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Regulating Synthetic Biology Under Environmental Laws

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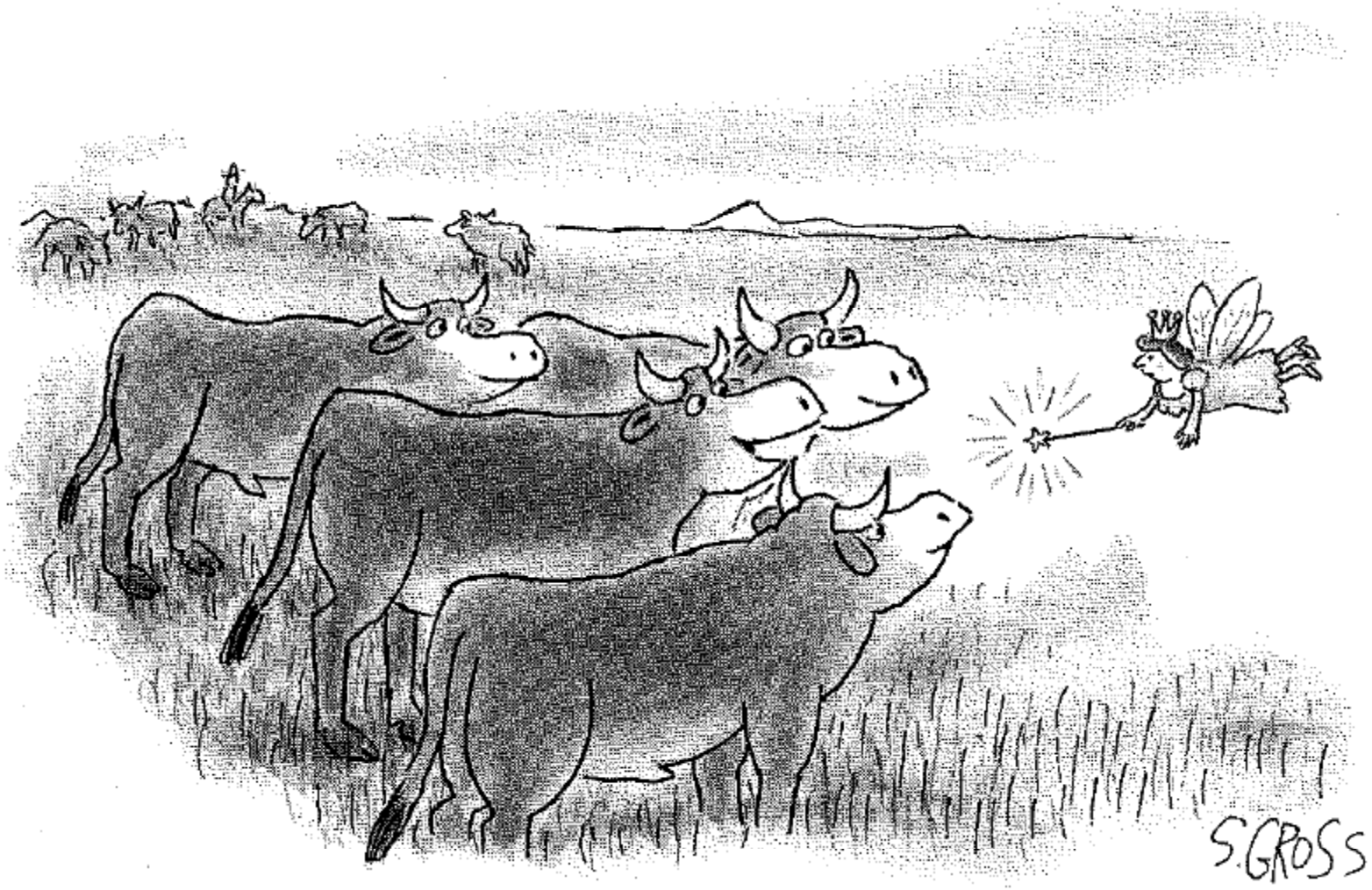


