governance challenge are consistent with those articulated in various government agencies. Dr. Jessica Tucker, AAAS science and technology fellow in the Office of the Assistant Secretary for Preparedness and Response of the Department of Health and Human Services, specifically addressed the oversight needs, tracing the history of U.S. governmental efforts from the NSABB report on Synbio in 2006.

Her focus was on one potential chokepoint—the gene synthesizers. To address that segment, HHS will develop U.S. government guidance to be published in 2009 to cover the following core elements:

- customer screening,
- sequence screening,
- screening software,
- records retention, and
- reporting and response mechanisms.

IV. A Scientist's Response

An important element in the discussion is the perspective of the scientific community. Dr. Carrie D. Wolinetz of the Federation of American Scientists for Experimental Biology provided her perspective by addressing ''The Other Three Rs: Research, Regulation and Responsibility.''

The potential challenge for scientists in an area like synbio was illustrated by analogy to the current environment for stem cell research. That area is replete with oversight, guidelines—both formal and informal through peer review processes, and substantial training. This has led to a situation where the regulatory burden is almost overwhelming, yet without any sort of investigatory or enforcement activity.

In this kind of environment, there are clear threats to pursuing the research at all. If the ultimate governance and regulatory structure is too onerous, research may well cease at responsible academic settings.

V. Striking the Balance

Much in synbio is new. Yet, as Randy Rettberg of the Massachusetts Institute of Technology (and the affiliated International Genetically Engineered Machine, or iGEM, competition) reminded participants, fears of a new technology taking over, creating havoc, and posing mass population threats have been heard before in our lifetime—for example, with respect to computers that can think or open access to the Internet. In each case, the challenges and threats were both theoretical and real. It was (and perhaps remains) important to choose the right model and allow that model to grow as the industry and the evaluated threats grow as well.

In the case of synbio, the promise is comparable, the opportunities great, and growth is moving in what may be an analogous path. As one of the current thought leaders, Drew Endy of Stanford University, points out, there is an opportunity to integrate engineering with the living world, creating large positive impacts on our security, supply chains, and economies.

But, the threats are real as well. Responsible dialogue and interaction with those charged with our protection, including the FBI and others, is to be both encouraged and applauded. Beyond that, while the open environment required for academia and commercial synbio activities must be preserved, a response to the FBI's willingness to engage in education, outreach, discussion, and collaboration can only yield benefits to all the interested parties.