



Governance for Gene Drives in Historical and Systems Context

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Environmental Release of Engineered Pests
October 6, 2016

Reboot the debate on genetic engineering

2016 | VOL 531 | NATURE | 165

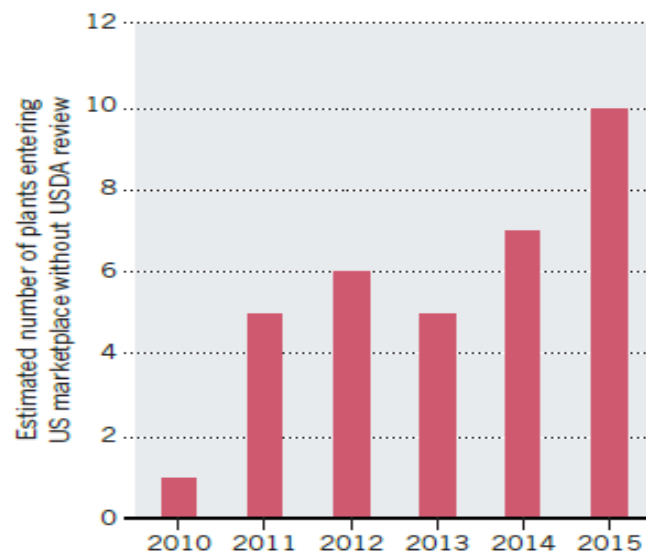
Arguments about whether process or product should be the focus of regulation are stalling progress, says **Jennifer Kuzma**.

In reality, it is impossible to be completely 'science based' in a regulatory system. Value judgements are embedded in all risk and safety assessments. For example, the dose-response curve for a certain food additive might be known, but such data do not by themselves tell regulators where to set an acceptable safety limit. More often, the dose-response curve is not well established, or known at all. This uncertainty leads to various interpretations of the data.

Empirical evidence matters, but human interpretation brings meaning to that evidence, and multiple perspectives can strengthen understanding. Thus, an over-

LOOSER SCRUTINY

Because of changes to genetic-engineering (GE) processes, several GE crops have entered the US marketplace without review from the US Department of Agriculture (USDA) in recent years.



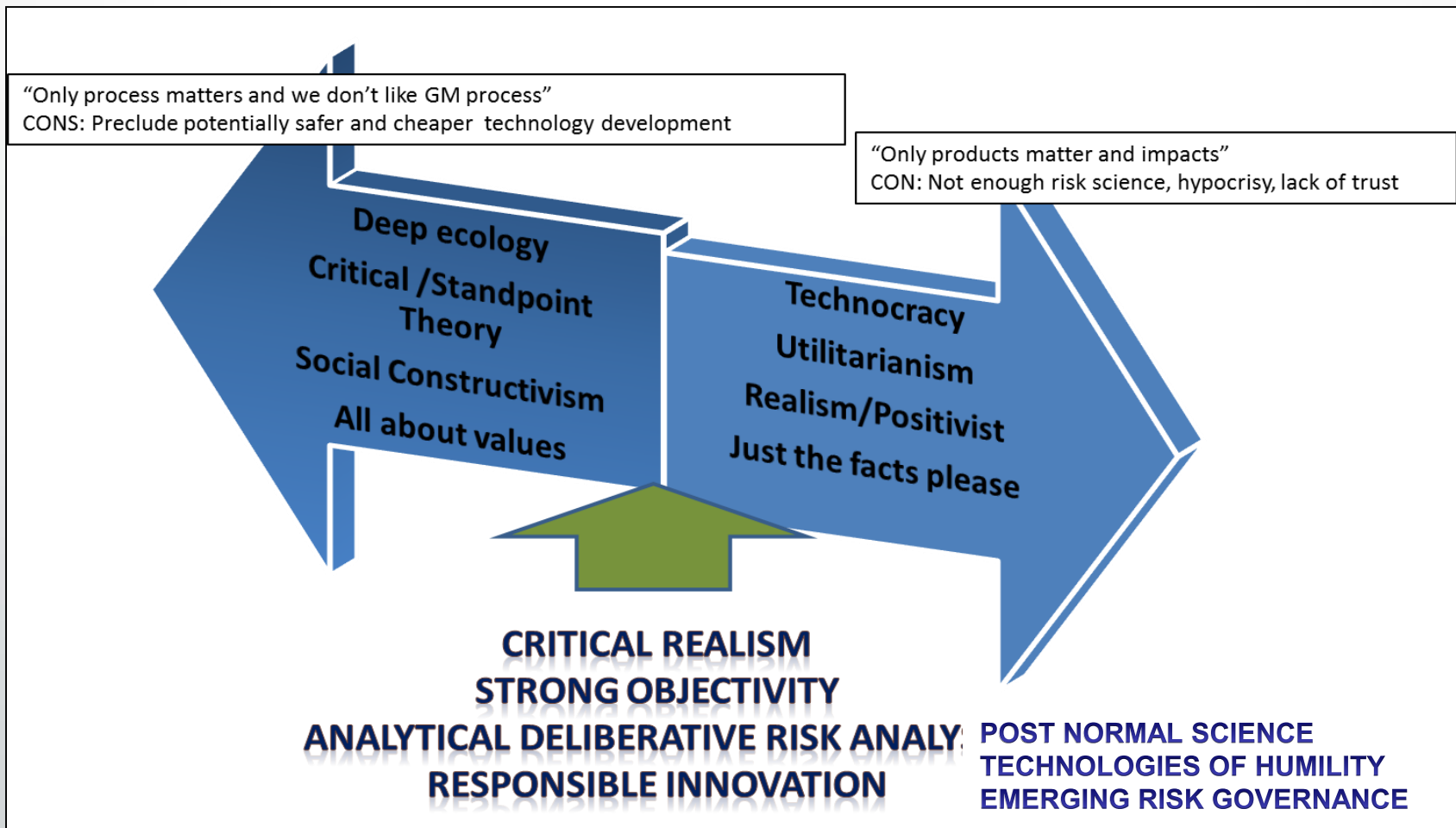
Within these efforts and others, stakeholders could do away with polarizing product-versus-process and science-versus-values framings, and help to establish a governance system that is both informed by the science and guided by the concerns and values of citizens. ■

“I have a dream...”

Martin Luther King, Jr.