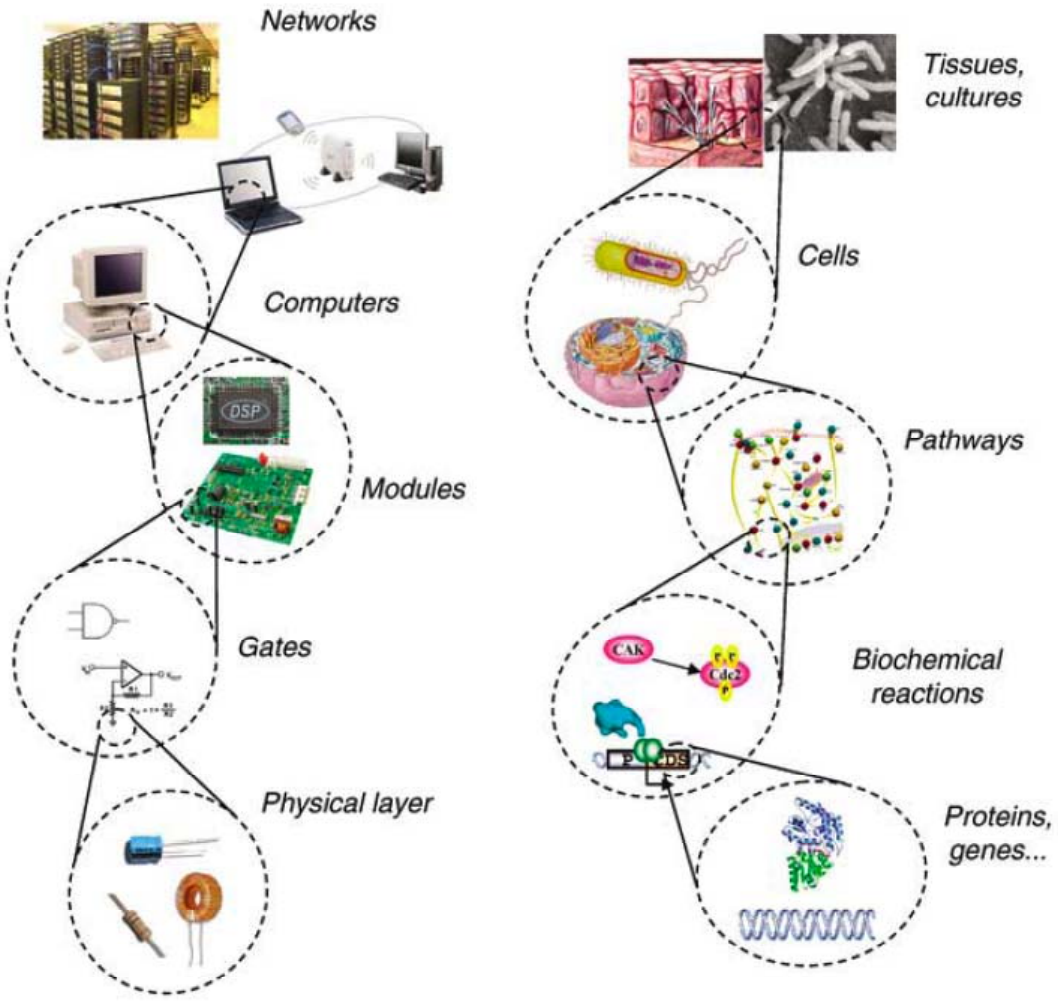
"We would like to be genetically modified to taste like Brussels sprouts."

