Synthetic Biology and the US Biotechnology Regulatory System

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Excerpted from: **SYNTHETIC BIOLOGY AND THE U.S. BIOTECHNOLOGY REGULATORY SYSTEM: Challenges and Options**

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This study addresses how well the current U.S. regulatory system for genetically engineered products is equipped to handle the near-term introduction of organisms engineered using synthetic biology. While the current regulatory system has generated debate from its inception, here we focus on whether the advent of synthetic biology will raise new issues for the regulation of these products. In particular, we focused on those engineered organisms (for example, bioenergy crops and biofuel-producing algae) intended to be used or grown directly in the environment, outside a contained facility.

Our research concludes that the U.S. regulatory agencies have adequate legal authority to address most, but not all, potential environmental, health and safety concerns posed by anticipated near-term microbes, plants, and animals engineered using synthetic biology. Such near-term products are likely to represent incremental changes rather than a marked departure from previous genetically engineered organisms. However, we have identified two key challenges to the current U.S. regulatory system posed by the introduction of organisms engineered using synthetic biology into the environment. For these challenges, we do not make specific policy recommendations, but rather set out options, including an analysis of the advantages and disadvantages of each option from a variety of perspectives for policy makers to consider. Policy responses will depend on the trade-offs chosen among competing considerations.

The key challenges and options to address them are:
Genetically engineered organisms are increasingly being developed in ways that leave them outside of the U.S. Department of Agriculture's Animal and Plant Health Inspection Service's (APHIS) authority to review, and synthetic biology will accelerate this trend. Currently, APHIS' oversight depends on whether plant pests or some component of a plant pest is used to engineer the plant. These regulations covered almost all plants made using older genetic engineering techniques, but will not apply to plants engineered using several of the newer techniques. This shift will leave many engineered plants without any regulatory review prior to their cultivation in the environment for field trials or commercial production.

- Option 1: Maintain existing regulatory system and rely on a voluntary approach for those genetically engineered plants not subject to review. APHIS could maintain a voluntary system similar to their current regulatory procedures or product developers could use industry-developed standards to ensure that environmental risks are assessed and addressed.
- Option 2: Identify the most likely risks from newer generations of plant biotechnology and apply existing laws best able to mitigate them. One approach may be to use APHIS' authorities over noxious weeds to regulate biotechnology products. In 2008, APHIS

issued a proposed rule for genetically engineered plants that incorporated both noxious weed and plant pest authorities, but even after extensive public comment and stakeholder input, the rule has not advanced.

- Option 3: Give APHIS additional authority to review and regulate genetically engineered plants. This option would require Congressional action, which might be difficult to achieve.
- Option 4: Promulgate rules under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) or the Toxic Substances Control Act (TSCA) for the Environmental Protection Agency (EPA) to regulate engineered plants. Both of these laws are broad enough to apply to genetically engineered plants, but such rules would be a major departure from the current regulatory system.

Synthetic biology will lead to an influx of genetically engineered microbes intended for commercial use, which may overwhelm EPA's Biotechnology Program. While EPA regulators have successfully reviewed such engineered microbes to date, this influx will include a larger number and more diverse set of microbes than the program has seen previously, including many with intended or possible environmental exposure. Moreover, as engineered microbes become increasingly complex, risk assessments will pose a greater challenge. EPA will require additional funding to meet the increased workload and expertise requirements. In addition, the agency may be constrained by the authority given to it under TSCA, which has been criticized as inadequate, both in the context of engineered microbes and more broadly. These issues could lead to regulatory delays for microbial products, inadequate review, and/or legal challenges.

- Option 1: If and when needed, provide additional funding for EPA's Biotechnology Program under TSCA and pursue efficiency measures to expedite reviews. Efficiency measures could include broadening exemptions for low-risk microbes and developing procedures to review environmental testing of engineered microbes on a programmatic basis (i.e. for multiple, similar microbes in a single submission).
- Option 2: Amend TSCA to strengthen EPA's ability to regulate engineered microbes. This option would require Congressional action and could either address engineered microbes specifically or could strengthen TSCA for all chemicals subject to the law.

In addition to these major challenges, we have identified three additional issues in the regulation of new engineered microbes that should be periodically revisited as the technology advances, but in our view, do not require action today. These issues include the regulatory treatment of two classes of microbes that are exempted or excluded from review by EPA and EPA's somewhat limited definition of "intergeneric microorganism."

In developing this report, we consulted with a wide range of experts to ensure a broad representation of knowledge and viewpoints, including U.S. federal agency regulators, legal and science policy experts, representatives from the biotechnology industry, and non-governmental organizations. This cross-section of views informed this report, but this study does not represent a consensus: the findings and conclusions here are the authors' alone, and not necessarily those of the institutions at which the authors work or the organizations that funded the study.