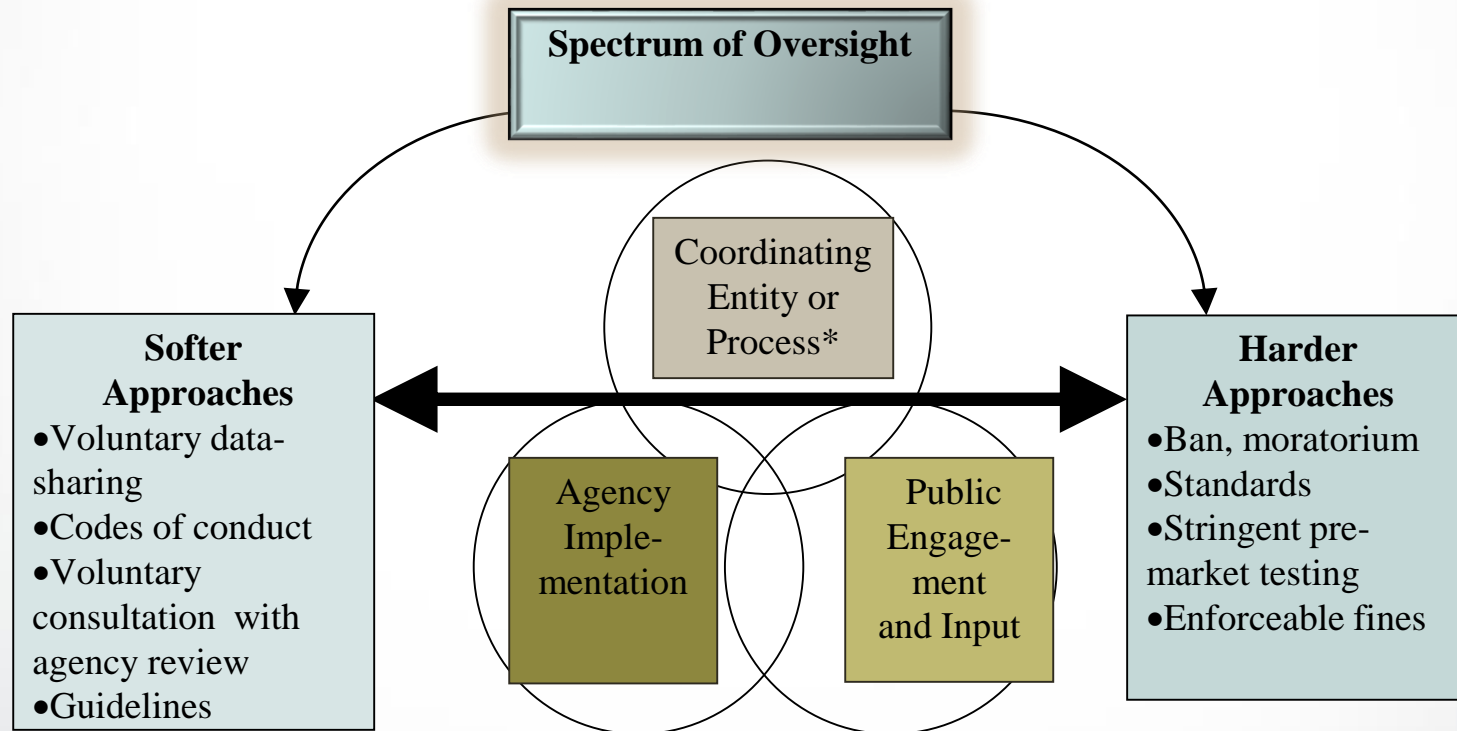
Future Innovation in Governance

- Need to move to “middle-ground” approaches (Kuzma in press)
- Plenty of policy models in the literature
- Lack of political and social will to change?
- But it is INNOVATION and regulatory innovation can also create jobs



Flexible, Coordinated, Inclusive Dynamic Oversight:

Ramachandran, Kuzma et al. 2011



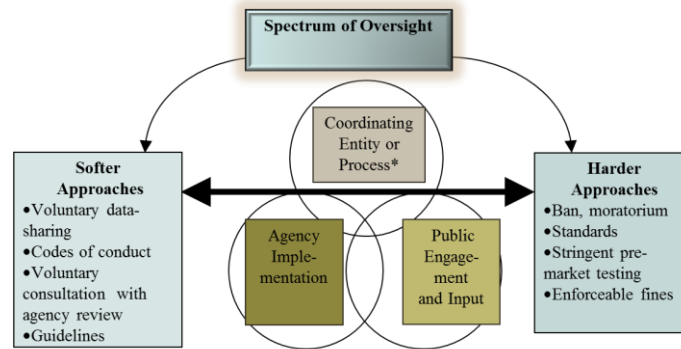
* with citizen, governmental, academic, industry, tribal, and NGO representation

Key Features

- Integrates (and mixes) soft and hard approaches to oversight, moving between these two dynamically as data become available, attitudes and analyses evolve, and technology changes.
- Provides strong coordination among various regulatory agencies, the various stakeholders and the public.
- Provides oversight throughout the life-cycle of the technology or product.
- Considers Life Cycle issues, relative risk and benefit, and asks question “do we need this option”, is it the lowest risk option?
- Stakeholders and public reps have a central role in providing input to the oversight framework. (note—they do not “vote”, but have a voice and are listened to in policy process)

Additional Principles

- Anticipates convergence
- Inclusive
- Public empowerment
- Learning among groups
- Respectful
- Multiple iterations
- Preparedness at all stages
 - (including post-market)
- Transparent
- Adequate resources
- Continuous
- Evolving
- Information-generating
- Information- and value-based



* with citizen, governmental, academic, industry, tribal, and NGO representation

Coordinating body has political teeth, but is not unduly constrained by legal barriers

OSTP IN U.S.?

CBD BSP INTERNATIONALLY?

Long-term view

**INDIGENOUS PEOPLES *AND*
YOUTH ARE ENGAGED**

ENGINEERING THE WILD: GENE DRIVES AND INTERGENERATIONAL EQUITY

Jennifer Kuzma* and Lindsey Rawls**

, Jurimetrics (2016)

Conservation of Quality
Conservation of Options
Conservation of Use
(Weiss 1989)

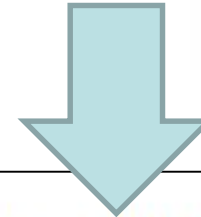


Table 1. Categories of Gene Drive Purposes and Effects

Effect on Population Carrying the Gene Drive*					
	Population Immunization	Population Suppression	Population Enhancement	Population Sensitization	
General Purpose	Human disease eradication	Block vector-species from carrying disease	Drive down population of disease vector-species with genetic sterility mechanism.	Enhance fitness of populations that prey on vector	Make vector species or disease agent newly susceptible to safer chemical or biological agent
	Agricultural safety and sustainability	Immunize agricultural commodity against disease	Drive down populations of insect or other pests with genetic sterility mechanism	Increase commodity abilities to thrive on fewer inputs; enhance fitness of prey of pests	Make pests newly susceptible to safer chemical or biological agent
	Control Invasive species	Immunize desirable species against invasive species	Drive down populations of invasive species with genetic sterility mechanism	Increase fitness or predation abilities of predators of invaders	Make invasive species newly susceptible to safer chemical or biological agent
	Protect threatened or endangered species	Immunize endangered species against disease	Drive down populations of predators of endangered species with genetic sterility mechanism	Increase fitness of endangered species towards any stressor	Make predator species newly susceptible to safer chemical or biological agent

*The species into which the gene drive would be introduced varies and is presented in italics for each category

Increasing intergenerational equity: A proposal

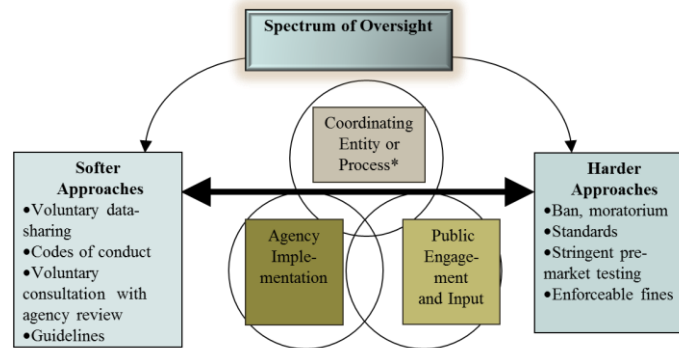
Next generation Voices in Next Generation GE

“next generation” biotechnologies such as gene drives present an area for which the input of the next generation is particularly important. The face of “nature” and human relationships with nature are shifting, yet those who are most likely to experience these changes, the young, are left out, and their voices are not heard by today’s decision makers. We can at least provide opportunities for youth to discuss and report their hopes, concerns, and attitudes about next generation GE, including gene drives, while we encourage policy makers to adopt a longer term perspective for other future generations.