Synthetic Biology

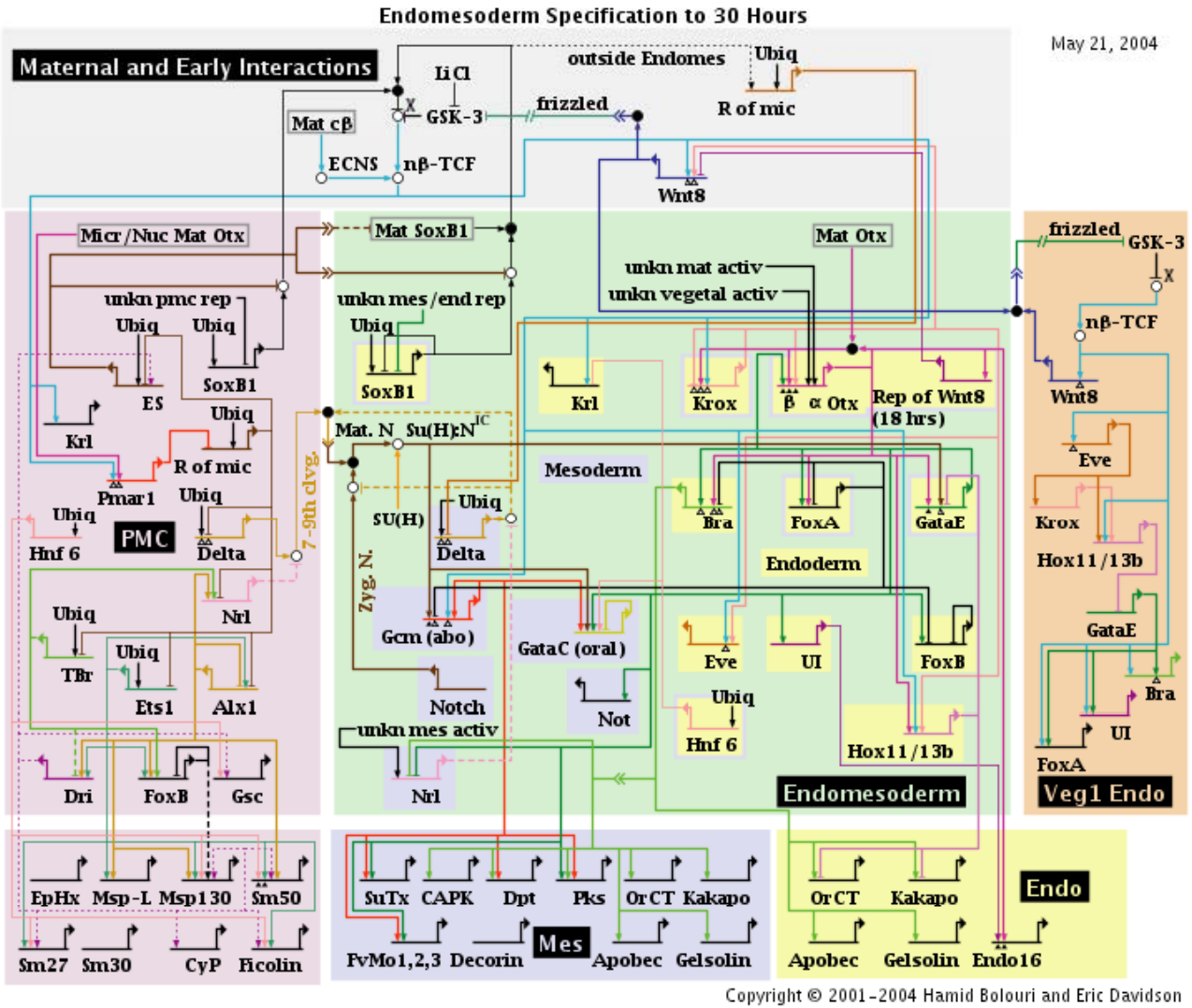
". . .[the application of] standardized engineering techniques to biology and thereby create organisms or biological systems with novel or specialized functions to address countless needs."

New Directions: The Ethics of Synthetic Biology and Emerging Technologies, Presidential Commission for the Study of Bioethics, Dec. 2010 at p. 2

What exactly does that mean?



