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# Evaluating Oversight Systems for Emerging Technologies: A Case Study of Genetically Engineered Organisms

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U.S. approaches to oversight of research and technological products have developed over time in an effort to ensure safety to humans, animals, and the environment and to control use in a social context. In modern times, regulatory and oversight tools have evolved to include diverse approaches such as performance standards, tradable allowances, consultations between government and industry, and pre-market safety and efficacy reviews.<sup>1</sup> The decision whether to impose an oversight system, the oversight elements, the level of oversight (for example, federal, state, local), the choice of approach (for example, mandatory or voluntary), and its execution can profoundly affect technological development, individual and collective interests, and public confidence in technological products.<sup>2</sup> Oversight is conducted by a range of institutions with various capabilities, cultures, and motives.<sup>3</sup> Avenues for disputing oversight decisions are also important, and some argue that the U.S. operates in an adversarial regulatory culture in which Congress, the media, and stakeholders regularly contest the decisions of federal agencies.<sup>4</sup>

Currently, there is debate about oversight systems for the products of nanotechnology. Nanotechnology has been defined by the U.S. National Nanotechnology Initiative as the “understanding and control of matter at dimensions of roughly 1 to 100 nanometers, where unique phenomena enable novel applications.”<sup>5</sup> Nanotechnology involves a broad set of methods, products, and applications at a very small scale, about the size of several atoms or a biological molecule like a protein. Nanotechnology products are rapidly entering the marketplace, with over 1,000 currently catalogued.<sup>6</sup>

The primary goal of this paper is to derive hypotheses and evidence-based lessons for the oversight of nanotechnology. For this, we turned to the evaluation of oversight of another emerging technology with which we have experience: genetic engineering. Genetic engineering (GE) has parallels to nanotechnology in multiple ways. It is an enabling or foundational technology, like nanotechnology, which can be used for many applications such as medicine, food and agriculture, environmental ones, and the industrial production of compounds. Both technologies use

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a set of tools for manipulating matter at molecular levels. In the U.S., the products of genetic engineering come under the purview of multiple federal agencies and laws, just like the products of nanotechnology. Nanotechnology can be applied to food and agriculture, just like genetic engineering, and in some cases it converges with GE, as it can be used to modify or deliver genes to plants or animals.<sup>7</sup> Thus, oversight of genetically engineered organisms (GEOs) in food and agriculture is a relevant historical case study for informing the development of nanotechnology oversight broadly, as well as for informing oversight of nanoproducts used for GE or applied to food and agriculture. However, there are some differences between the two technologies, in that nanotechnology does not always involve the manipulation of biological matter, and it is sometimes conducted at an even smaller scale than GE, the atomic scale. Regardless, there are good reasons to believe that historical insights from GEOs oversight can be used to inform the debate about nanotechnology oversight.

### GEOs Oversight History

Genetic engineering has been used in the last 20 years to produce plants with desirable qualities, such as pest and disease resistance and enhanced processing characteristics, and for faster production of these crops in comparison to the use of conventional plant breeding techniques. In the past decade, genetically engineered (aka GE or biotech) crops have permeated markets across the world. In 2007, 23 countries grew biotech crops: 12 developing countries and 11 developed countries.<sup>8</sup> Herbicide tolerance (Ht) and insect resistance (IR) are the prominent traits in GE crops grown world wide. In 2007 approximately 90 percent of soybeans acres in the United States were planted with Ht GE soybean; 45 percent of maize acres with IR or Ht GE maize; and 65 percent of cotton acres with Ht GE cotton.<sup>9</sup>

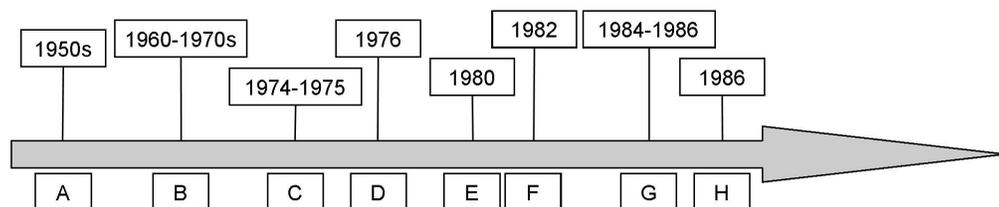
GEOs have been formally overseen by the U.S. government for about three decades. Three stages of U.S. GEOs oversight can be identified from the literature: development, implementation, and adaptation (Figure 1). The development phase began with the Asilomar conference<sup>10</sup> and the involvement of National

Figure 1

### Timeline for GEOs Oversight in the U.S.

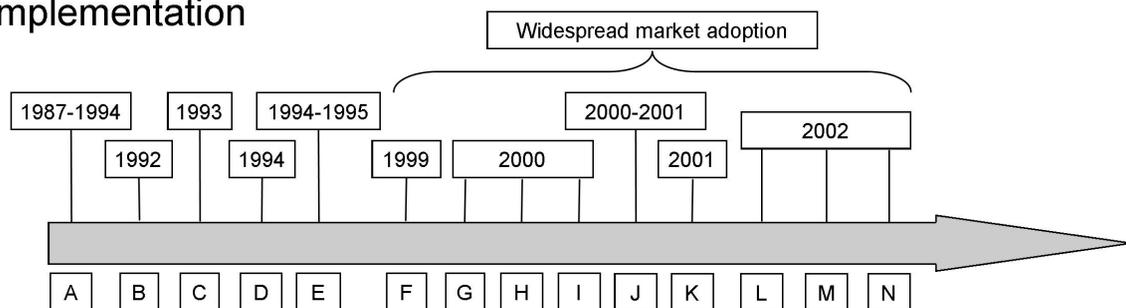
Three phases were identified in the timeline for GEOs oversight: a) evolution, b) implementation, and c) adaptation.