– Giving Kids Voice in Next Generation Genetic Engineering

- Educational goals
 - Social science research
 - Ethical Imperative
-
- Kids & Teens 11-17 years old
 - Interactive café style dialogues
 - Coupled with National survey
 - Report back to decision makers in DC (kids taking leadership)
 - In proposal and fundraising stage



* with citizen, governmental, academic, industry, tribal, and NGO representation

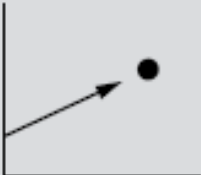
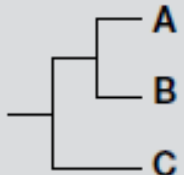


Infeasible to do such an approach for EVERY SINGLE PRODUCT

**THREE-BODY GROUP WOULD
LOOK AT *CLASSES* OF
PRODUCTS**

Typologies of Uncertainty

Emerging Risks

IRGC 2015

		Deep Uncertainty			Total Ignorance
		Level 1	Level 2	Level 3	
Determinism	Context	A clear enough future 	Alternate futures (with probabilities) 	A multiplicity of plausible futures 	Unknown future 
	System Model	A single system model	A single system model with a probabilistic parametrization	Several system models, with different structures	Unknown system model: know we don't know
	System Outcomes	A point estimate and confidence interval for each outcome	Several sets of point estimates and confidence intervals for the outcomes, with a probability attached to each set	A known range of outcomes	Unknown outcomes: know we don't know
	Weight on Outcomes	A single estimate of the weights	Several sets of weights, with a probability attached to each set	A known range of weights	Unknown weights: know we don't know

Risk governance and public engagement

Figure 4: The Risk Management Escalator and Stakeholder Involvement (from simple via complex and uncertain to ambiguous phenomena)

- IRGC 2006

			<i>Risk Trade-off Analysis & Deliberation necessary</i> + Risk Balancing + Probabilistic Risk Modelling
		<i>Risk Balancing Necessary</i> + Probabilistic Risk Modelling	
	<i>Probabilistic Risk Modelling</i>	Remedy	Remedy
		• Cognitive • Evaluative	• Cognitive • Evaluative • Normative
	Remedy	Type of Conflict	Type of Conflict
<i>Statistical Risk Analysis</i>	Cognitive	• Agency Staff • External Experts • Stakeholders	• Agency Staff • External Experts • Stakeholders
Remedy	Type of Conflict	• Industry • Directly affected groups	• Industry • Directly affected groups • General public
Agency Staff	• Agency Staff • External Experts		
Actors	Actors	Actors	Actors
Instrumental	Epistemological	Reflective	Participative
Type of Discourse	Type of Discourse	Type of Discourse	Type of Discourse
Simple	Complexity induced	Uncertainty induced	Ambiguity induced
Risk Problem	Risk Problem	Risk Problem	Risk Problem
Function: Allocation of risks to one or several of the four routes Type of Discourse: Design discourse Participants: A team of risk and concern assessors, risk managers, stakeholders and representatives of related agencies			

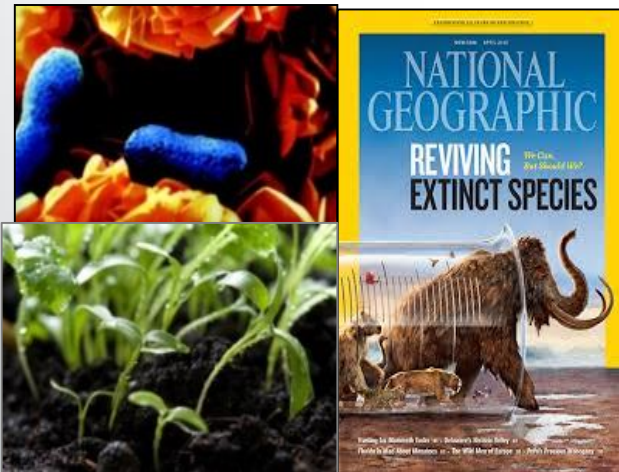
Example: Policy Delphi for Anticipatory Governance of SB



ALFRED P. SLOAN
FOUNDATION

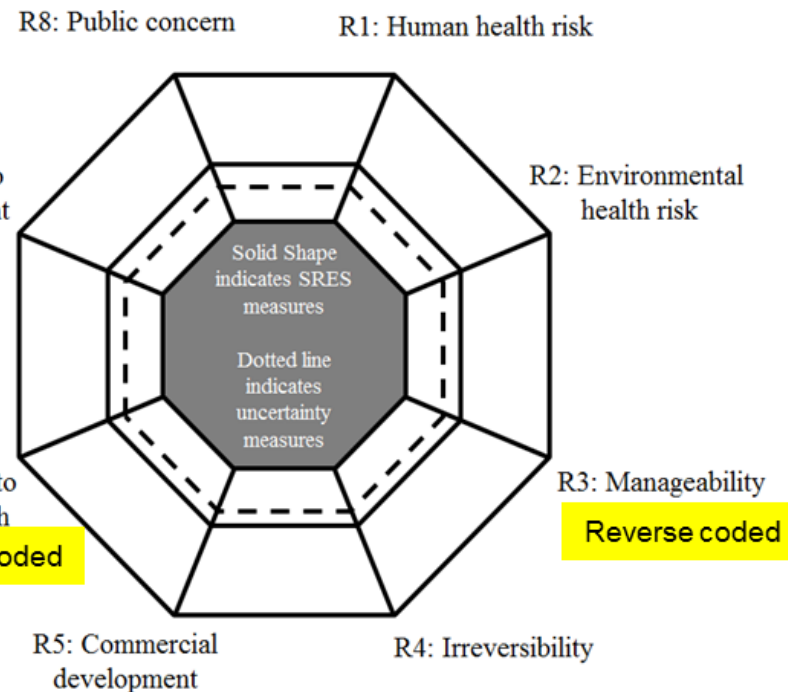
Societal Risk Evaluation Scheme

- Future Studies
- Upstream Technology Assessment
- Cases of longer-term development
- Risk Analysis, and Governance questions
- Policy Delphi process in 4 rounds
 - Interviews, Survey, Workshop, Survey