Picture the cell as a network - literally



Differences between conventional genetic engineering and synthetic biology

- GE: relies on existing genetic material and expression

  Synthetic biology: allows creation of completely new genes and pathways

- GE: focuses on transfer of existing traits or suppression of current functions

  Synthetic biology: allows engineering of entirely new capabilities or traits

- For short term, products looks similar (artesimin, biofuels).

- For long term, offers possibility of radically new products

Challenges to Environmental Law from Synthetic Biology

- How do you assess risk for the entirely novel?
- Assessing risk from self-replicating organisms?
- Low barriers to entry
  - Expenses have dropped dramatically with time
  - As standardization and accessible instructions become available, expertise not required

BioBrick™ Assembly Manual

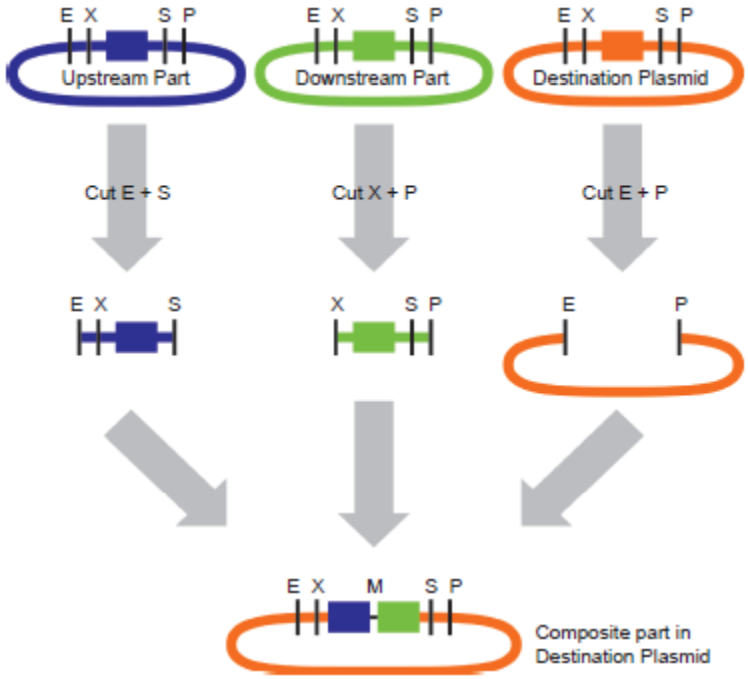
ginkgobioworks

NEW ENGLAND BioLabs Inc.

This manual describes the major steps of BioBrick assembly using BioBrick Assembly Standard 10. The input to the protocol is DNA for the two parts to be assembled and a destination plasmid. The manual includes protocols for the digestion of the three input DNA molecules and the ligation of the digested DNA to form a circularized plasmid containing the composite part. The product of the ligation reaction can be used to transform competent cells with the composite part. To read more about the BioBrick system and browse the BioBrick collection, visit the Registry of Standard Biological Parts at http://partsregistry.org.

BioBrick assembly overview

E=EcoRI-HF™
X=XbaI
S=SpeI
P=PstI
M=Mixed site



1 Start with two BioBrick parts and a BioBrick destination plasmid. The destination plasmid contains a toxic gene, *ccdB*, in the BioBrick cloning site and a different antibiotic resistance marker to the upstream and downstream parts.