## Evolution



- **A:** (1950s) The structure of DNA was discovered.
- **B:** (1960s-70s) Scientists develop recombinant DNA techniques and eventually are able to synthesize and replicate genes resulting in the ability to produce human growth hormone.
- **C:** (1974-75) The leading genetic scientists convene at the Asilomar meeting and encourage the U.S. Govt. to develop guidelines for regulating experimentation concerning recombinant DNA.
- **D:** (1976) U.S. Govt. sets up the Recombinant DNA Advisory Committee (RAC) through the National Institutes of Health (NIH 1978).
- **E:** (1980) Laboratory applications (such as the development of a gene-synthesizing machine) and industrial applications (such as Exxon's oil-eating microorganism) were emerging.
- **F:** (1982) RAC reviews its 1st proposed environmental release – the introduction of "ice minus" bacterium during the process of field trials.
- **G:** (1984-86) Legal controversy emerges involving the "ice minus" bacterium and its release into the environment (USC 1983).
- **H:** (1986) The Office of Science and Technology Policy (OSTP) forms a working group, called the Biotechnology Safety Coordinating Committee (BSCC), and develops a three agency jurisdictional model known as the Coordinated Framework for the Regulation of Biotechnology (CFRB).

Figure I (continued)

**Timeline for GEOs Oversight in the U.S.****Implementation**

- **A:** (1987-1994) USDA, FDA, and EPA interpret existing laws (such as the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), the Toxic Substance Control Act (TSCA), and the Federal Plant Pest Act (FPPA)) and promulgates regulations and policies concerning GEOs.
- **B:** (1992) FDA issues novel foods policy, which states that foods derived from new plant varieties do not substantially differ from conventional counterparts.
- **C:** (1993) USDA issues regulatory guidelines for how a plant would become commercialized, or brought to the market.
- **D:** (1994) EPA develops rules for plant incorporated protectants (PIPs).
- **E:** (1994-95) The first commercial GEO products, such as the Flavr Savr tomato, emerge on the market.
- **F:** (1999) A study raises concerns about possible negative effects of Bt corn on Monarch butterflies, however, subsequent field research has shown little possibility of harm.
- **G:** (2000) StarLink, a form of Bt corn that could cause allergic reactions in small numbers of people and is therefore not allowed in the food supply, is found in food supply causing recalls of some food and controversy over biotechnology regulation.
- **H:** (2000) EPA conducts meeting of its Scientific Advisory Panel (SAP) and considers re-registering Bt corn.
- **I:** (2000) The National Research Council (NRC) publishes a report on EPA's review of pest-protected GE plants (NRC 2000). FDA asks for comments on a mandatory pre-market safety review of GE foods.
- **J:** (2000-01) The Office of Science and Technology Policy (OSTP) and the Council on Environmental Quality (CEQ) conduct 6 case studies on the federal regulation of agricultural biotechnology for emerging products.
- **K:** (2001) The FDA publishes draft labeling guidance for companies that wish to label their foods as containing, or not containing, genetically modified ingredients and for making the agency's review process mandatory (FDA 2001). The process is still not mandatory (2009).
- **L:** (2001) The EPA publishes its finalized rules for the regulation of PIPs.
- **M:** (2002) The NRC publishes a report stating that the USDA should more rigorously review the potential environmental effects that transgenic plants may cause before approval for commercial use (NRC 2002).
- **N:** (2002) Prodigene Inc. was fined for tainting soybeans in Nebraska with experimental corn used for producing human vaccines.

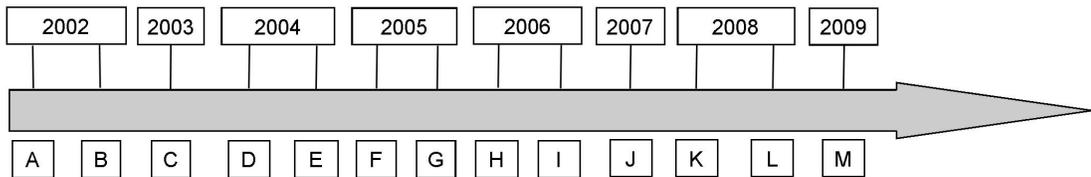
Institutes of Health (NIH) Recombinant DNA Advisory Committee (RAC) for oversight of laboratory experiments involving GEOs.<sup>11</sup> NIH RAC still governs the use of GEOs in the laboratory, and this point of oversight is the focus of the gene therapy case study in this symposium. Likewise, laboratory oversight of nanomaterials would occur through the Occupational Safety and Health Administration (OSHA), which is the focus of the chemicals in the workplace case study in this symposium.

This paper focuses on oversight for approval of GEOs through the Coordinated Framework for the Regulation of Biotechnology (CFRB).<sup>12</sup> The CFRB was formulated in 1986 in the final stages of the development phase in Figure 1a (H) and designed for the regulation of environmental release and use of GEOs outside of the laboratory. CFRB instructed three federal agencies — the U.S. Environmental Protection Agency

(EPA), the U.S. Food and Drug Administration (FDA), and the U.S. Department of Agriculture (USDA) — to use the Toxic Substances Control Act (TSCA), Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), Federal Food Drug and Cosmetic Act (FFDCA), and the Federal Plant Pest Act (FPPA) to regulate the products of biotechnology and GEOs. The framework relied on the policies that the “product not process” should be the focus of regulation and no new laws were needed to cover GEOs and products from them. The political will to adopt this framework stemmed in part from controversies, court cases, and congressional hearings about the proposed release of a GEO, the “ice minus” bacterium, into the environment.<sup>13</sup>

Twenty years later this framework is still operational, although it has evolved over time, particularly in the most recent phase of adaptation (Figure 1b&c). In the CFRB, the boundaries of various statutes were signifi-

Figure 1 (continued)