Reverse coded

R7: Benefits to
the environment



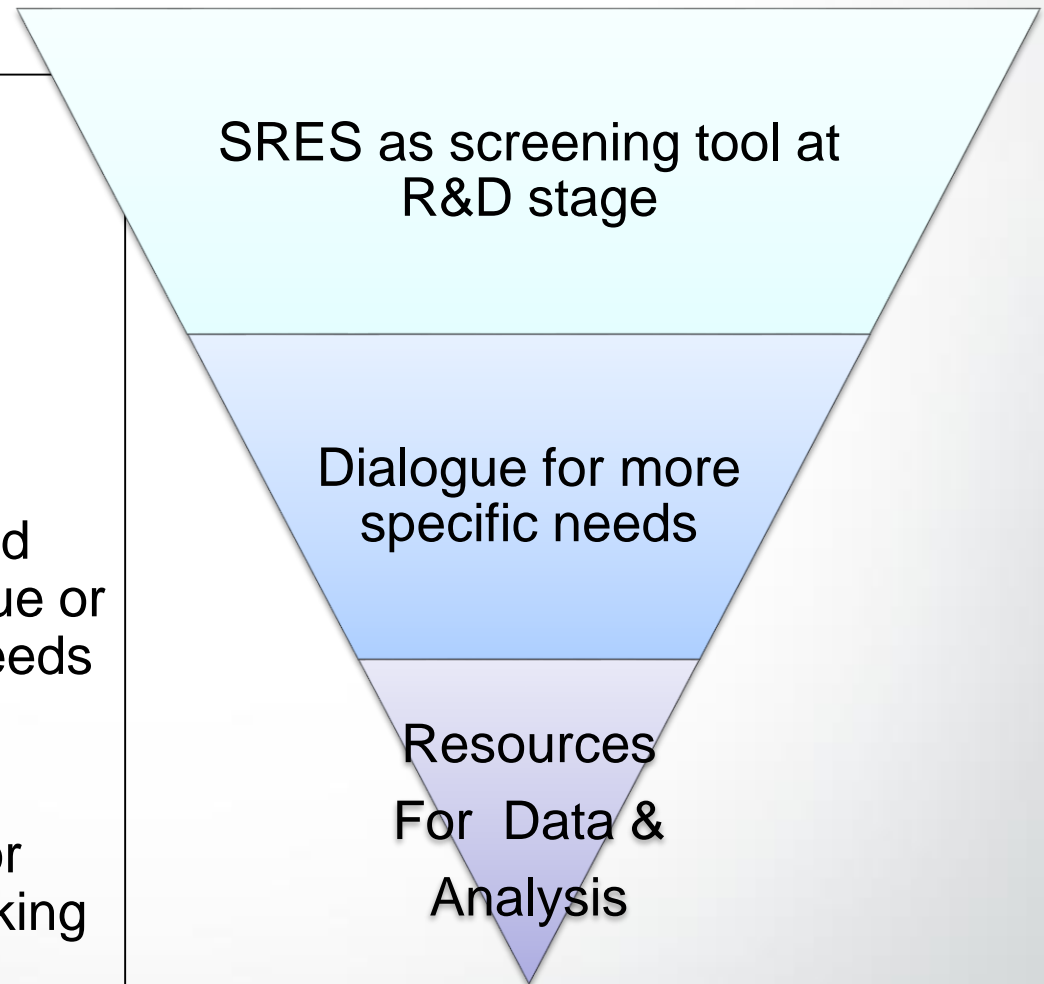
Cummings & Kuzma in review

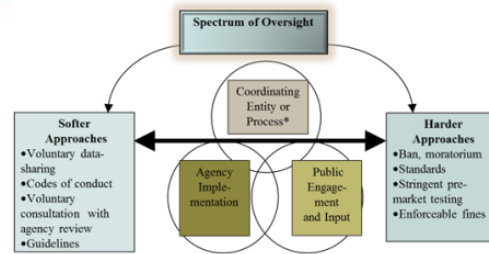
Anticipatory Governance

Deploy SRES in Anticipatory Governance at early stages of product development (before investment)

As product categories developing (e.g. CRISPR gene drives or RNAi), gather more information and data in high SRES areas—dialogue or interviews for specific research needs

These activities as foundation for resource allocation and funding for information to inform decision making





* with citizen, governmental, academic, industry, tribal, and NGO representation

Who should convene the screening process to decide what categories of products go through rigorous engaged and iterative process?

Academic or think tank centers that have minimal CONFLICTS serve as a technical resource group for the process or convener?

Consortium of Centers funded by OSTP,(CBD or WHO or IPPC) or ...?.

CENTER & FOR
SCIENCE & TECHNOLOGY
POLICY RESEARCH

GES
CENTER

NC STATE UNIVERSITY

ASU center for
science, technology and
environmental policy studies
ARIZONA STATE UNIVERSITY



tpac Technologies in Context

ISSP

INSTITUT DE RECHERCHE SUR LA SCIENCE,
LA SOCIÉTÉ ET LA POLITIQUE PUBLIQUE
INSTITUTE FOR SCIENCE, SOCIETY AND POLICY

US

University of Sussex

SPRU – Science Policy Research Unit

A Roadmap for Gene Drives: A Deliberative Workshop to Develop Frameworks for Research and Governance

February 24-26, 2016

- **Typologies, Systems and Intersectionality**
- Governance issues and research needs with attention to
 - ecological risk analysis,
 - **political economy**,
 - governance
 - and ethical analysis.
- **12 Peer Reviewed Papers**



Special issue of the ***Journal of Responsible Innovation*** (open access) early 2017

Editors: Delborne, Kuzma, Gould, Leitschuh, Sudweeks, Frow eds

Program committee: Brown, Collins, Delborne, Esvelt, Frow, Gould (coPI), Guston, Kuzma (PI), Leitschuh, Oye

Research Typology from Maps

How to consider values around animals & nature in economic-based decisions?

New context-dependent economic models --gene drives type, geographical scale, who controls?

Distribution of risks and benefits?

Changes in employment/jobs ?

Technological access as a democratizing or destabilizing force in small industry vs. large or organic vs. non users?

Economic

Ecologic
al &
Human
Health

Ethics

Socio-
cultural

Framing effects and effects on perception & governance?

How to consider & engage marginalized groups appropriately?

Protocols on containment?

Anticipate potential ecosystem surprises?

Pest ecology?

Technology efficacy to achieve end goal?

Policy

Institutional structures for collective and adaptive governance? (Commons analogy)

Stakeholder identification methods?

What gives social license to operate?
To inform?
To participate?

What are public perceptions about gene drives?

* How much risk science is enough for DM?

Design of systems to measure long-term eco effects?

Translational Governance Research

Kuzma 2015

- *Experiments with Governance Systems*³

- (1) Test ways to anticipate and prepare for future technologies in governance systems with side-by-side comparisons of different features for these systems.
- (2) Explore a creative set of emerging, interested and affected parties within these systems.

- *Methods to Deal with Uncertainty and Ambiguity in Governance*

- (1) Improve upstream methods within governance systems to explore a broad range of harms and benefits and characterize uncertainty.
- (2) Test decision-science and future-studies approaches (scenario planning, Bayesian approaches, systems mapping, etc.) in governance systems.

- *Improve Ways to Explore Claims in Contested Areas*

- (1) Develop balanced and more inclusive approaches for determining 'weight of evidence' and for ways to understand and mitigate bias in interpretations of evidence.
- (2) Understand and acknowledge values behind multiple perspectives and interpretations of evidence.
- (3) Explore assumptions, contradictions, and correlation arguments on multiple sides of controversies.