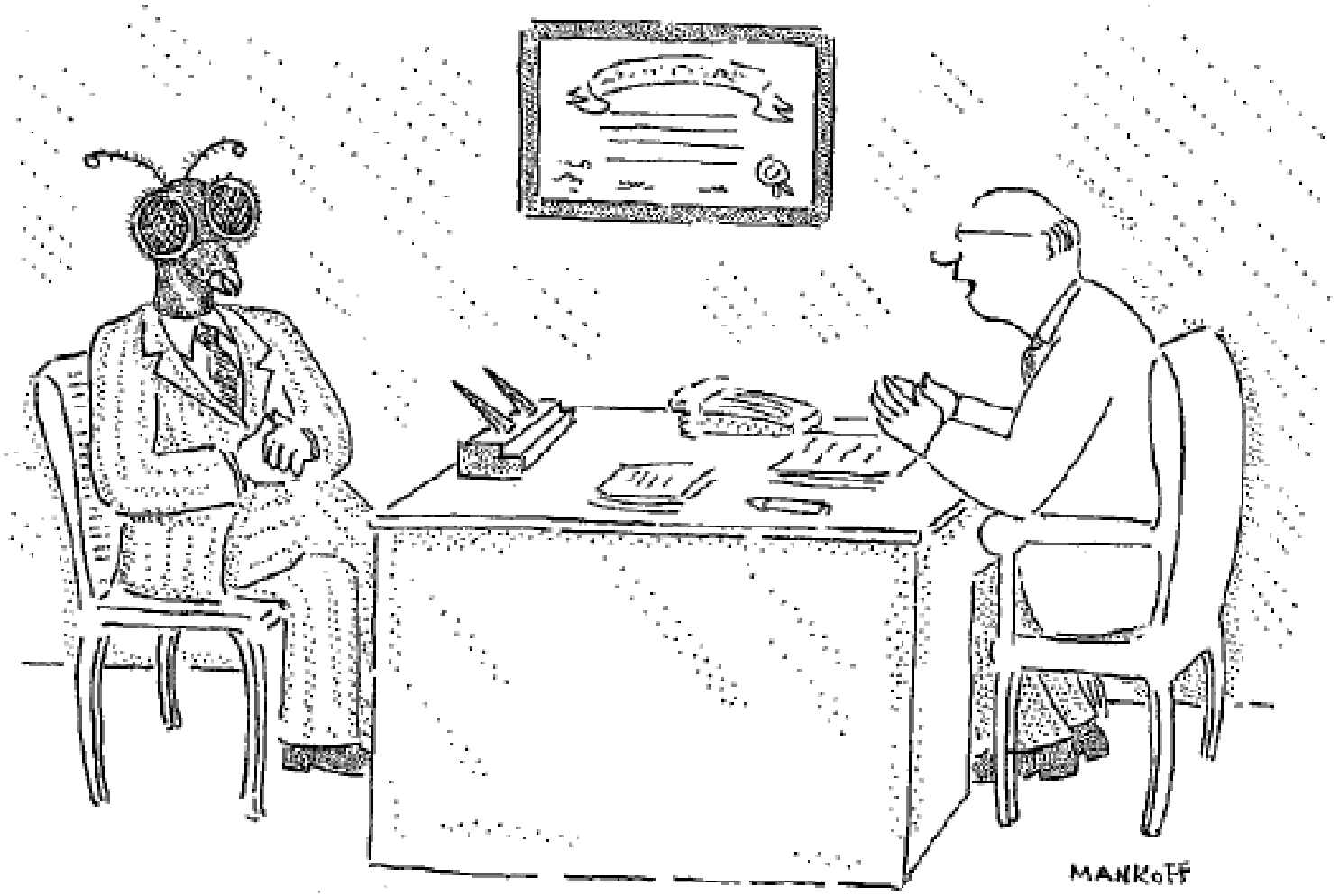
2 Digest each of the parts with the appropriate restriction enzymes.

3 Mix the digests together and perform a ligation step. One of the ligation products formed will be the correctly assembled composite part in the destination plasmid. You can use the ligation mix to transform competent cells with the new composite part.

The BioBrick™ Assembly Kit from NEB and Ginkgo BioWorks has been designed for use with this manual. Download this manual from http//ginkgobioworks.com/support

Version 1.0

http://parts.mit.edu/registry/indEx.php/Main_Page



"We think it has something to do with your genome."

How to regulate synthetic biology?