**Timeline for GEOs Oversight in the U.S.****Adaptation**

- **A:** (2002) OSTP publishes a notice in the Federal Register proposing actions to update field test requirements for industrial plants, although it concerns mainly harvesting and extraction.
- **B:** (2002) Government Accounting Office calls for enhancement of FDA's voluntary evaluation process for GE foods.
- **C:** (2003) USDA introduces enhanced safety guidelines—including more stringent confinement measures for field trials of pharmaceutical and industrial GE plants—creating the permitting process interim rule.
- **D:** (2004) The NRC and the Institute of Medicine (IOM) publishes a report about the unintended consequences of GE foods in which they recommend that greater scrutiny be given to foods containing new compounds (NRC/IOM 2004).
- **E:** (2004) The FDA issues draft guidance for industry regarding the Early Food Safety Evaluation of new non-pesticidal proteins produced by new plant varieties intended for food use (FDA 2004).
- **F:** (2005) USDA introduces finalized safety guidelines for field trials on industrial and pharmaceutical GE plants—creating the permitting process Final rule.
- **G:** (2005) Syngenta's Bt-10 corn is found in food supply, however FDA deems it no risk and therefore not illegal (although planting Bt-10 corn in the U.S. is illegal). Field trials of Ht Creeping Bentgrass contaminate wild grass varieties in Oregon.
- **H:** (2006) FDA finalizes its guidelines to industry regarding Early Food Safety Evaluation.
- **I:** (2006) Bayer notifies FDA and USDA that trace amounts of LLRICE601 (a form of Ht rice) has been detected in commercial rice varieties and may have entered the food supply. The USDA then determines that LLRICE601 does not pose a threat based on available data (provided by Bayer) and deregulates it.
- **J:** (2007) The Animal Plant Health Inspection Service (APHIS) publishes its first Environmental Impact Statement (EIS) in compliance with the National Environmental Protection Act (NEPA) concerning its regulation of GEOs. This occurred partially in response to lawsuits challenging USDA for improperly regulating GE plants.
- **K:** (2008) Currently, there is still uncertainty about how GE animals, insects and bio-industrial or pharmaceutical crops will be regulated.
- **L:** (2008) Unapproved GE corn seed inadvertently sold to farmers by Dow Agrosiences affiliate Mycogen Seeds (Reuters 2008).
- **M:** (2009) USDA proposes revisions to its rule for GEOs under the FPPA, sparking thousands of public comments.

cantly stretched to promulgate agency regulations for diverse products. Genetically engineered (GE) plants are regulated as “plant pests” under FPPA, because they often contained engineered sequences from viruses and bacteria that cause plant disease and can be considered plant pests in themselves.<sup>14</sup> GE plants engineered with pesticidal-like proteins are regulated under FIFRA and FFDCAs as pesticides (plant-incorporated-protectants) by the EPA.<sup>15</sup> GE microorganisms are regulated as “toxic chemicals” under TSCA.<sup>16</sup> GE or bioengineered foods are reviewed under FFDCAs by the FDA through a voluntary consultation mechanism.<sup>17</sup> Genetically engineered animals are likely to come under consideration by the FDA as “investigational new animal drugs.”<sup>18</sup>

Although the laws and their interpretations have largely remained the same since GE crops were first commercialized in 1996, several guidance documents

and regulatory policies have been published to adapt to emerging GE products over time (Figure 1). These adaptations were in part prompted by public and stakeholder reactions to new risk information or perceived failures of the system. To this day, several interest groups are opposed to the Coordinated Framework approach and believe that new and focused policies and laws are needed to fully cover the risks and societal impacts associated with GEOs and their products. Some argue that biotechnology is a “process” that presents new risks and requires special regulation, running counter to the U.S. policy of focusing on products being the “same in kind” as those that are bred by conventional means or mutagenesis.<sup>19</sup> The current regulatory system is reviewed in detail by Alan McHughen and Stuart Smyth.<sup>20</sup> These authors detail laws and agencies involved and current controversies over the adequacy of GE crop regulation. In the past few years,

several court challenges have been made by NGOs. In 2007, USDA's Animal Plant Health Inspection Service (APHIS) lost two district court cases for inadequate data to support its decision to allow deregulation of GE alfalfa and for ignoring evidence of environmental harm in field trials of GE bentgrass.<sup>21</sup>

Debates about the oversight of GEOs in food and agriculture (also known as agricultural biotechnology oversight) have operated in an adversarial culture<sup>22</sup> and controversy has been periodically fueled by mishaps in the system (Figure 1). Some believe that a lack of clear consumer benefits from the initial phase of developing GE products has led to rejection of the technology; however, U.S. citizens are either largely unaware or fairly neutral in their thinking about GEOs.<sup>23</sup> In the European Union (EU), on the other hand, there has been greater public and stakeholder resistance. The U.S. and EU were involved in a protracted WTO dispute over the EU's de facto moratorium on importing GE products from the U.S. from 1998 to 2004.<sup>24</sup> It has been estimated that U.S. farmers lost \$200 million per year in trade during the moratorium on several U.S. GE crop varieties. The EU regulatory documents cite a more precautionary approach to oversight, including mandatory product labeling above a threshold of 0.9 percent GE ingredients. The U.S. does not have a mandatory labeling policy, although products can be voluntarily labeled as containing or not containing GE ingredients.

In more recent times, concerns over cross-contamination issues have been prominent. For example, herbicide tolerant (Ht) genes from creeping bentgrass in field trials have shown potential to migrate into natural grasslands in Oregon, unapproved Ht rice varieties were discovered in the human food supply, and GE pigs from research labs entered the human food supply without regulatory approval (Figure 1c). Safety issues surrounding agricultural biotechnology include engineered genes introgressing into and impacting wild relatives (for example, Bt gene introgressing into native maize in Mexico), adverse effects from GEOs on nontarget species in the environment (for example, concerns in 1999-2001 about Bt pollen from corn killing monarch butterfly larvae), and changes in the levels of toxicants or allergens in food due to introduced genes (for example, *cry 9C* gene and protein with similarities to human allergens in Starlink corn entering the human food supply without approval).<sup>25</sup> Broader impacts of GE crops include those on the sustainability of ecosystems (for example, reduced or increased use of water or pesticides), economies, markets, research and innovation, and social and cultural systems. Ethical issues are also prominent in the development and

application of GEOs, including the rights to know and choose products (autonomy), the distribution of the risks and benefits (justice and equity), and the opportunities to object to the technology on moral grounds (intrinsic).<sup>26</sup>

Oversight is broader than formal government regulation,<sup>27</sup> and the social, ethical, regulatory, and scientific issues intersect in GEOs oversight in a variety of ways.<sup>28</sup> Multiplicity of types of issues and their intricate relationships suggest the need for multi- and interdisciplinary assessments of oversight systems. However, analysis of oversight systems has historically been conducted through one or a few perspectives using a small set of evaluation criteria.<sup>29</sup> Criteria used by the federal government are primarily limited to human and animal safety, environmental risks, and costs and benefits, as mandated by presidential executive orders and various statutes.<sup>30</sup> Recent reviews of the oversight system for GEOs in food and agriculture have considered the breadth of federal statutes and agencies, as well as the ability of the system to cover significant potential human health and environmental risks.<sup>31</sup> Historical narratives of GEOs oversight from social and cultural perspectives have also been published.<sup>32</sup> Ethicists have reviewed dimensions of oversight for GEOs.<sup>33</sup> Despite the examination of oversight programs and policies by scholars from several different fields, few comprehensive evaluations exist, and there is no consensus on what constitutes "good oversight," how to measure it, or how it changes with the nature and context of what is overseen.