- *Historical Analyses of Governance Systems*

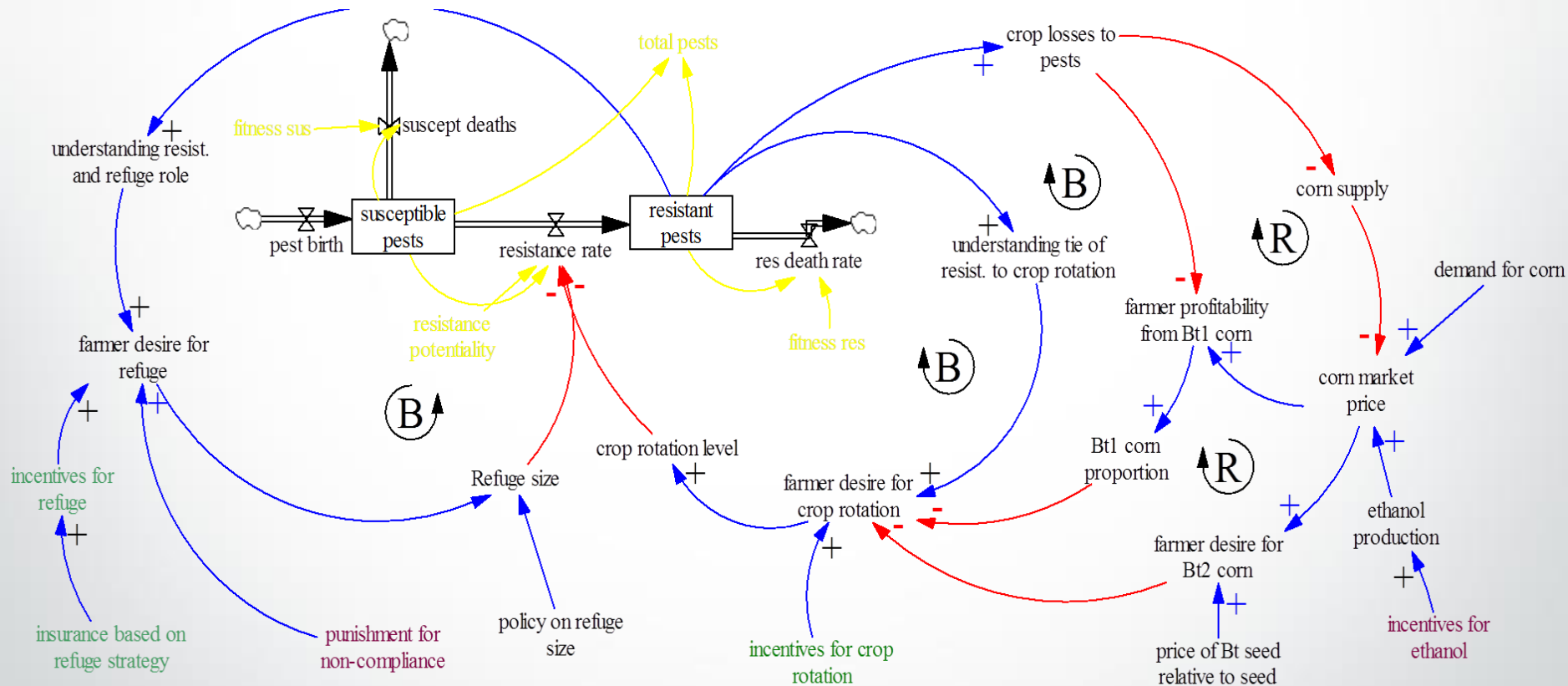
- (1) Explore the use of multiple natural and social science and ethical criteria and how to integrate them to analyse the historical cases of governance and uncover patterns or features that are indicators of systems that lead to desirable outcomes for multiple stakeholders.

Who funds in U.S.?
No one really...

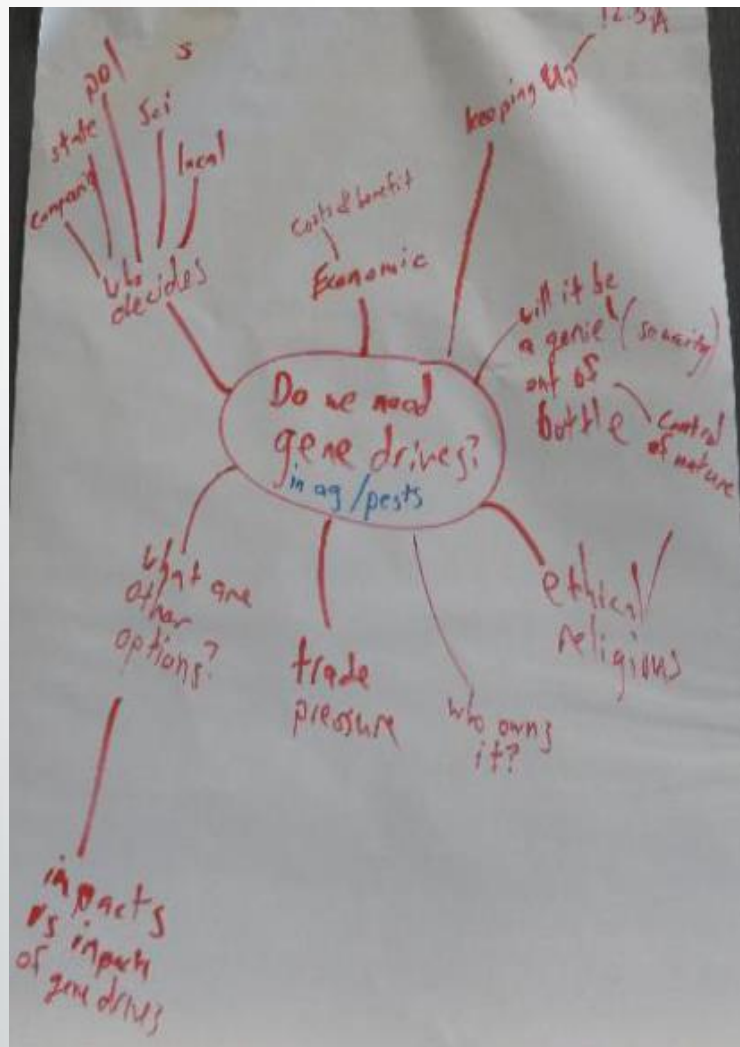
Policy Learning

- Instrumental policy learning (single loop)—reactive learning
 - Effectiveness of policy tools
 - Learning about how a policy works and making adjustments to improve or replace techniques
- Social learning (double loop)—causal learning
 - Social causes of problems and interventions to solve them
 - Thinking and learning also about the fundamental assumptions and structures
 - Systems and behavior over time

Recent Example—Bt resistance (SESYNC group)



Cockerill et al. 2010



OK, NOW REALITY HITS....

**SOCIAL AND POLICY
SCIENCES RESEARCH**

I am increasingly dismayed by the barriers having studied biotech policy for 20+ years.....

BIOTECH REGULATION

A missed opportunity for U.S. biotechnology regulation

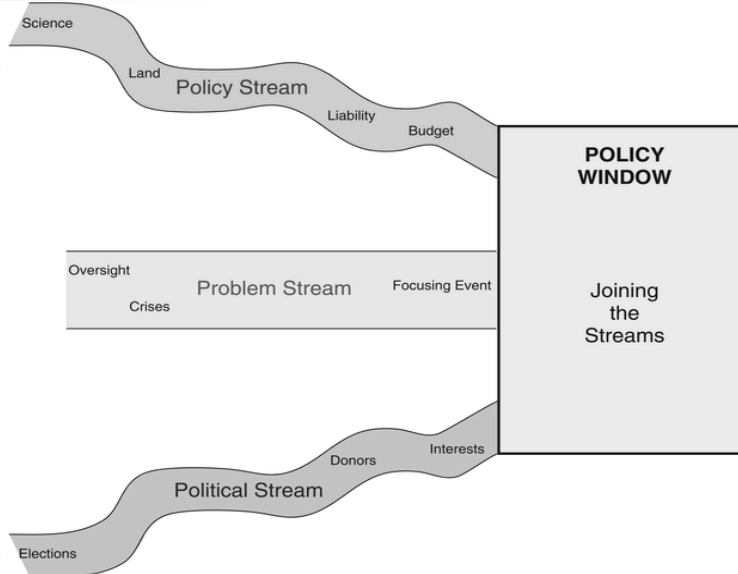
Policy options for change were not on the table

