Institute on Science for Global Policy

Governance of Synthetic Biology**

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Summary

Synthetic biology is … biotechnology. From a policy perspective, synthetic biology is a new set of methods for genetic engineering that offers new opportunities, brings several new challenges, and just as important, does little to alter the controversies that have surrounded the use of biotechnology for the last several decades.

I will first review the current governance of synthetic biology and biotechnology to address five key societal concerns: 1. biosecurity, 2. laboratory biosafety, 3. harm to the environment, 4. human health, and 5. ethical issues. I then briefly discuss the potential benefits and risks to society, and finally, present some governance options for policymakers to consider.

Current realities

Over the past eight years, the J. Craig Venter Institute (JCVI), in collaboration with several other institutions, has examined a broad range of societal issues raised by synthetic biology with a view to disentangling the set of concerns that are either *unique to synthetic biology*, or where the use of synthetic biology *significantly adds to societal concerns about the use of biotechnology* in general. Our goal has been to identify governance options that address the new issues raised by, or significantly changed by, this next-generation biotechnology. To provide context, I will first review current governance of synthetic biology in the United States.

Biosecurity was the first societal concern related to synthetic biology to reach the attention of policymakers, beginning with the synthesis in 2002 of an infectious polio virus constructed in the laboratory directly from nucleic acids by Eckard Wimmer and colleagues. The paper demonstrated for the first time in a post-September 11 world the feasibility of synthesizing a complete human pathogen using only published DNA sequence and mail-ordered raw materials.

Over the following decade, two governance activities have been most significant. In 2004, the National Institutes of Health (NIH) established the National Scientific Advisory Board for Biosecurity (NSABB), a federal advisory committee chartered to provide advice about "dual-use" biological research (i.e., legitimate research that might also be misused for nefarious intent), including synthetic biology. The NSABB functions at the national level; there are no requirements for individual research institutions to establish mechanisms to review the dual-use implications of the research undertaken by their scientists, though some do. In 2010, the U.S. Department of Health and Human Services (HHS) published the *Screening Framework Guidance for Providers of Synthetic Double-Stranded DNA,* with the goal "to minimize the risk that unauthorized individuals or individuals with malicious intent will obtain 'toxins and agents of concern' through the use of nucleic acid synthesis technologies." It is now standard practice for suppliers of synthesized DNA to screen orders to see if they contain dangerous "sequences of concern" and to make sure their customers are legitimate research users.

Biosafety concerns related to genetic engineering research have been under the purview of NIH since 1976, when the agency first issued the *NIH Guidelines for Recombinant DNA Research*. Though the NIH retains some oversight responsibility at the federal level, most is delegated to Institutional Biosafety Committees (IBCs) required at institutions that receive government funding. The *NIH Guidelines* have been revised frequently since that time to stay current with the evolving science. The next revision, which will take effect in March 2013, is the first that will explicitly address synthetic biology research and will be renamed *NIH Guidelines for Research Involving Recombinant*

or Synthetic Nucleic Acid Molecules. Other than making clear the *NIH Guidelines* apply to research with synthetic, as well as recombinant, DNA, few substantive changes were made.

Commercial products that might cause harm to the environment or human health are regulated by a long list of federal laws and regulations. The oversight and regulatory framework in the United States for products developed using biotechnology stems from the 1986 *Coordinated Framework for Regulation of Biotechnology*. The *Coordinated Framework* assigned primary responsibility for regulating the products of biotechnology to three agencies: the Food and Drug Administration (FDA), the Animal and Plant Health Inspection Service (APHIS) of the U.S. Department of Agriculture (USDA), and the Environmental Protection Agency (EPA), using an array of laws in place at the time. Figure 1 summarizes the products that are regulated, by which agency and under what law, as well as the societal risks addressed.

Ethical issues related to synthetic biology were reviewed by the Presidential Commission for the Study of Bioethical Issues. The 2010 study, *New Directions: The Ethics of Synthetic Biology and Emerging Technologies*, recommended that the government "remain forward-looking about the potential benefits and risks to the public," but did "not recommend that additional agencies or oversight bodies need to be created to oversee synthetic biology."

Opportunities and challenges

Synthetic biology combines methods for the chemical synthesis of DNA with computational techniques for DNA design. These new techniques have the potential to accelerate scientific and technological progress in a variety of areas: from basic research to understand how living cells function; to biofuels to power our cars; and to high-value pharmaceuticals, including vaccines to respond quickly to emerging threats.