Policy analysis approaches are a way to integrate a diversity of perspectives through the use of several types of criteria and different forms of evidence.<sup>34</sup> Yet, they are seldom used in the formal evaluation of oversight for emerging technologies. Technologies affect multiple stakeholders with various viewpoints, values, and concerns, which make legal, economic, ethical, social, scientific, and safety criteria all relevant to assessing oversight for them. Some stakeholders are most concerned about economic impacts or job opportunities that result or are lost with technological adoption. Others care primarily about the health and environmental impacts of new products. Most consumers value parameters that affect their daily life, such as improved health, lower costs, better local environments, convenience, and quality. Government regulators focus on health risks, costs, and benefits.<sup>35</sup> Barry Bozeman and Daniel Sarewitz (2005)<sup>36</sup> discuss the pervasive use of "market valuation" and judgments about science and technology based upon avoiding "market failures." However, they urge that "public failures" of science and technology are equally impor-

tant and can occur with or without market failures. Public failure can stem from many factors, including inadequate congruence with public values and short time horizons.<sup>37</sup> Incorporating several criteria into the analysis of oversight helps to address both public values and private marketing goals. From a global perspective, there are emerging concerns that risks and benefits of technological products be fairly distributed within and among nations.<sup>38</sup> From an ethical perspective, emerging technologies may fundamentally conflict with moral principles, and questions arise as to whether the oversight process respects these values.<sup>39</sup> Although not every group or individual viewpoint can be accommodated in an oversight system, in a democracy such as the United States, an oversight system should respond to a range of viewpoints, values, and concerns.<sup>40</sup>

In this study, we use an integrated, multi- and mixed methodological approach to address three goals: (1) the development of methodology for evaluating oversight systems from multi- and interdisciplinary perspectives; (2) the formal evaluation of the U.S.'s GEOs oversight system using several lines of evidence and multiple disciplinary perspectives; and (3) the derivation of lessons for the oversight of nanotechnology. Nanotechnology involves the manipulation of matter and a broad set of methods, products, and applications at a very small scale, about the size of several atoms or a biological molecule like a protein. Its products are rapidly entering the marketplace, and there is currently debate about oversight systems for nanotechnology products.

We set out to evaluate the oversight system for GEOs by using multiple types of criteria which span several societal impacts and values. We use qualitative and quantitative methods, including expert elicitation, semi-structured expert and stakeholder interviews, and analysis of literature relating to the history of GEOs oversight in a triangulation approach representing a variety of data, methods, and theories.<sup>41</sup> Different types of data are related to strengthen the development of theories and conclusions and overcome the shortcomings of each individual approach.<sup>42</sup> We also include normative analyses based on ethical principles. Our process largely follows a policy analysis approach, in which a problem is noted (that is, the need to develop effective oversight for emerging technologies such as nanotechnology and biotechnology); criteria are derived for description and evaluation; evidence is gathered; outcomes are examined; and conclusions about oversight policy options are reached. In this case, we analyze U.S. oversight for GEOs in agriculture and food for the past 30 years to identify strengths and weaknesses of the system and

develop hypotheses for important elements of technology oversight.

In our previous work, we devised descriptive and evaluative criteria for oversight assessment through multiple methods including review of the relevant legal, public policy, and ethics literature; group consensus; and quantitative expert and stakeholder elicitation.<sup>43</sup> The approach was based in part upon multi-criteria decision analysis (MCDA). MCDA relies on the notion that no single outcome metric can capture the appropriateness or effectiveness of a system, allows for integrating heterogeneous information, and enables incorporation of expert and stakeholder judgments.<sup>44</sup> MCDA refers to a range of approaches in which multiple criteria are developed, ranked, and used to compare alternatives for decision making.<sup>45</sup> In this sense, it is related to policy analysis. General categories of criteria for evaluating policies or decisions have been described, such as utility-based criteria (focusing on cost, risk-benefit comparison, or outcomes), rights-based criteria (focusing on whether people have consented to risk and their rights are being respected), and best available technology-based criteria (focusing on using the best technologies available to reduce risk to the extent possible with them).<sup>46</sup> From our previous work, a set of 28 criteria to evaluate oversight was chosen from an initial list of 66.<sup>47</sup>

In this study, we apply this set of 28 criteria to GEOs oversight in the U.S. in order to test our methodology, evaluate GEOs oversight, and derive lessons for the oversight of other emerging technologies, particularly nanotechnology. We blend literature analysis, expert and stakeholder interview data, and expert elicitation to strive for a holistic picture of how the oversight system for GEOs has performed in society. This type of analytical approach has been suggested in order to school the development of nanotechnology oversight.<sup>48</sup> It can be instructive for assessment of specific oversight systems, and for developing hypotheses more broadly about how certain features of oversight systems and policies affect outcomes that are important to society. Ultimately, we hope our work contributes to a better understanding of how to both evaluate oversight from multiple perspectives and formulate good policies and systems for overseeing emerging technologies.