By Jennifer Kuzma

16 SEPTEMBER 2016 • VOL 353 ISSUE 6305 1211

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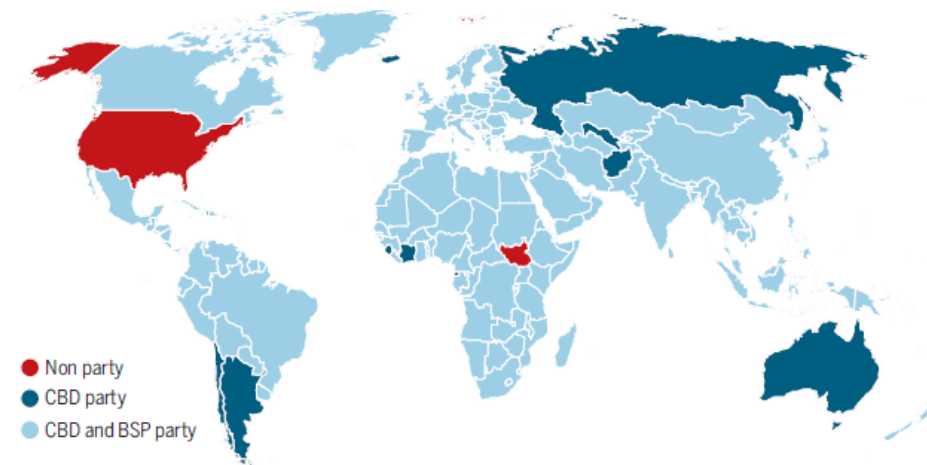


“...opportunities [for] meaningful...change... were missed at this key juncture in the biotech revolution...”

- Policy window cracked for first time in 25 years
 - No policy options for change on the table
 - Little meaningful participation
 - Little to no thought about harmonization

Parties to agreements on biodiversity

The countries that have ratified or accessioned the Convention on Biological Diversity (CBD) and its Cartagena Protocol on Biosafety (BSP) are shown, as well as nonparties.



Policy Efforts

- OSTP interagency process to clarify Coordinated Framework for Regulation of Biotechnology (3 public meetings)—completed
- Agency processes in the “long term strategy” document
 - EPA to possibly have a role in GE insects or animals that act like pesticides?
- National Academies of Sciences study committee on the Future of Biotechnology (nas-sites.org/biotech) and risk assessment preparedness for emerging products (full disclosure, I am on it)
- USDA proposed Environmental Impact Statement for new rule on GEOs
- EPA guidance revision for GE algae and microbes

The Pacing Problem

9. Properly paced? Examining the past and present governance of GMOs in the United States

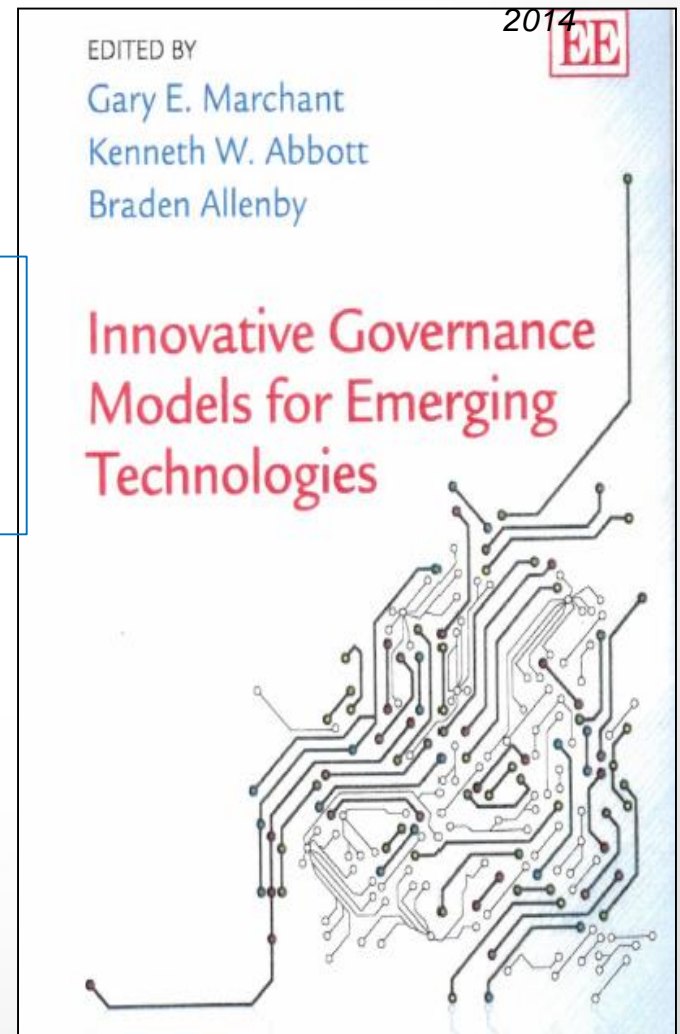
Jennifer Kuzma

9.1 INTRODUCTION

A case study of genetically modified organisms (GMOs)¹ in US agriculture and the environment illustrates the problem of policy systems to keep up or pace with advances in emerging technologies. This chapter describes the history of GMO governance in four phases, examining the oversight system's ability to pace with technological developments in each phase. In general, government decisions for oversight of GMOs, particularly GM crops, seemed to pace well with technology in a temporal sense. However, they continue to be contested and do not seem appropriate in the longer term for ensuring safety, transparency and public confidence. The GM crop oversight system exhibited temporal pacing through flexible legal frameworks, but not proper pacing. This chapter argues for a broader notion of pacing that incorporates not only elements of timeliness, but also notions of appropriateness in dynamic societal contexts. It will conclude with proposed lessons from the US GMO oversight experience for developing a new prototype model of governance for emerging technologies that properly paces with technological advancements. This model is based upon three pillars: (i) upstream oversight assessment (a subset of anticipatory governance); (ii) dynamic oversight; and (iii) strong objectivity through more extensive public and stakeholder engagement in decision making.

¹ Natural scientists prefer the term genetically engineered; however, we use genetically modified (GM), as it is more in line with international policy discussions. We use GM to indicate any organism modified by recombinant DNA or newer biotechnology methods.

How has oversight
kept pace
with changes in GE
products and
technologies?

