Gene Drives and the U.S. Biotechnology Regulatory System

Sarah R. Carter, Ph.D.
Policy Analyst
J. Craig Venter Institute

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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

- Policy Center
  - Focused on the policy and societal implications of 21st Century biology

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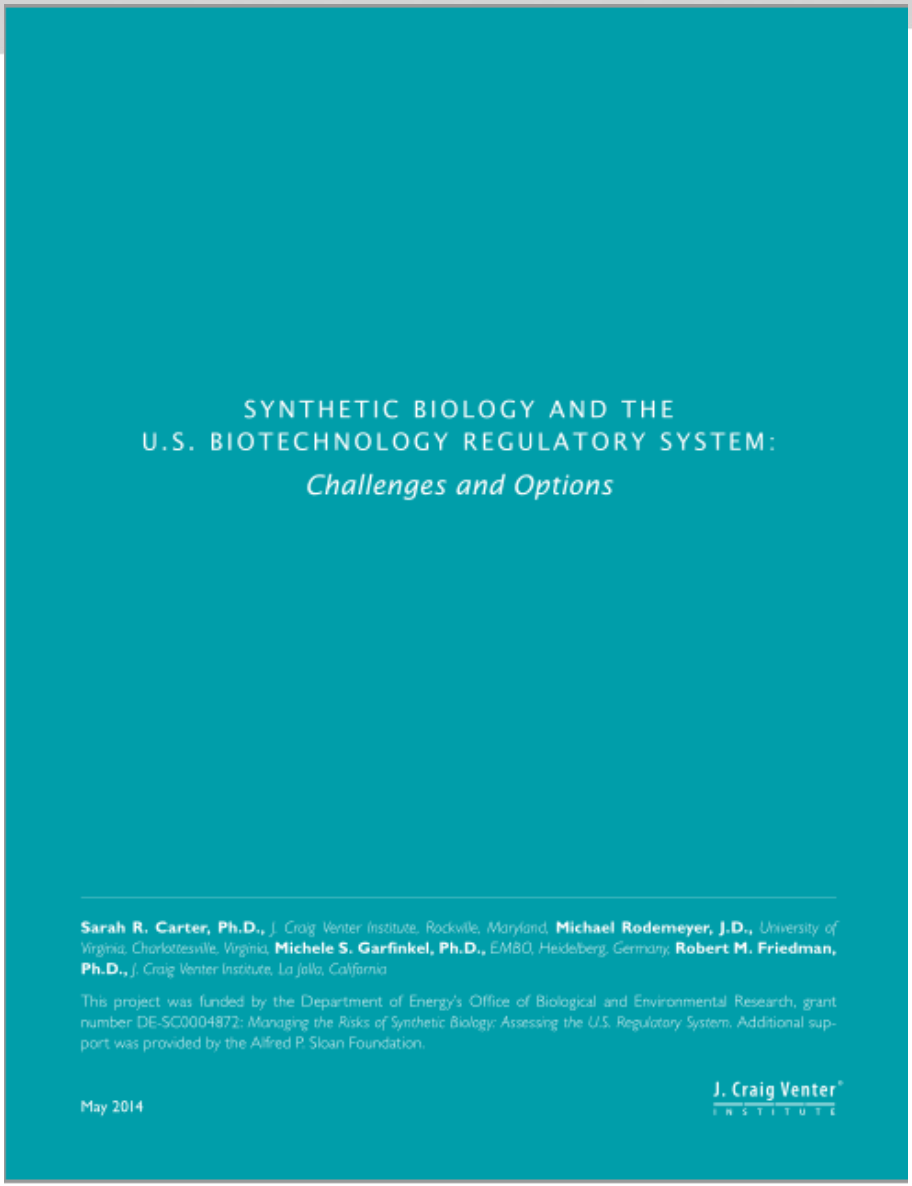
Regulation of Synthetic Biology



2014 Report

- How well will Coordinated Framework handle next generation biotechnology?
- Focused on environmental release: microbes and plants
- CRISPR/Cas9 has greatly expanded possibilities for animals

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Non-regulatory Safety Mechanisms

- Regulatory system focuses on commercial products
- NIH Guidelines and Arthropod Containment Guidelines
  - Laboratories: NIH Guidelines and IBCs for transgenic organisms
  - APHIS Guidelines for plant pest containment
  - American Committee of Medical Entomology's Arthropod Containment Guidelines
- NEPA (National Environmental Policy Act)
  - Applies to major federal action (regulatory approvals and deregulation decisions)

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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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 a commercial purpose not covered elsewhere	EPA / Human, animal, and ecosystem health
Any gene(s) inserted into an animal	Used for any purpose (with some exceptions)	FDA / Human and animal health

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Gene Drives?

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Gene Drives in Animals

- Constructs, including gene drives, inserted into animals likely will be considered animal drugs and so regulated by FDA
  - Examples: gene drives in mosquitos, rodents (?)
  - Exceptions: plant pests, as covered by USDA/APHIS
- FDA standards of “safe and effective” will have to be met
- Environmental assessment done as part of compliance with NEPA

Gene Drives?

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Gene Drives in Plant Pest Insects

- USDA/APHIS regulates plant pests
  - Maintains a list of pests for important crops and trees
  - Regulates importation, transport of plant pests, including engineered varieties
    - Examples of engineered organisms: pink bollworm, diamondback moth
  - Performs facility inspections for labs working with plant pests

Gene Drives in Biocontrol Organisms

- USDA/APHIS also regulates plant pest biocontrol organisms
  - Examples of biological control organisms: sterile insects, parasitoids targeting plant pests
  - Evaluation and monitoring of field releases of biocontrol organisms
  - Environmental assessment (for NEPA) is performed before a new organism is released

Gene Drives in Plants

- Engineered plant products are regulated by USDA/APHIS if they use a plant pest vector or include plant pest DNA
  - Traditionally, plant transformation depended on the use of agrobacteria
  - Many recent applications are not regulated
  - Recent CRISPR successes in plants have used pest vectors, but gene drives can be inserted other ways
  - Ongoing process to update these regulations

Ongoing updates to the Regulatory System

- APHIS, March 2015: withdrew 2008 Proposed Rule to re-open stakeholder input on regulation of engineered plant products
  - Bringing in “noxious weed” authorities (likely)
  - Considering gene editing techniques

Ongoing updates to the Regulatory System

- OSTP, July 2015: Memorandum to the agencies on a process to review the Coordinated Framework; stakeholder engagement
  - Initial focus on “clarifying” roles of the agencies
  - Streamlining processes
  - Long-term strategy

Key Points and Remaining Questions

- Most gene drive products will fall within existing authorities
  - Plants transformed without plant pests may present a challenge – updated regulations may help
- Risk assessments will include environmental assessment for compliance with NEPA
  - But, agency authorities do not cover environmental endpoints; what will regulatory process look like?
- Does EPA have a role?
  - Authorities over pesticides
  - TSCA as back-up for Coordinated Framework

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Thank you!

Sarah R. Carter: scarter@jcvi.org

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