TABLE 1. FEDERAL LAWS POTENTIALLY APPLICABLE TO GE ORGANISMS AND PRODUCTS DERIVED FROM THEM

Title of Act	Abbreviation	Agency	Cite
The Federal Insecticide, Fungicide, and Rodenticide Act	FIFRA	EPA	7 USC § 136
The Toxic Substances Control Act	TSCA	EPA	15 USC § 2601
The Food, Drug, and Cosmetic Act	FDCA	FDA; EPA	21 USC § 301
The Plant Protection Act	PPA	USDA	7 USC § 7701
The Virus Serum Toxin Act	VSTA	USDA	21 USC § 151
The Animal Health Protection Act	AHPA	USDA	7 USC § 8031
The Federal Meat Inspection Act	FMIA	USDA	21 USC § 601
The Poultry Products Inspection Act	PPIA	USDA	21 USC § 451
The Egg Products Inspection Act	EPIA	USDA	21 USC § 1031
The Animal Damage Control Act	ADCA	USDA	7 USC § 426
The Animal Welfare Act	AWA	USDA	7 USC § 2131
The National Environmental Protection Act	NEPA	(All)	42 USC § 4321

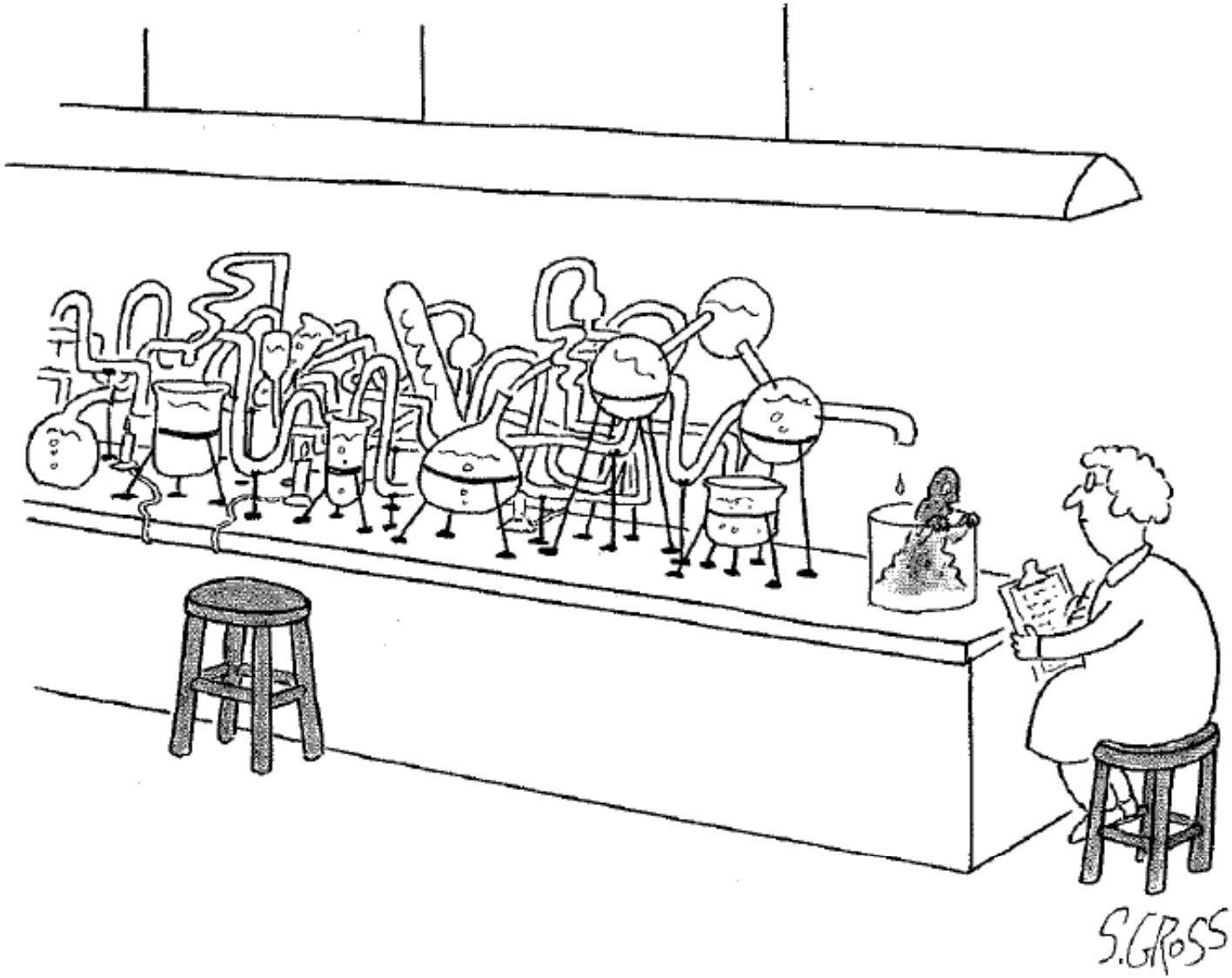
Source: Pew Initiative on Food and Biotechnology (2004).