## Methodology

### *Context and Previous Work*

The criteria used for the expert elicitation in this study are based on a previous study by Jennifer Kuzma et al. (2008)<sup>49</sup> as discussed above. They were initially derived from an extensive search of literature on oversight evaluation and reduced by expert elicitation and consensus processes from a total of 66 to 28. The

final 28 criteria (see Table 1 and the “Generic Expert Elicitation Survey, Appendix A” in J. Paradise et al.’s article in this symposium) are ones that a majority of experts rated highly for evaluating oversight systems for emerging technologies (over 70 percent of experts rated the importance of these criteria over 70 on a scale from 1-100). The 28 criteria are grouped into 4 categories relating to how oversight systems develop (development criteria), operate (attribute criteria), change over time (evolution criteria), and impact society (outcome criteria) (Figure 2). This evaluation of GEOs oversight is part of a larger effort to evaluate possible oversight models for nanotechnology. These criteria are applied to other historical oversight systems in this symposium, including gene therapy, workplace chem-

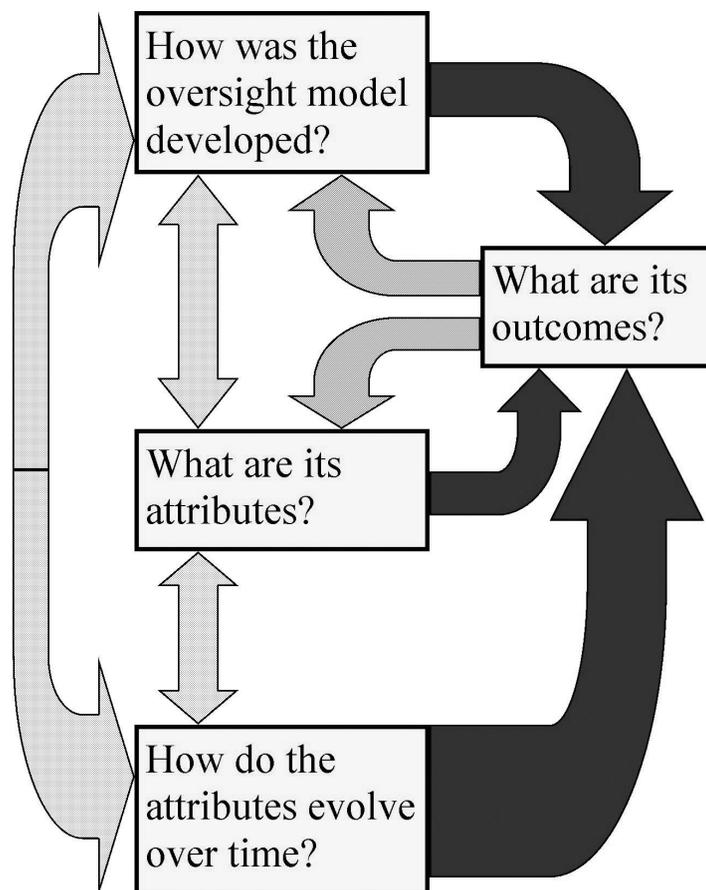
icals, drugs, and devices. Through a comparative case study approach<sup>50</sup> among these five oversight systems, hypotheses generated from the work in this paper can be tested.

A systems analysis approach was taken to explore relationships among criteria in the four categories (Figure 2, Table1). Systems analysis is useful in cases where mental models (that is, people’s understandings of systems) are crucial for analysis given high degrees of complexity, limited empirical information, and multiple types of parameters.<sup>51</sup> It has been suggested that effective methods for learning about complex, dynamic systems include elicitation of participants in the system for their perceptions, creation of maps of

Figure 2

### Developing Dynamic Hypotheses about Oversight Systems

Criteria were placed into categories of development, attributes, or outcomes of oversight systems, as well as how systems change over time. Solid arrows indicate relationships in which outcome criteria are the dependent variables and used for evaluating oversight systems. Dotted arrows indicate relationships between other categories of criteria, which may include independent or dependent variables and evaluative or descriptive criteria. Striped arrows indicate feedback from outcomes into features of oversight systems, and in these cases, outcomes impact dependent variables in other categories of criteria.



the feedback structure of a system from those perceptions, and stronger group processes.<sup>52</sup>

In this paper, we initially consider outcomes that are widely agreed upon as results of good oversight as key dependent variables and evaluative criteria (that is, the five outcome criteria of public confidence, justly distributed health impacts, positive environmental impacts, health and safety, and increased research and innovation). A central question of our approach

to assessing GEOs oversight is whether criteria in the attributes, evolution, and development categories (initially considered as independent variables) positively or negatively impact key outcome criteria (initially the dependent variables) (Figure 2, solid arrows). For example, the literature suggests that transparency in development or operation of oversight systems promotes public confidence<sup>53</sup> (Table 1, O24). In this case, transparency would be considered the independent or

Figure 3

### Summary of Expert Scores on Criteria and Levels of Agreement

Data from the expert elicitation survey is summarized by mean, median, and standard deviation. SD=Standard deviation, N=number of experts rating that criterion, n=number of experts who rated that criterion within the range of scores indicated. Qualitative assessment of agreement was obtained by viewing the distribution of scores: L=low agreement, M=moderate agreement, H=high agreement.

	Mean	Median	SD	N	n	n	n	Qual. Assessment
					1 to 39	40 to 59	60 to 100	Visual
<b>Development</b>								
D1. Impetus	52	50	34	17	5	4	8	L
D2. Clarity of technological subject matter	69	70	19	17	1	2	14	H
D3. Legal grounding	39	30	24	17	9	3	5	M
D4. Public input	46	50	27	17	6	6	5	L
D5. Transparency	34	30	23	16	10	3	3	H
D6. Financial resources	38	35	26	14	7	4	3	M
D7. Empirical basis	45	45	26	17	6	6	5	L
<b>Attributes</b>								
A8. Legal grounding	45	40	23	16	6	4	6	L
A9. Data requirements and stringency	53	50	28	17	5	4	8	L
A10. Post market monitoring	27	20	23	17	13	1	3	H
A11. Treatment of uncertainty	43	40	30	15	6	3	6	L
A12. Empirical basis	57	50	25	17	4	5	8	M
A13. Compliance and enforcement	47	40	29	17	7	5	5	L
A14. Incentives	53	45	30	17	7	3	7	L
A15. Treatment of intellectual property	37	33	26	16	9	2	5	M
A16. Institutional structure	77	80	24	17	2	0	15	H
A17. Flexibility	62	70	19	17	1	6	10	H
A18. Capacity	37	30	23	17	11	2	4	H
A19. Public input	40	35	27	17	9	3	5	M
A20. Transparency	41	35	26	17	9	2	6	M
A21. Conflict of interest	37	35	29	16	8	4	4	M
A22. Informed consent	26	20	24	17	12	3	2	H
<b>Evolution</b>								
E23. Extent of change	47	40	24	17	6	5	6	L
<b>Outcomes</b>								
O24. Public confidence	54	50	25	17	3	6	8	M
O25. Research and innovation	55	50	21	17	3	7	7	M
O26. Health and safety	61	60	28	17	2	6	9	M
O27. Distributional health impacts	58	60	31	15	4	2	9	L
O28. Environmental impacts	61	65	30	16	3	3	10	M

descriptive variable and public confidence the dependent or evaluative one.

