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Comments Regarding the Request for Information: Building a 21st Century Bioeconomy (76 FR 62869, October 11, 2011)

To the Office of Science and Technology Policy:

In October, 2011, OSTP issued a Federal Register notice titled "Request for Information: Building A 21st Century Bioeconomy."[1] The comments below are in response to the questions therein on the role of regulation in and for an expanding bioeconomy (questions 13, 14, and 15).

For context, the authors of this letter are policy analysts, who for many years have focused on public policy aspects of biotechnology in general, and in particular of synthetic biology, an emerging technology that has potential to be an important driver of this coming century's bioeconomy. Dr. Friedman leads JCVI's Policy Group and is a coauthor of a 2007 report focusing on the biosecurity and biosafety aspects of synthetic biology.[2] Dr. Carter is also a policy analyst at JCVI. Mr. Rodemeyer, currently at the University of Virginia, was the Executive Director of the Pew Initiative on Food and Biotechnology from its inception in 2000 through 2005. In 2009, he authored an early review of the regulations that apply to synthetic biology for the Woodrow Wilson International Center for Scholars in 2009.[3]

The three of us are also investigators on an ongoing DOE-funded study to assess how well the current Federal regulatory framework applies to the anticipated products of synthetic biology, and to provide options for addressing any gaps or shortcomings. This two-year project will include two workshops as well as multiple consultations with experts both within and outside the Federal government. A full report should be available by late 2012. However, though preliminary, we feel our insights to date will be helpful to OSTP's current request for information.

The 1986 Coordinated Framework for the Regulation of Biotechnology has generally been successful: the government has been able to assess products for safety and biotechnology developers have been able to move those products to market. The regulatory system has served an important role in the marketplace as well; product developers benefit from the public's trust in the government's oversight. On the other hand, as others have observed, regulatory requirements increase costs and contribute to the challenges faced by smaller companies and independent entrepreneurs.[4] Moving forward, any changes to the

[1] 76 FR 62869, Oct 11, 2011
[2] Garfinkel M, D. Endy, and G.L. Epstein. *Synthetic Genomics | Options for Governance*, The J. Craig Venter Institute, Rockville MD, 2008, 57 pp.
[3] Rodemeyer, M (2009) New Life, Old Bottles: Regulating First-Generation Products of Synthetic Biology.
[4] Pew Initiative on Food and Biotechnology and Animal and Plant Health Inspection Service (2004) Impacts of Biotech Regulation on Small Business and University Research: Possible Barriers and Potential Solutions, Washington, D.C.

regulatory system must strike an appropriate balance between minimizing risks and avoiding roadblocks to the development of beneficial new products. At the same time, the regulatory system must provide the rigor, clarity, and transparency needed for both the public and technology developers to understand, and have confidence in, the process.

The current regulatory framework has evolved over time, both as the agencies have gained experience with the products and as the technology has advanced. In 2001, CEQ and OSTP undertook an assessment of the Coordinated Framework in part to "ensure that U.S. regulations keep pace with the latest scientific and product development."[5] Given the rapid pace of scientific advancement, particularly in synthetic biology and related technologies, we believe that another such assessment is needed. We believe that our report, building on previous work by us and others, will provide a solid foundation for this review.

In our research to date, we have found areas where products developed using new biotechnologies may not be covered clearly by the current regulatory regime. We have also found areas where more clarity in the regulatory process would help create more predictability for the approval of new bio-based products. Such gaps and uncertainties lead to delays as product developers try to determine the appropriate regulatory path to take; reducing uncertainties, filling such gaps, and providing clarity are critical to reducing regulatory barriers for the bioeconomy.

We give two examples below, one addressing genetically engineered plants and the other, engineered microbes. However, given the early stage of our project, we cannot provide a comprehensive review of all issues that need resolution. And, at this early stage of research, it is still premature for us to offer options for the directions that the Federal government might take regarding regulatory policies or risk assessments.

Clarity is needed on what types of plant biotechnology products should be reviewed by USDA and which, if any, might not need to be reviewed. USDA's Animal and Plant Health Inspection Service (APHIS) has authority to assess and regulate "plant pests" and "noxious weeds." Until recently, biotechnology developers depended on techniques that incorporated sequences from known plant pests into their products, and so were regulated by APHIS based on its authority over "plant pests." However, using new technologies, product developers will increasingly avoid using plant pests to modify plants, rendering APHIS's regulatory authority inapplicable[6] [7] and thereby creating a gap in pre-market assessment.[8] [9] It remains unclear whether and to what extent APHIS will apply its

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[5] CEQ/OSTP Assessment: Case Studies of Environmental Regulation for Biotechnology (2001)

[6] USDA's decision not to regulate modified Kentucky Bluegrass: 76 FR 39812, July 7, 2011.

[7] USDA's decision not to regulate Maize altered with zinc-finger nucleases: http://168.68.1.70/foia/foia_requests//2011/Biotechnology%20and%20Regulatory%20Services%20(BRS)/11-089%20-%20Correspondence%20Concerning%20Regulatory%20Status%20of%207%20CFR%20Part%20340/11-089%20Records.pdf

[8] Kuzma J and Kokotovich A (2011) Renegotiating GM Crop Regulation. *EMBO Reports*, Volume 12, p. 883–888.

[9] "GM grass eludes outmoded USDA oversight" (2011) *Nature*, Volume 29, No. 9, p.772

authority to regulate "noxious weeds" to plant biotechnology, as was suggested in their 2008 Proposed Rule.[10] Also, EPA has previously indicated that it has the authority to regulate modified organisms under the Toxic Substances Control Act (TSCA),[11] but whether that authority could be applied to new plant products that fall out of APHIS's system remains to be seen. Given the shifting landscape, technology developers are left with some uncertainty regarding their products.

As synthetic biology techniques and applications expand, microbes will likely grow to become a major component of the bioeconomy. The regulatory system must begin to anticipate an influx of these products; EPA in particular will need the resources to meet the risk assessment needs for these technologies. For product developers, it will be helpful for EPA to generate and release guidance on the types of data that they consider necessary to conduct a risk assessment on genetically modified microbes, particularly those that have the potential for environmental release (e.g. algae used to generate biofuels). To generate this data, it is likely that experiments involving limited release of these microbes into the environment will be required. While EPA has a TSCA Environmental Release Application (TERA) process that has been used for individual products, more general guidance on appropriate precautions to take may provide clarity for product developers as they move through this process.

The Coordinated Framework has provided guidance for both the public and developers for a quarter of a century and demonstrated its ability to adapt with experience. However, new technologies and the increasing pace of technological change are likely to create challenges for the Framework. Legal gaps and questions about regulatory pathways can create uncertainty for the public and developers alike. While there are strong arguments for maintaining the basic structure of the Framework, there will be a need to review regulatory authorities to meet the challenges of new technologies, including synthetic biology. Such a reassessment inevitably involves making difficult, but extremely important, judgments about striking the appropriate balance between regulation intended to prevent harm to public health and the environment and the desire to bring beneficial and safe products to market.

We would be happy to discuss these topics further and we will keep you apprised on the status of our upcoming report on the regulatory system for synthetic biology products.

Sincerely,

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[10] Available: http://www.aphis.usda.gov/biotechnology/340/340_index.shtml
[11] CEQ/OSTP Assessment: Case Studies of Environmental Regulation for Biotechnology (2001).