Preparing for Future Products of Biotechnology

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Report Release Event

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Impetus for the Study

2015 White House Memorandum calling for modernization of the biotechnology regulatory system:

- Update the Coordinated Framework
  - Clarify the roles and responsibilities of the agencies that regulate to “products of biotechnology”

- Formulate long-term strategy for biotechnology regulatory system
  - Efficiently assess risks associated with future products of biotechnology
  - Support innovation, protect health and environment, promote public confidence in regulatory process, increase transparency and predictability, reduce unnecessary costs and burdens

- Commission an external, independent analysis of the future landscape of biotechnology products
Statement of Task

What will the likely future products of biotechnology be over the next 5-10 years? What scientific capabilities, tools, and/or expertise may be needed by the regulatory agencies to ensure they make efficient and sound evaluations of the likely future products of biotechnology?

(1) Describe the major advances and the potential new types of biotechnology products likely to emerge over the next 5-10 years

(2) Describe the existing risk analysis system for biotechnology products ... and each agency’s authorities as they pertain to the products of biotechnology

(3) Determine whether potential future products could pose different types of risks relative to existing products and organisms. Where appropriate, identify areas in which the risks or lack of risks are well understood

(4) Indicate what scientific capabilities, tools, and expertise may be useful to support oversight of potential future products of biotechnology

(Human drugs and medical devices are not in the purview of the study)
Committee on
Future Biotechnology Products

Richard M. Murray (Chair), California Institute of Technology

Martha Krebs, Pennsylvania State University

Raul F. Medina, Texas A&M University

Steven P. Bradbury, Iowa State University

Barbara J. Evans, University of Houston Law Center

Steven L. Evans, Dow AgroSciences

Mary E. Maxon, Lawrence Berkeley National Lab

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Jennifer Kuzma, North Carolina State University

Jeffrey Wolt, Iowa State University

David Rejeski, Woodrow Wilson Center for International Scholars

Farren Isaacs, Yale University

Biotechnology (academic and industrial)
Biotechnology Law, Regulation, and Policy
Energy Science and Policy
Entomology and Evolutionary Ecology
Environmental Toxicology

Genetics and Genomics
Microbial Physiology and Biochemistry
Molecular Biology and Synthetic Biology
Plant Biochemistry and Genomics
Risk Analysis and Governance

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## Study Relevant Activities

### Committee activities

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<th>Jul’15</th>
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- **April 18-19:** Meeting 1 (2 days; DC)
- **June 1-3:** Meeting 2 (3 days; DC)
- **June 27-28:** Meeting 3 (2 days; SF)
- **July:** 8 Webinars
- **August 1-5:** Writing Meeting (5 days; Irvine)
- **Oct-Nov:** Report review
- **Dec-Jan:** Report revision in response to review
- **Feb-Mar:** Final approval and release of report

### Information gathering

- 74 speakers (acad, industry, NGO)
- 180 papers, books and reports
- Public sessions, comments (100+)
- 17 federal offices; public databases

### Report review

- 17 external experts
- Response to all comments
- Report review committee

### US Government activities

- **July 2015:** Establishment of Biotechnology Working Group (BWG)
- **June 2016:** Passage of New TSCA (Toxic Substances Control Act)
- **Sep 2016:** Updated Coordinated Framework (draft) + National Strategy
- **Jan 2017:** Release of final updated Coordinated Framework

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What is a Biotechnology Product?

Products developed through genetic engineering or genome engineering or the targeted or \textit{in vitro} manipulation of genetic information of organisms, including plants, animals, and microbes

- Includes products where the engineered DNA molecule is itself the “product” as in an engineered molecule used as a DNA information-storage medium
- Also covers some products produced by such plants, animals, microbes, and cell-free systems or products derived from all of the above
Cross-Cutting Themes

• The bioeconomy is growing rapidly and the U.S. regulatory system needs to provide a balanced approach for consideration of the many competing interests in the face of this expansion

• The profusion of biotechnology products over the next 5-10 years has the potential to overwhelm the U.S. regulatory system

• Regulators will face difficult challenges that go beyond contained industrial uses and traditional environmental release

• The safe use of new biotechnology products requires rigorous, predictable, and transparent risk-analysis processes that mirror the scope, scale, complexity, and tempo of biotechnology development

• Agencies involved in regulation of future biotechnology products would benefit from adopting recommendations made by previous National Academies’ committees
(1) Describe the major advances and the potential new types of biotechnology products likely to emerge over the next 5-10 years

- The *scale, scope, complexity, and tempo* of biotechnology products are *likely to increase* in the next 5–10 years. Many products will be similar to existing biotechnology products, but they may be created through new processes, and some products may be wholly unlike products that exist today.
Risk Analysis System

(2) Describe the existing risk analysis system for biotechnology products including, but perhaps not limited to, risk analyses developed and used by EPA, USDA, and FDA, and describe each agency’s authorities as they pertain to the products of biotechnology

- The Coordinated Framework for Regulation of Biotechnology appears to have considerable flexibility to cover a wide range of biotechnology products, though in some cases the jurisdiction of the agencies has the potential to leave gaps in regulatory oversight (for future products)