Other relationships among criteria can be explored with our approach. Several attributes and development criteria are normatively considered good features of oversight, and these can be used on their own to judge an oversight system. Transparency is thought to be a good feature of oversight (Figure 3 and Table 1, D5 & A20) in that it promotes ethical principles of autonomy and “rights to know.”<sup>54</sup> Regarded this way, transparency is an evaluative and independent criterion. Yet, other criteria in development or attributes categories, such as institutional structure (A16), can impact transparency, making transparency a dependent and evaluative variable (Figure 2, dotted arrows). Furthermore, with feedback, transparency could become a dependent and evaluative variable based

upon an outcome criterion (Figure 2, striped arrows). Therefore, transparency can be placed into multiple categories depending on the relationship being explored. As such, we did not place all criteria into categories of “evaluative” versus “descriptive” or “independent” versus “dependent” variables at the onset of our evaluation of GEOs oversight. We focus instead on criteria that impact outcomes or are considered defensible based on ethical principles. More complex relationships may be discovered after these criteria and our approach are applied to many historical models.

#### *Expert Elicitation*

Expert elicitation is an evidence gathering methodology in the face of high uncertainty and little information.<sup>55</sup> We set out to gather information and opinion about GEOs oversight from experts and stakeholders

Table 1

#### **Criteria for Expert Elicitation**

Experts were asked, on a scale of 1 to 100 (see details in Appendix 2), to evaluate how they believed the U.S. GEOs oversight system performs with regard to or reflects that criteria. (See also Appendix A in J. Paradise et al. in this symposium.)

#	Criteria	Low (1)	High (100)
D1	Impetus	Reactive	Proactive
D2	Clarity of Technological Subject Matter	Not clear	Clear
D3	Legal Grounding	Weak	Strong
D4	Public Input	Minimal	Significant
D5	Transparency	Low	High
D6	Financial Resources	Not at all	Sufficient
D7	Empirical Basis	Weak basis	Strong basis
A8	Legal Grounding	Weak	Strong
A9	Data Requirements and Stringency	Weak	Strong
A10	Post-market Monitoring	Little	Extensive
A11	Treatment of Uncertainty	Limited	Extensive
A12	Empirical Basis	Weak basis	Strong basis
A13	Compliance and Enforcement	Weak	Strong
A14	Incentives	Few	Many
A15	Treatment of Intellectual Property	Closed	Open
A16	Institutional Structure	Simple	Complex
A17	Flexibility	Low	High
A18	Capacity	Inadequate	Adequate
A19	Public Input	Minimal	Significant
A20	Transparency	Low	High
A21	Conflict of Interest	Prominent	Avoided
A22	Informed Consent	Little	Extensive
E23	Extent of Change	None	Extensive
O24	Public Confidence	Low	High
O25	Research and Innovation	Negative	Positive
O26	Health and Safety	Negative	Positive
O27	Distributional Health Impacts	Inequitable	Equitable
O28	Environmental Impacts	Negative	Positive

and ask them to evaluate the oversight system with respect to the set of 28 criteria. One of the greatest challenges of expert elicitation is determining an appropriate set of experts for participation. A list of experts was generated from extensive literature searches, the authors' knowledge of the U.S. GEO oversight system, media reports, government contacts, and national reports. Purposive sampling,<sup>56</sup> relying on the authors' specialized knowledge of GEOs oversight, was used to identify categories of experts. Experts were categorized according to affiliations, terminal degrees obtained, perspectives, biases, and expertise. The list contained over 50 people who have dealt with the oversight system for GEOs or study agricultural biotechnology and fit the definition of expert. These include substantive contributions to the scientific or technical literature,<sup>57</sup> status in the scientific community, membership on editorial committees of key journals,<sup>58</sup> membership on advisory boards, or peer nomination.<sup>59</sup> The experts were chosen based upon their knowledge; prominence in the literature, debates, and other studies on oversight for agricultural biotechnology; or their key roles as actors in agencies, think-tanks, non-governmental agencies, and industry during the formation and execution of the GEOs oversight in the U.S. Many of the chosen experts are also key representatives of stakeholder groups. Fundamentally, all experts could be considered members of stakeholder groups; for example, most academic experts are members in professional societies and make up the stakeholder group of "researchers." Similarly, stakeholders have specialized expertise in their area; for example, consumer group representatives have expertise in consumer viewpoints and concerns. Thus, there is not a clear distinction between experts and stakeholders in either direction.

Experts were sent a description of the project, and a survey instrument asking them to rate how, on a scale of 1 to 100, the oversight system for GEOs performed with regard to each of the 28 criteria (Table 1). A definition and example were provided to help them interpret the criteria (see "Genetically Engineered Organisms Expert Elicitation Survey Instrument," available online). They were assured that no individual responses would be attributed to them and that their individual participation would remain confidential, although their type of affiliation and expertise area would be listed with the data. A total of 17 responses (approximately a 33 percent response rate) were obtained from most categories of expertise and affiliation, with the exception of farming and trade organizations (Table 2). Following completion of the survey instrument, the experts were asked if they were willing to be interviewed by the authors. Eleven experts

agreed to be interviewed over the phone. Interviews were conducted using a semi-standardized interview approach,<sup>60</sup> which focused on the following general questions, although conversations were allowed to diverge from these questions:

- How generally did the criteria survey capture your experiences with oversight for genetically engineered organisms?
- How did the development and the characteristics of the GEO oversight system affect outcomes such as: consumer/public confidence, health and environmental effects, or innovation and economic development?
- Any other comments on GEO oversight? (If no response, then we asked about the strengths and weaknesses of the oversight system or other follow-up questions.)
- With respect to oversight in general, describe the features that you think are the greatest predictors of effects or outcomes?
- Please explain the most important lessons from the history of the GEO oversight system for the oversight of nanotechnology products (recognizing nanotechnology products will fall into many categories of products)?
- Any other comments on nanotechnology oversight?