However, these advancements present several new challenges. Synthetic biology can be dual-use: in addition to useful advances for society, it provides those with nefarious intent new ways to harm. Improvements in the speed and cost of DNA synthesis are also opening the field to new participants (e.g., engineers and computer scientists). This influx of new practitioners must be trained to work safely in the lab.

The public will likely expect that any living organisms modified by synthetic biology and intended for market will first be reviewed for possible adverse effects to the environment or human health. Though the *Coordinated Framework* for the regulation of products of biotechnology has been in place for more than 25 years, it is still controversial. Known harms to the environment or human health from introduced products have been minimal. However, some view our current system as too lax, others as too burdensome. But two areas appear particularly challenged by the new technology: many plants modified using synthetic biology techniques may no longer be covered by USDA rules, and the increasing number and diversity of microbial products that synthetic biology will enable will likely create a challenge for EPA.

Policy issues

Biosecurity

- Current HHS Guidance for screening synthetic nucleotides applies to providers of synthetic double-stranded DNA. Similar guidance could be directed to providers of oligonucleotides (single-stranded nucleotides), from which pathogenic viruses can also be constructed (though with greater difficulty, and with greater technical challenges for affected companies).

- The currently mandated roles and responsibilities of IBCs could be broadened to include review of dual-use research of concern. IBCs would continue to carry out the duties outlined in the *NIH Guidelines* but with review expanded to consider of dual-use concerns.

Biosafety

- NIH and the Centers for Disease Control and Prevention (CDC), who currently publish the "gold-standard" lab biosafety manual, could prepare a companion manual for biosafety in synthetic biology laboratories, geared to the background and needs of the new generation of synthetic biologists.

Harm to the Environment

JCVI's ongoing review of the *Coordinated Framework for Regulation of Biotechnology* has identified two key challenges:

- **USDA's current rules will not cover many plants modified using synthetic biology techniques.** Newer plant technologies, including synthetic biology, will be less likely to use plant pests during the transformation process and so will largely not be subject to the assessment process that has been a staple of traditional biotechnology regulation. Options to address this gap include:
  - No action: APHIS maintains a voluntary assessment process for genetically modified plants, but review is required for only those organisms with a potential to be plant pests.
  - APHIS incorporates its noxious weed authorities into biotechnology regulation to add another significant risk to ecosystem health.