- The current biotechnology regulatory system is complex and fragmented, resulting in a system that can be difficult for individuals, nontraditional organizations, and small- and medium-size enterprises to navigate, that might cause uncertainty and a lack of predictability for developers of future biotechnology products, and that has the potential for loss of public confidence in regulation of future biotechnology products
(3) Determine whether potential future products could pose different types of risks relative to existing products and organisms. Where appropriate, identify areas in which the risks or lack of risks relating to the products of biotechnology are well understood

- **The risk-assessment endpoints are not new**, but the pathways to those endpoints have the potential to be very different in terms of complexity

- The **profusion** of future biotechnology products will challenge the federal agencies’ ability to handle significant increases in the rate, number and complexity of biotechnology products, and the diversity of actors

- To enable effective regulation, it would be beneficial to have a **single point of entry** into the regulatory system

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**Product Complexity and Novelty**

**A**
- Domesticated organisms
- Transgenic / recombinant DNA
- One or only a few gene-pathway engineering
- Ample comparators

**B**
- Domesticated & Undomesticated organisms
- Transgenic, new genome engineering
- Multiple pathway engineering
- Few to no comparators

**C**
- Many candidate organisms
- Genome engineering, gene drives
- Genome refactoring, recoding, cell-free synthesis
- Few to no comparators

**D**
- Synthetic communities of microbes and synthetic, multicellular plants & animals
  - Metagenome & microbiome engineering
  - Population and ecosystem engineering
  - No or ambiguous comparators
A Single Point of Entry

- Enable the federal agencies to decide early in the product development cycle which authorities are relevant
- Over time product types might “move” from right to left, as experience gained in evaluating additional products

Many different ways to implement similar ideas (this is just one)

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Opportunities for Enhancement

(4) Indicate what scientific capabilities, tools, and expertise may be useful to the regulatory agencies to support oversight of potential future products of biotechnology

- The staffing levels, expertise, and resources available in EPA, FDA, USDA, and other agencies that have interests related to future biotechnology products may not be sufficient to handle the expected scope and scale of future biotechnology products.
Recommendation #1

EPA, FDA, USDA and other agencies involved in regulation of future biotechnology products should *increase scientific capabilities, tools, expertise, and horizon scanning in key areas of expected growth* of biotechnology, including *natural, regulatory, and social sciences*

- Build and maintain capacity to rapidly triage products, focused on new pathways to risk-assessment endpoints
- Scan the horizon for new products that present novel risk pathways and develop new approaches to assess and address more complex risk pathways
- EPA, FDA and USDA should work together to
  - Implement mechanisms for keeping aware of the emerging technologies
  - Pilot new approaches to problem formulation, uncertainty characterization, and risk-benefit assessments
  - Pool skills and expertise across the government for first-of-a-kind cases
- Pre-competitive “data commons” to provide information to developers
- Implement a more permanent, coordinated mechanism to measure progress
Recommendation #2

EPA, FDA, and USDA should increase their use of *pilot projects to advance understanding and use of ecological risk assessments and benefit analyses* for future biotechnology products that are unfamiliar and complex and to *prototype new approaches for iterative risk analyses that incorporate external peer review and public participation*

- More iterative processes for risk assessments that span development cycles
- Advances in ecological risk assessments/benefit analyses for open-release products
- Probabilistic estimates of risk to assess likelihood of adverse effects of future biotechnology products compared to existing alternatives
- New methods of outreach to the public and developer community (horizon scanning, capability growth, improving understanding)
- Engage with federal and state consumer and occupational safety regulators
Recommendation #3

The National Science Foundation, the Department of Defense, the Department of Energy, the National Institute of Standards and Technology, and other agencies that fund biotechnology research with the potential to lead to new biotechnology products should *increase their investments in regulatory science and link research and education activities to regulatory-science activities*

- Develop long-term strategy for risk analysis of future biotechnology products
- Establish appropriate federal funding levels for sustained, multi-year research to develop the necessary advances in regulatory science
- Provide linkages to market-path requirements for regulatory success
- Invest in new methods of understanding ethical, legal, and social implications associated with future biotechnology products
- Increase graduate and post-graduate knowledge of the regulatory system
Outline of the Report

1. Introduction and Context

2. Emerging Trends and Products of Biotechnology
   • Setting the Stage: Understanding the Key Drivers for Future Biotechnology Products
   • Future Biotechnology Products

3. The Current Biotechnology Regulatory System
   • Overview of U.S. Regulatory System
   • Consumer and Occupational Safety
   • Environmental Protection

4. Understanding Risk Related to Future Biotechnology Products
   • Risks from Future Biotechnology Products: Similarities to the Past and Gaps Going Forward
   • Existing Federal Capabilities, Expertise, and Capacity

5. Opportunities to Enhance the Capabilities of the Biotechnology
   Regulatory System
   • Consistent, Efficient, and Effective Decision Making for Future Products of Biotechnology
   • Technical Toolbox and Capabilities for Risk Assessment and Regulatory Science

6. Conclusions and Recommendations
Acknowledgments

• National Academies staff
• Fellow committee members
• Reviewers
• Speakers and members of the public

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Thank you!

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Questions?
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