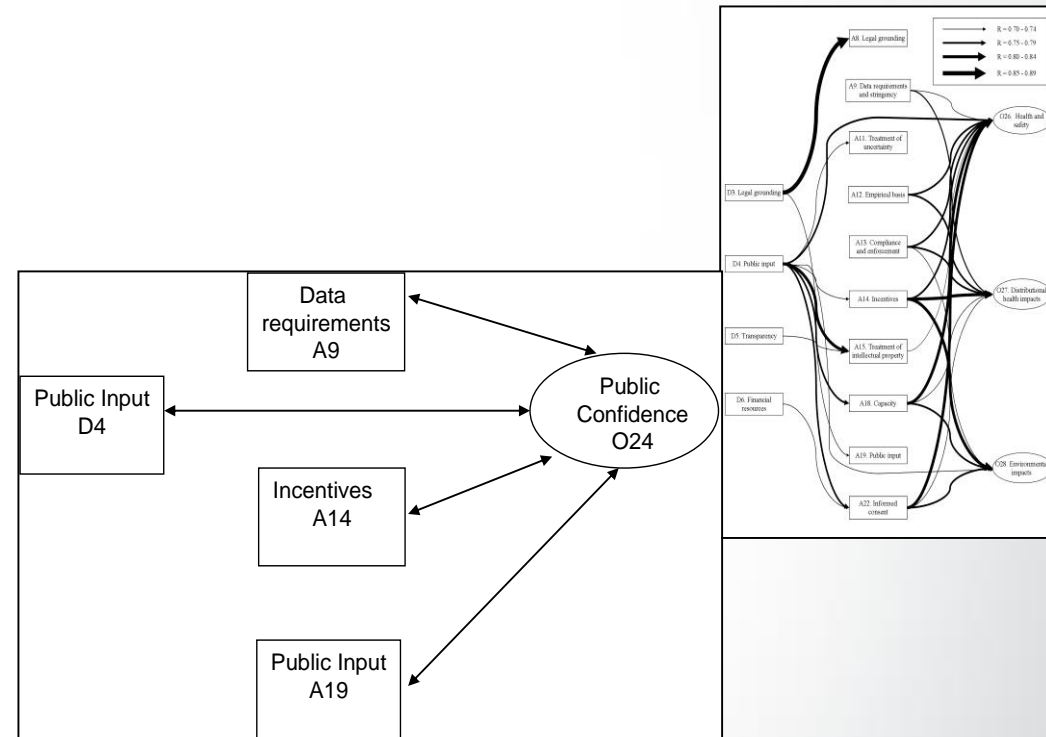
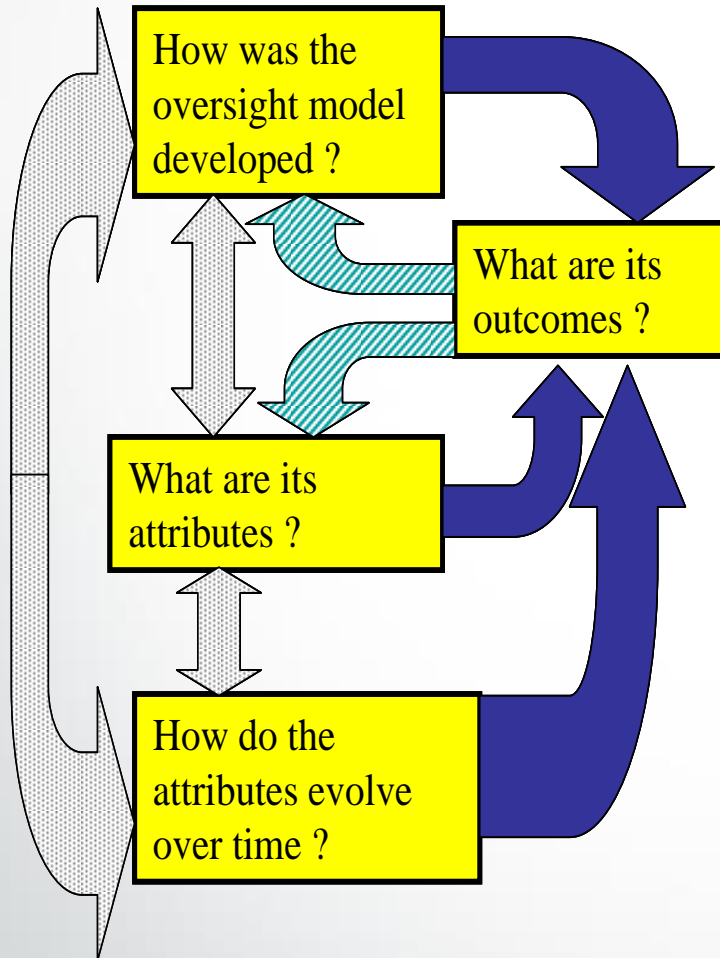


Integrated Oversight Assessment— A multi-criteria evaluation approach

Kuzma,, Paradise, et al Risk Analysis(2008)

Kuzma, et al. JLME (2009)

Kuzma et al. Policy & Socceity (2009)

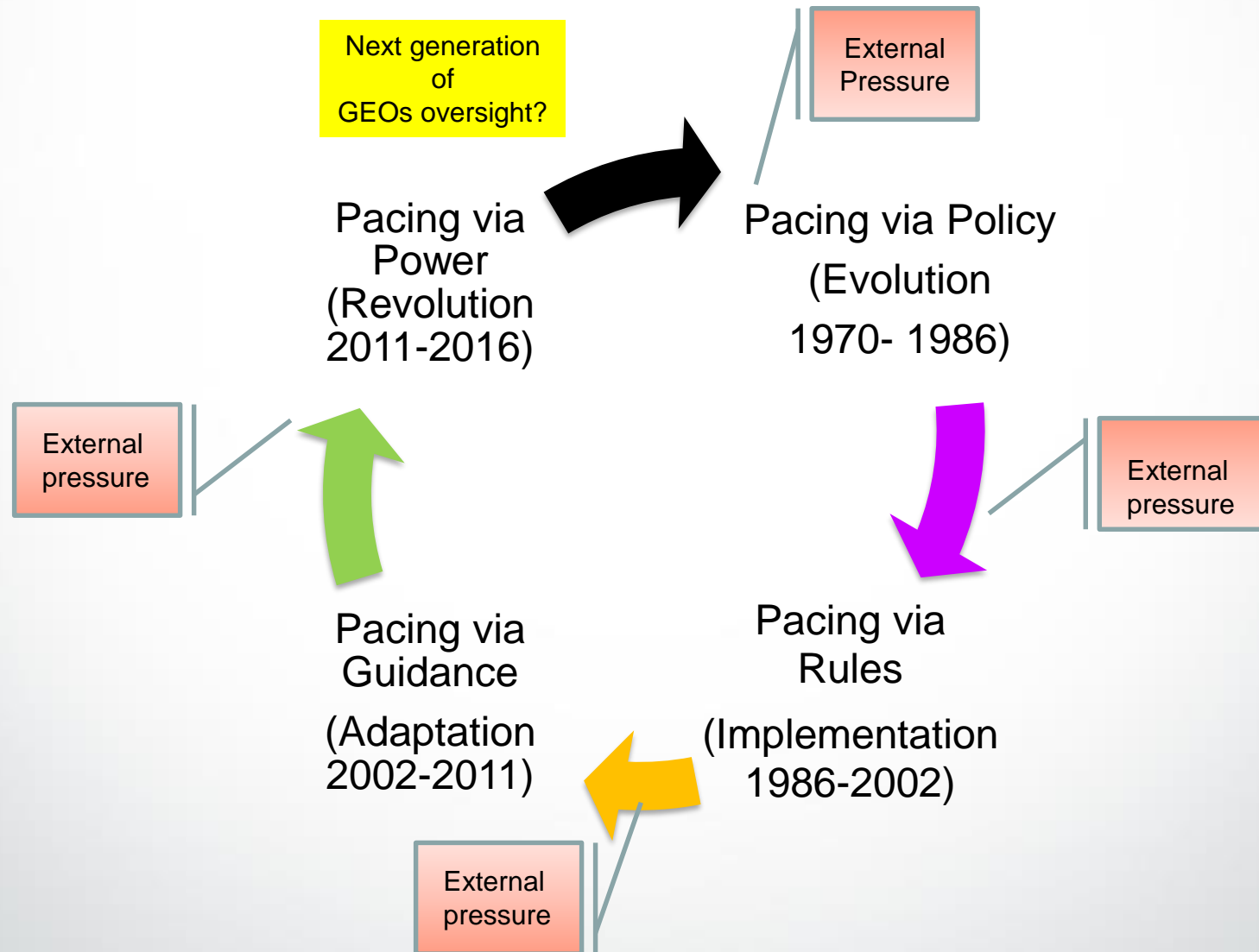


• Findings

- **Complex System of GEOs Governance:**
- **Normative, Empirical, and Institutional Criteria are Intertwined**

Cycle of oversight for GEOs

Conflict and Reaction



GMO Oversight: Coordinated Framework and Proper pacing?

(Kuzma et al JLME 2009)

- | | |
|---|---|
| <ul style="list-style-type: none">• High flexibility• Weak legal grounding allowing for multiple interpretations• Complex institutional structure | <ul style="list-style-type: none">• Little transparency• Low level of informed consent• Few opportunities for public input• Low capacity |
|---|---|

More controversy, delay, rejection?