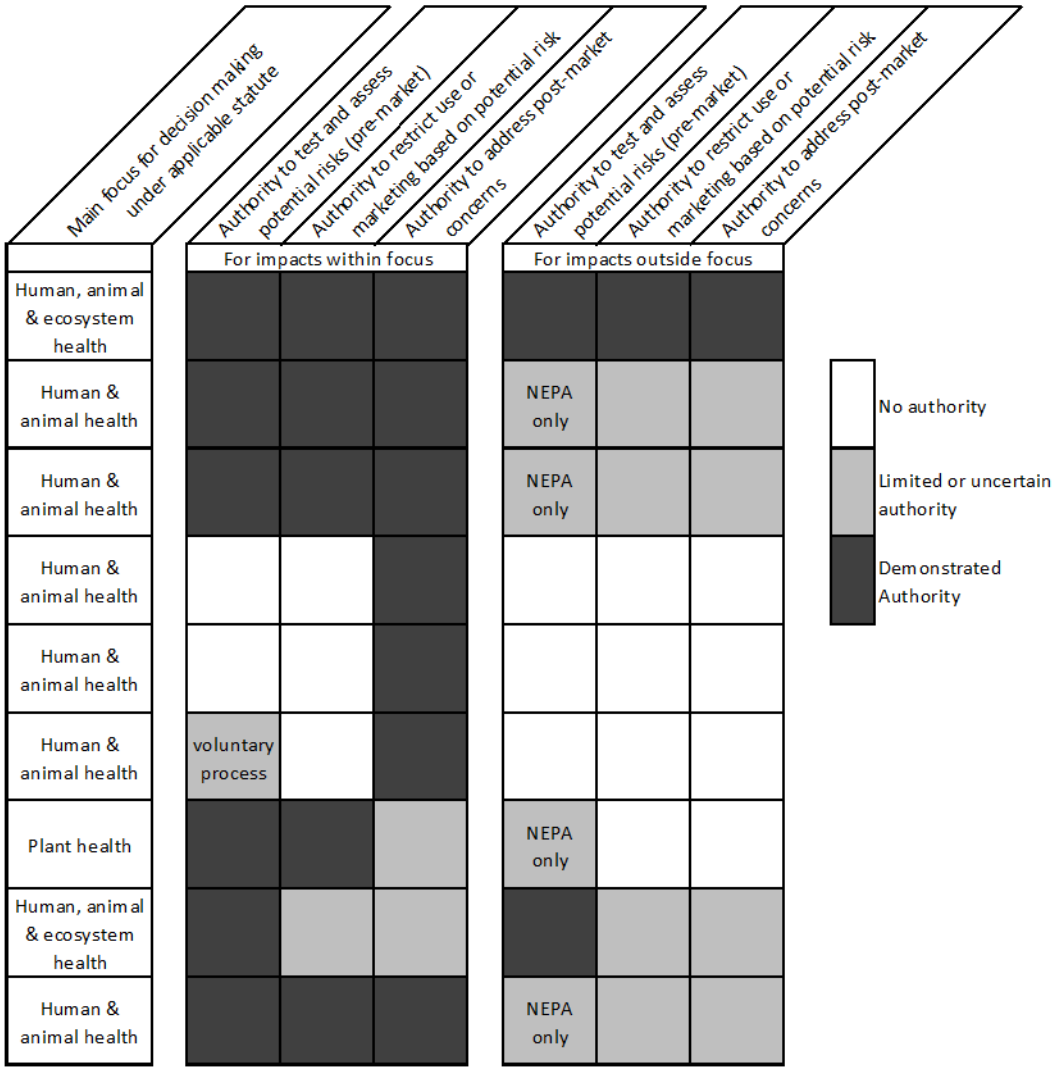
- **The increasing number and diversity of microbial products that synthetic biology will enable will likely create a challenge for EPA.** The Toxic Substances Control Act (TSCA), the primary law governing commercial, genetically engineered microorganisms, was not intended for this purpose and in the view of some, is ill-suited to be the primary regulatory mechanism, particularly as the number of microbes requiring assessment increases. Options to address these challenges include:
  - Congress ensures that EPA is given sufficient resources to adequately undertake the regulatory reviews needed to evaluate the risks posed by commercial microbial products engineered using synthetic biology techniques or, more aggressively, amends TSCA to strengthen EPA's ability to regulate such microbes.
  - EPA develops a voluntary assessment process for noncommercial microbes, which are currently exempt from regulation.

References

Garfinkel, M.S., Endy, D., Epstein, G.L., & Friedman, R.M. (2008) *Synthetic Genomics: Options for Governance*. Rockville, MD: The J. Craig Venter Institute. Retrieved from http://www.jcvi.org/cms/fileadmin/site/research/projects/synthetic-genomics-report/synthetic-genomics-report.pdf

Figure 1: Biotechnology products are largely regulated based on the following regulatory definitions; synthetic biology products will meet many of these same definitions. Each applicable statute has a main focus; the application of authorities are displayed based on potential risks both within and outisde of that main focus.

Product type	With this characteristic	Meets this definition
Any product, including modified plants, animals, and microbes	That will be used as a pesticide or to produce pesticides	Pesticide or Plant-incorporated protectant (EPA/FIFRA)
	That will be used as a drug or to produce drugs	Drug or Animal Drug (FDA/FDCA)
	That will be added to food and is not generally recognized as safe	Food additive (FDA/FDCA)
	That will be used as or will produce a dietary supplement	Dietary Supplement (FDA/FDCA)
	That will be used as or produce a cosmetic	Cosmetic (FDA/FDCA)
Any modified organism	That will be used as a food	"Substantially equivalent" (FDA/FDCA)
	That incorporates DNA sequences from a known plant pest	Regulated Article (APHIS/PPA)
Any intergeneric microorganism	That is used for any commercial purpose not listed above	Intergeneric microorganism (EPA/TSCA)
Any gene(s) inserted into an animal	That will be used for any purpose	Animal drug (FDA/FDCA)



Acronyms: APHIS (Animal and Plant Health Inspection Service), EPA (Environmental Protection Agency), FDA (Food and Drug Administration), FDCA (Federal Food, Drug, and Cosmetics Act), FIFRA (Federal Insecticide, Fungicide, and Rodenticide Act), GRAS (Generally Recognized as Safe), NEPA (National Environmental Protection Act), TSCA (Toxic Substances Control Act)