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Synthetic Biology and the U.S. Biotechnology Regulatory System

Challenges and Options

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JCVI Policy Center: Who We Are

- JCVI is an independent, 501(c)(3) non-profit research institute
  - Campuses in Rockville, MD and San Diego, CA
  - Major efforts in genomics, metagenomics, infectious disease, synthetic biology
  - May, 2010: Announcement of the first synthetic cell

- Policy Center
  - Focused on the policy and societal implications of genomics, synthetic biology, and other 21st Century biology

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U.S. Regulatory System Project

- Project Team
  - Sarah Carter, JCVI
  - Bob Friedman, JCVI
  - Michael Rodemeyer, University of Virginia
  - Michele Garfinkel, EMBO
- Methods:
  - Workshops including federal regulators, outside experts, stakeholders
  - Extensive review and commenting on drafts
  - No consensus sought

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Coordinated Framework, OSTP, 1986

- Biotechnology poses no *inherent* risks, but some individual products might
- Thus, regulate the product, not the process
- Existing laws are adequate for now (1986)
- Address gaps through coordination and lead agencies
- The framework can and should evolve over time as experience is gained

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U.S. Regulatory System Project

Synthetic biology *is* biotechnology, thus biotech regulations apply

Key questions:

- Are today's biotech regulations adequate for anticipated products of synthetic biology?
- Do challenges exist? Will new ones emerge?

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Evaluation of Coordinated Framework

- Determined the regulatory process for different types of products and organisms, with focus on:
  - Environmental assessment
  - Strength of regulatory authority as applied today at different stages of the process

- Intent was NOT to revisit old controversies, but to identify challenges that might arise from the next generation of biotechnology products

Product-based Laws and Regulations

Product type	***Characteristic***	***Agency/Main focus***
Any product, including modified plants, animals, and microbes	Used as or produces a pesticide	EPA / Human, animal and ecosystem health
	Used as or produces a human or animal drug	FDA / Human and animal health
	Used as or produces a food additive	FDA / Human and animal health
	Used as or produces a dietary supplement	FDA / Human and animal health
	Used as or produces a cosmetic	FDA / Human and animal health
	Is or could be a plant pest	APHIS / Plant health

Process-based Laws and Regulations

Product type	***Characteristic***	***Agency/Main focus***
Any modified organism	Used as or produces a food	FDA / Human and animal health
Any intergeneric microorganism	Used for any commercial purpose not listed above	EPA / Human, animal, and ecosystem health
Any gene(s) inserted into an animal	Used for any purpose	FDA / Human and animal health

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Overarching Conclusions

- The regulatory system is adequate to address most environmental, health, and safety concerns from these newer techniques. Examples:
  - FDA practices will generally be unaffected by new engineering techniques (with some exceptions).
  - EPA authority over pesticides will be unaffected.
  - USDA authority over organisms engineered using plant pests or that could be plant pests will remain strong.
- However, some challenges will arise.

Key Challenges and Options

- Challenges
  - Plant products
  - Microbial products
- Options to address those challenges
  - Small fixes to new regulation to Congressional action
  - Bias toward simplest possible solution

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Key Challenge: Plant Products

Synthetic biology and other new genetic engineering techniques enable development of engineered plants that are outside of USDA's authority to review.

- USDA's authority depends on the use of plant pests (esp. agrobacterium) for transformation.
- With newer techniques, plant pests no longer necessary for transformation.

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Key Challenge: Plant Products

Shift is already underway

- APHIS website: “Am-I-Regulated” letters show several recent examples of plants engineered using new techniques, with APHIS declining to regulate

- Examples:
  - Switchgrass engineered for use as biofuel feedstock
  - Kickstarter “Glowing Plants” project used biolistics and will distribute plants to supporters shortly

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Key Challenge: Plant Products

Implications for other agencies

- EPA
  - Early field trials for plants with plant incorporated protectants (e.g. Bt) are currently managed by APHIS
  - Plants that produce industrial compounds are not covered by TSCA (even if the compound is)
- FDA
  - Plants producing pharmaceuticals may not be covered by FDA in early trials

Plant Products: Options

1. Maintain existing regulatory system and rely on a voluntary approach for those genetically engineered plants not subject to review.
   - Could rely on APHIS or on industry-developed standards
   - NEPA would not be triggered

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Plant Products: Options

2. Identify the most likely risks from newer generations of plant biotechnology and apply existing laws best able to mitigate them.

- APHIS' 2008 Proposed Rule:
  - Plant pest and noxious weed authorities combined
  - Tiered system – risk-based
  - Many comments, not yet advanced

Plant Products: Options

3. Give USDA's Animal and Plant Health Inspection Service APHIS additional authority to review and regulate genetically engineered plants.

   - Envisions Congressional action
   - Could be a system similar to Canada's (or other countries')

Plant Products: Options

4. Promulgate rules under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) or the Toxic Substances Control Act (TSCA) for EPA to regulate engineered plants.

   - For FIFRA: authority over “plant regulators”

   - For TSCA: authority over “new chemical substances” – the same as for microbes

Key Challenge: Microbial Products

EPA may be constrained by inadequate funding and by the authority given to it under TSCA to address the anticipated influx of genetically engineered microbes for industrial use.

- To date, EPA's TSCA Biotechnology program has been adequate, given low numbers of microbes.
- TSCA's provisions for new chemical substances (including microbes) haven't been challenged legally and could come under increased scrutiny.

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Key Challenge: Microbial Products

Influx may have already begun. According to EPA website:

- EPA received 23 TSCA Experimental Release Applications between 1998-2012
- They received 7 in 2013
- Example: algae biofuels

Microbial Products: Options

1. If and when needed, provide additional funding for EPA's Biotechnology Program under TSCA and pursue efficiency measures to expedite reviews.

2. Amend TSCA to strengthen EPA's ability to regulate intergeneric microbes.

   - Requires Congressional action

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Additional Issues for Microbial Products

TSCA excludes microbes that fall under other authorities, including dietary supplements and cosmetics

- FDA practices do not include premarket review
- It is not clear how FDA would consider post-market environmental concerns
- Example: algae producing vitamin D

- An evaluation of this type of product could be helpful (including likely market penetrance and regulatory path)

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Additional Issues for Microbial Products

TSCA exempts non-commercial microbes

- Certain microbes may be released without oversight
  - Including, potentially, some DIYBio microbes
- Institutions in compliance with NIH Guidelines may be prevented from experimental environmental release
  - NIH Guidelines require oversight from a federal agency
  - The Guidelines apply to nearly all U.S. research institutions
  - May prevent useful research from being done
- An evaluation of these issues would be helpful

Additional Issues for Microbial Products

EPA's definition of "intergeneric microorganism" may need to be updated to accommodate microbes constructed using synthetic biology

- Current definition does not include synthetic sequences
- Nevertheless, current product developers anticipate regulation by EPA

- If and when a rule change is made, a clarification would be helpful

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Thank you!

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