Too much regulatory uncertainty for developers of new GM products?

Fundamental Issues and Challenges

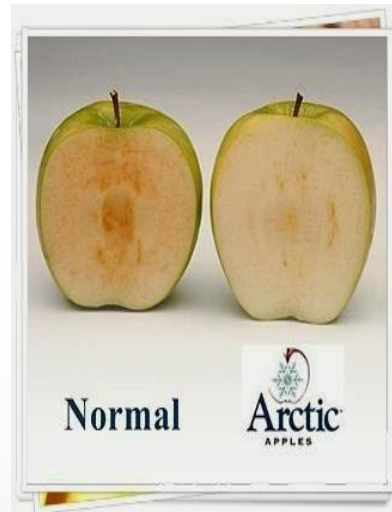
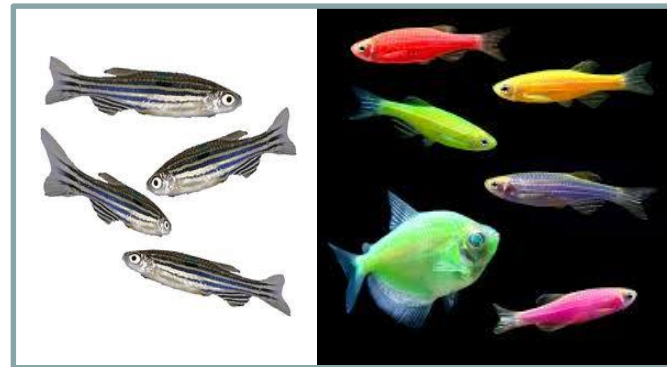
Issues

- Science is uncertain
- Sound science cannot tell society what to do
- Values are embedded in all types of assessment and regulatory policy
- Therefore, Who gets to decide? Whose values count?
- Industry and Govt. Scientists are not the only ones who should have a “voice”

Challenges

- **Technological Elitism**
 - (luddite shaming, deficit model, accusations of social apathy)
- **“Science Based” system in face of uncertainty/ambiguity**
 - leads to biased interpretations of evidence on all sides.
- **Sticking to the science**
 - marginalizes other world views, local and specialized knowledge
- **Creates distrust, skepticism**

2nd Generation Genetic Engineering



Evaluation of Risk Governance for GM insects as precursor to gene drive

Kuzma & Meghani, in prep *Buffalo Law Review*

Figure 2: Criteria for legitimate, appropriate, and accountable risk assessment processes

Humility

- Social foundations of vulnerability
- Distributive impacts
- Public input into framing
- Learning as object of deliberation

Reflexivity

- Examine assumptions & framing
- Acknowledge alternative explanations
- Reflect on quality of organizational processes
- Reflect on what error means to outcomes and reputation

Procedural Validity

- Assessing the quality of the process that led to the outcomes.
- Scientific validity of the approaches used
- Openness and transparency
- Consistency
- Use all available information including subjective probabilities
- Acceptability to those who provide inputs

Inclusion

- Engage new voices in discussion of ends and means of innovation

Anticipation

- Ask 'what if...?' consider contingency,-- what is known, plausible, possible, unknown



Hubris or Humility?

Jasanoff 2003

Technologies of Hubris

- Blindness toward ambiguity and uncertainty
- Claims of objectivity tend to hide values
- Predictive analysis pre-empts societal discussion
- Lack of capacity to deal with challenges outside of framing assumptions.
- Lack of not just knowledge to fill gaps, but also processes and methods to elicit what the public wants, and to use what is already known

Technologies of Humility

- Public input into **framing** problems and analysis
- Analyze social foundations of **vulnerability**
- Expose the **distributive** impacts of innovations upstream
- **Learning** as an object of citizen deliberation, collectively reflect on the ambiguity of experiences and alternative explanations.

Evaluation of Risk Analysis for Population Suppression as Precursor to Gene Drives

	FDA-Oxitec EA/FONSI	USDA- DBM EA/FONSI	CSIRO
Humility <ul style="list-style-type: none"> Social foundations of vulnerability Distributive impacts Public input into framing Learning as object of deliberation 	None	None	Some
Reflexivity <ul style="list-style-type: none"> Examine assumptions & framing Acknowledge alternative explanations Reflect on quality of organizational processes Reflect on meaning of errors to outcomes and reputations 	Minimal to none	Minimal to none	Minimal
Procedural Validity <ul style="list-style-type: none"> Assessing the quality of the process that led to the outcomes. Scientific validity of the approaches used Openness and transparency Consistency Use all available information including subjective probabilities Acceptability to those who provide inputs 	Minimal to none	Minimal to none	Moderate
Inclusion <ul style="list-style-type: none"> Engage new voices in discussion of ends and means of innovation 	None	None	Moderate
Anticipation <ul style="list-style-type: none"> Ask 'what if. . .?' consider contingency,-- what is known, plausible, possible, unknown 	Minimal	Minimal	Moderate

Conclusions

Gene drives as a “constitutional moment” in technology development

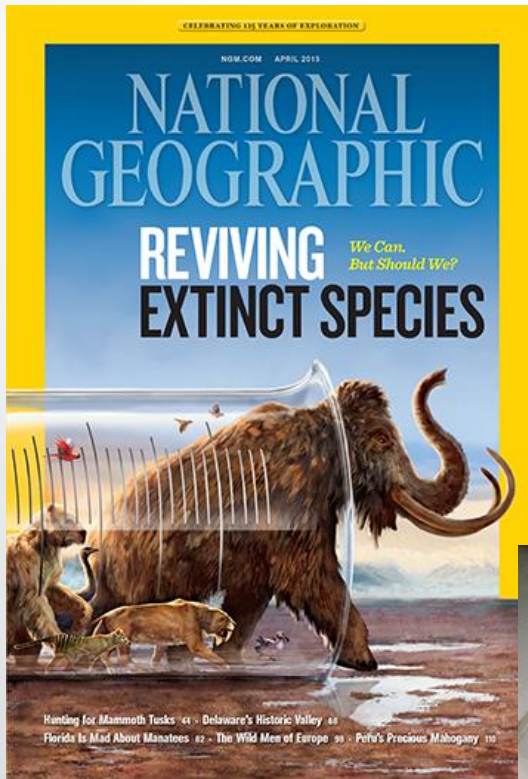
- **Problematic regulatory risk analysis process in a fundamental way**
 - SPREAD go against fundamental purpose of GEOs regulation of containment and confinement.
 - Without SPREAD cannot evaluate impacts
 - Little guidance on moving from near full confinement in lab to field trials (Phase 1 to 2 in NASEM report)—is that “release” or not
- **Serious deficiencies in the US regulatory assessment approach for GE insects that jeopardize legitimacy, procedural validity, and likely the acceptability**
 - “hubris” not humility
 - strong neoliberal orientation of Coordinated Framework and agencies

Recommendations

- **Pilot , and then formalize, “good governance” approaches, technologies of humility, and practices of responsible innovation in oversight system**
- **But first MUST address systemic and causal system issues**
 - Bias, worldview, power, and policy lock-in (funding, agency predispositions, etc.)
- **Engage just around the question of elitism, bias, power, and world view?**
 - must be honest
 - Reboot & dispense of arguments that obfuscate our world views in the name of “sound science’ or on the other hand the unreasonable expectation of “no risk”

3rd Generation

and beyond?



**I think I still have a dream?
BUT OH, the BARRIERS....**

Political Will

Policy Feedback and Power Effects

Bias against “Other Side”

Engage around those specifically?