Interviewees were also encouraged to share stories about their interactions with the GEO oversight system. Data collection took place over the period of five months in summer to fall 2007. Experts were asked to consider the GEOs system as a whole, over time, and not within a particular time period. Interviews typically took 30-45 minutes. Notes were taken during the interviews, which captured the essence of the interviewees' statements as well as verbatim quotes. The interviews were not audio-recorded to encourage more candid conversation given the sensitivity of the subject and the prominence of the experts and stakeholders interviewed. Appendix 1 depicts statements given by the interviewees in their own words.

#### *Data Analysis*

Quantitative criteria survey data were analyzed using Excel (Microsoft) and @Risk (Pallisade Corp). Excel was used for most basic calculations, and @Risk (Pallisade Corp) and Excel were used to generate distributions of expert scores. Expert data was not standardized (that is, normalized to account for systematic differences in rating by different experts) because we did not want to lose the diversity of opinion among experts and stakeholders, which we felt was essential

to capture the experience and controversy with GEOs oversight, as well as to shed light on potential biases in the oversight system (that is, are particular stakeholder groups more satisfied with GEOs oversight?).

Statistical analysis of the data was performed using a program written in Matlab 7.0. For each criterion, the mean and median scores, standard deviation and number of responses (n) were determined, and a 10-bin histogram was created. Within each bin of the histograms responses were analyzed according to expert affiliation

Pearson correlation coefficients (r) between each pair of criteria were calculated using the intrinsic Matlab function "corrcoef." This function takes an input matrix X (the matrix of data) and returns a square matrix R in which each entry is a correlation coefficient between 2 criteria. The equation for r is shown below, where  $\sigma$  represents the standard deviation, and  $C(i,j)$  is the element of the covariance matrix (C) located at the intersection of row  $i$  and column  $j$  of the matrix.

$$R(i, j) = \frac{C(i, j)}{\sqrt{C(i, i)C(j, j)}} = \frac{C(i, j)}{\sigma_i \sigma_j}$$

A correlation coefficient cutoff of  $r=0.7$  or, equivalently a product moment of  $r^2=0.49$ , was initially chosen as a minimum for determining significant correlations. Influence diagrams were then constructed showing links between significant pairs of criteria, with the size of the double-headed arrow indicating the strength of the correlation. The "corrcoef" function was also used to return a matrix of p values, indicating the probability of getting by random chance a correlation as large as that observed. Data was exported into an Excel spreadsheet for further analysis.

Qualitative data from the interviews were analyzed with the help of the content analysis software QSR's NVivo7. Notes from the interviews were read first and then coded using the software. The coding scheme was based on concepts as units.<sup>61</sup> The concepts are related to the criteria and oversight literature. The codes, also called nodes, were divided into two types: free nodes and tree nodes. Free nodes did not easily fit into a hierarchical structure. Tree nodes were organized in a hierarchical structure, moving from the general umbrella category (the parent node) to more specific categories (child nodes). Once the coding scheme was developed, the interviews were searched to identify occurrences of each node. The results were coded if a particular node was directly quoted in the interview notes, or if the interview response referred to the concept of the node but did not quote it verbatim. If a reference was coded to a tree node but did not apply to a specific child node, it was coded to the parent node of

that tree. The coding results are summarized in Figure 7 (see discussion below), which shows the number of references occurring for each node.

#### *Literature Searches*

Comprehensive literature searches were conducted to obtain information on the performance of the oversight system for GEOs, its impacts on research and innovation, and public perceptions of and confidence in it. Google Scholar, PubMed, Agricola, government websites, and web-based Google were initial points of searches which subsequently led in many different directions. Search terms included combinations of "oversight," "biotechnology," "genetic engineering," "genetically engineered," "regulation," "public confidence," "trust," "public perception," and "policy" among others. Searches on particular topics were stopped when the same articles emerged several times. Literature searches ended in spring 2008. More detail on the literature analysis can be found in Kuzma et al.<sup>62</sup>

#### *Limitations*

Limitations of this study include the reliance on expert opinion (including stakeholders) and the literature. Public confidence in GEOs oversight was not directly assessed through public surveys; however an extensive literature review was conducted on studies relating to this criterion. Although the number of experts (n=17) falls well within other expert elicitation studies (for example, 5-20),<sup>63</sup> we estimate that there are close to 100 people who could be classified as experts on GEOs oversight in the United States. Therefore, our sample is limited. Nine of the 17 experts come from academe which is another limitation, although this is not surprising given the broad and deep expertise in many disciplines related to oversight in this sector.

Another limitation is that experts and stakeholders were asked to score the criteria by looking at the system as a whole, although the system has changed over the course of time. Expert scores might depend on the different phases in Figure 1. We chose this route to get impressions of the system as it has operated since its formulation to the present. An additional limitation is that some experts might have rated criteria for which they were unsure in the middle of the score range (that is, around 50). Some experts chose not to rank criteria with which they were unfamiliar, although other experts might have given unfamiliar criteria a value of 50. Finally, correlation coefficients between criteria which were found in this study do not indicate that one causes the other with regard to oversight. Correlations should be interpreted carefully, and we use them to generate hypotheses, as opposed to determining causation or making definitive conclusions.

## Results and Conclusions

### *Agreement among Experts*

Expert elicitation data was gathered from 17 experts (Figure 3). We began to analyze the data by asking the question, "Upon which criteria do experts largely agree or disagree?" Criteria upon which diverse experts agree are instructive for highlighting strengths and weaknesses of the oversight system, whereas criteria upon which experts disagree indicate points of contention.

