

New Life, Old Bottles

Regulating First-Generation Products of Synthetic Biology



Michael Rodemeyer
University of Virginia

Synthetic
BIOLOGY
PROJECT

What is synthetic biology?

An emerging set of tools and techniques driven by rapid improvements and cost reductions in gene sequencing and synthesis

The application of an engineering perspective to biology

"[T]he design and construction of novel artificial biological pathways, organisms or devices, or the redesign of existing natural biological systems." (Royal Society)

The logo for the Synthetic Biology Project, featuring the word "Synthetic" in a script font, "BIOLOGY" in a bold sans-serif font, and "PROJECT" in a smaller sans-serif font below it.

Synthetic
BIOLOGY
PROJECT

Research & Applications

Much activity at basic research level

Bio-based manufacturing most likely near-term products

Focus on re-engineering metabolic pathways in microbes (bacteria, yeast, algae) to create a biological platform for useful chemicals, such as *biofuels* and *pharmaceuticals*

“What is this like?”

Synthetic biology: new and different, or deja vu?

“Framing” issue can be critical

Consider genetically-engineered crops and food,
and U.S. and European divide

“Deja vu” is reassuring to public, gives clear path to
regulators and industry

Assumption that synthetic biology already covered
by 1986 “Coordinated Framework” for biotechnology

Scope of Report

Looked at how U.S. biotechnology laws and regulations would apply to the likely first generation microbial synthetic biology products

Focus is on biosafety, the potential for accidental or unintentional harm

Focus is *not* on biosecurity – the intentional misuse of a technology for harm

Does not address broader social, economic, ethical issues or intellectual property issues – all likely to be important

Biosafety Risks Are the Same

Synthetic microbes pose the same *kind* of risk as genetically-engineered microbes

Risk: Living organisms can reproduce and spread

Scenarios:

-- accidental release of an engineered organism from containment (e.g., lab)

--unintenc o(n.R@d an)frof ad organisunintenc fd aueaseutscci

Risk Management Tools Are the Same

NIH biosafety guidelines for federally-funded grantees require biological and physical containment measures

Regulatory oversight and controls depend on the "product"

FDA: Food, food additives, drugs, animal drugs, medical devices

EPA: Pesticides, pesticide food residues, "new" chemicals

USDA: Potential plant pests

Adequacy of current system is debatable

The logo for the Synthetic Biology Project, featuring the word "Synthetic" in a script font, "BIOLOGY" in a bold sans-serif font, and "PROJECT" in a smaller sans-serif font below it, all contained within a light blue rectangular box.

Synthetic
BIOLOGY
PROJECT

Risk Assessment?

First products unlikely to be significantly different than GE cousins

No *a priori* reason to believe that synthetic microbes any riskier (or safer) than GE ones

Key risk management strategy for potentially harmful microorganisms is containment (biological and physical); containment is scaled to risk assessment

But as technology develops more complex synthetic organisms, risk assessment will be a challenge

Risk Assessment?

Risk assessment based on familiarity and experience with similar organisms and structures

Assessing organisms designed from scratch in lab or that combine elements from large variety of sources

Potential for emergent properties -- the total may be more than the predicted sum of the parts

Risk of mutation and evolution in environment with selective pressures

Risk Assessment?

Only imperfect ability to predict function from structure given complex genetic interactions

Likely low risk but difficult to quantify

Therefore focus is on containment – but how much is necessary? (Cost vs. risk)

Many synbio organisms unlikely to survive outside of lab

But organisms designed for environment pose challenges

Applying the Biotech Regulatory Framework

NIH

Guidelines are the first line of defense against accidental releases from research labs

- EPA, FDA, other agencies defer to NIH
- Need to amend guidelines to cover synthetic biology research that poses risks similar to rDNA molecules
- Need to provide risk assessment guidance to IBCs
- On right track: 74 Fed. Reg. 9411 (March 4 2009)

Underlying issues:

Self-regulation

Capacity of IBC's



Applying the Biotech Regulatory Framework

EPA

Legal authority under Toxic Substances Control Act (TSCA) already stretched

EPA may need to revise regulations to cover synthetic microbes

Limited authority to gather information for risk assessment, especially for field trials or non-contained uses

Limited experience with GE microbes

May be an issue in near future for scale up of biofuel production

Applying the Biotech Regulatory Framework

USDA

Covers “unknown” organisms that could be plant pests; no authority to look at health risks

Likely to need revisions to regulations

FDA

Broad authority for drugs; different process for other products (food, dietary supplements)

Applying the Biotech Regulatory Framework

Cross cutting issues:

- Risk assessment challenges (information, models, validation)
- Resources – scientific, technical and monitoring
- Risk management for uses outside of containment (e.g., biosensing, biofuels)
- Shoe-horning new technologies into older laws and regulations

Garage Biology

Regulatory framework assumes a regulated community (industry, universities) that knows the rules and plays by them

Open source model and low barriers to entry raise the prospect of backyard biologists

- biosecurity focus on pathogens and select agents
- but the issue of accidental or unintended consequences is just as real
- federal regulatory model irrelevant
- role for state and local regulations?

Conclusions

With some changes, current U.S. regulatory framework for biotechnology could cover likely first generation synthetic biology products

First synbio products unlikely to raise novel issues of risk assessment or management, but challenges in the longer term, especially for use outside of contained facilities

Regulatory framework may not be sufficiently agile for new technologies and new issues

Risk research urgently needed

Garage biology requires new approaches