A bit more complicated with Synthetic Biology….

TABLE 4. REGULATION OF SYNTHETIC BIOLOGY PRODUCTS UNDER U.S. BIOTECHNOLOGY FRAMEWORK

Product	Scope	Agency / Authority	Legal Tools	Comments	Risk Management Issues
R&D in Contained Facility					
NIH or federally-funded research	all R&D with rDNA molecules (*proposed: synthetic nucleic acids)*	NIH Guidelines & IBCs	Contract; violations threaten future federal funding	Reliance on IBCs and self-reporting	Uncertainty of risk; guidance to IBCs
Privately-funded basic				Not covered directly	
Industrial chemicals - commercial R&D	covered intergeneric microorganisms not regulated by other agencies (i.e., drugs)	EPA TSCA	Pre-manufacturing notification	Exempt if comply with NIH or functional equivalent; definition may not cover synthetic microorganisms	Relies on NIH; uncertainty in risk assessment; agency must show risk; limited resources
Human or animal drugs, biologics, medical devices	all (functional definition)	FDA FDCA	Mandatory pre-market approval; approval for investigational new drugs and devices	Some pre-commercial research phase not covered	

Commercial Production or Use in Contained Facility					
Human or animal drugs, biologics, medical devices	all (functional definition)	FDA FDCA	Can withdraw product approval; regs for good manufacturing practices; reporting		Limited resources
Industrial chemicals - commercial R&D	covered intergeneric microorganisms not regulated by other agencies (i.e., drugs)	EPA TSCA	Pre-manufacturing notification	Certain low-risk microorganisms in containment are exempt	Uncertainty in risk assessment; agency must show risk; resources
Microbial pesticides	all (functional definition); modified microbes	EPA FIFRA	Prior approval for use in non-contained facility	Exempts testing in facilities meeting NIH Guidelines or functional equivalent	Authority to require developer to test for environmental risks
Use in Non-Contained Settings					
Non-commercial research	GE microorganisms of unknown or unclassified organism	USDA APHIS	Permit required for transport or field trials	Does not cover public health risk	Uncertainty re: environmental risk assessment
Human or animal drugs, biologics, medical devices	all (functional definition)	FDA FDCA; NEPA	Mandatory pre-market approval for safety	Limited environmental authority	Clinical trials for safety and efficacy; environmental risk info limited
Industrial chemicals - commercial R&D	covered intergeneric microorganisms not regulated by other agencies (i.e., drugs)	EPA TSCA; USDA APHIS; NEPA	Pre-manufacturing notification; pre-release approval	Exempts some low-risk field trials; excludes noncommercial releases; overlap with APHIS	Uncertainty in risk assessment; agency must show risk; limited resources
Microbial pesticides	all (functional definition); modified microbes	EPA FIFRA	Mandatory pre-market approval for unreasonable risk; prior approval for field trials		Authority to require developer to test for environmental risks
Microbial animal and plant pests	GE microorganisms of unknown or unclassified organism	USDA APHIS; NEPA	Notification or permit for field trials; deregulation for commercialization	Does not cover public health risk	EIS might be required



"Are you my mommy?"

Questions?

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