Agreement can be determined in several ways, and we considered it in three. The first was whether a majority of experts rated the criteria in a particular score range. We chose ranges of 1 to 39, 40 to 59, and 60 to 100 (Figure 3). A majority of experts rated the following criteria in one of these score groups: clarity of technological subject matter during development (clear 60 to 100); legal grounding during development (weak 1 to 39); transparency during development (low 1 to 39); post-market monitoring (little 1 to 39); treatment of intellectual property (closed 1 to 39); institutional structure (complex 60 to 100); flexibility (high 60 to 100); capacity (low 1 to 39); public input dur-

ing operation (minimal 1 to 39); transparency during operation (low 1 to 39); and informed consent (little 1 to 39). The outcomes of health and safety impacts (positive 60 to 100), distributional health impacts (positive 60 to 100) and environmental impacts (60 to 100) also indicated agreement among experts by this standard.

The second way in which we considered agreement was through the magnitude of the standard deviations (SD) of the expert scores (Figure 3). Criteria that had standard deviations that were under the average SD of 26 are shown in Figure 3. In addition to the 14 criteria mentioned above, impacts on research and innovation (O25, Table 1) (mean=54) had a relatively low standard deviation (SD=21, average SD was 26). Seven out of the 17 experts rated impacts of GEOs oversight on research and innovation as positive (scores 60-100), and 7 rated these impacts as fairly neutral (40 to 59).

A more qualitative way to assess agreement, and the third way in which we did, involved viewing the distribution of expert scores for each criterion and using subjective judgment to rate the profile of the distribu-

Table 2

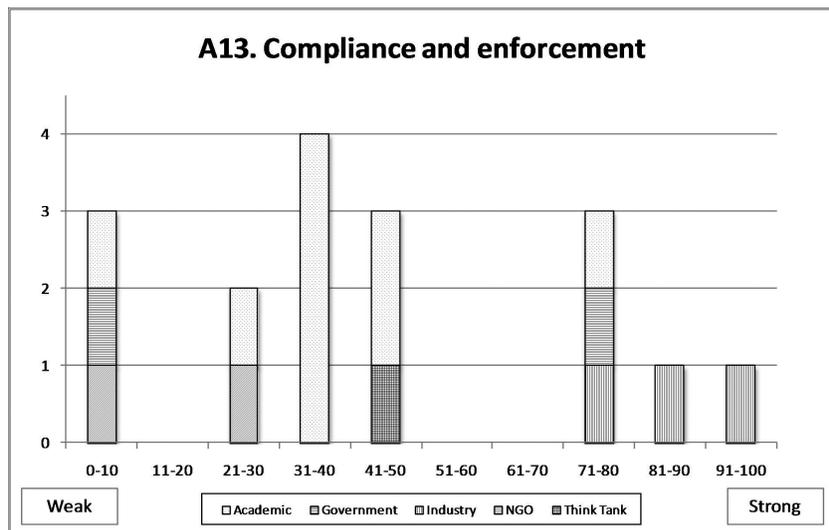
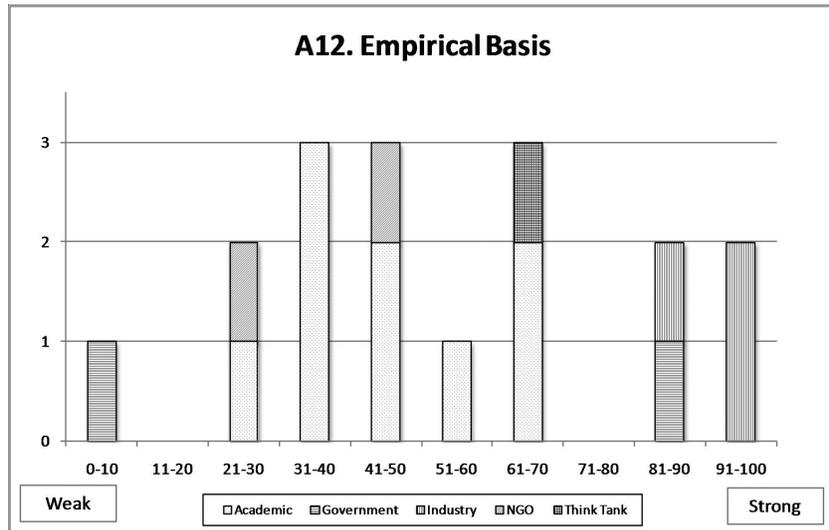
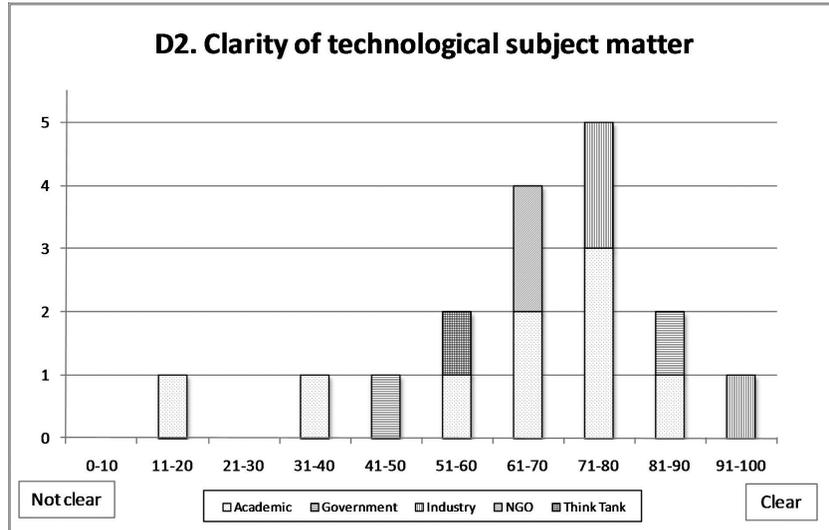
### **Expert and Stakeholder List: Affiliation, Degree, Expertise**

\*Indicates that the expert was also interviewed, in addition to filling out the survey.

1	academic, economics, agricultural biotechnology economics
2	academic (previous government), pediatrics/epidemiology, regulation
3*	academic, ecology, GEOs risk assessment
4*	academic, molecular genetics, GEOs risk assessment
5	academic, plant genetics, GEOs gene flow
6	academic, science and technology studies, regulation and society
7*	academic, sociology, agriculture and development
8*	academic, sociology, public participation
9*	academic, sociology & communications, public perception
10*	government, genetics & forestry, GEOs regulation
11	government, microbiology, regulation
12*	industry (consulting), law, GEOs regulation
13*	industry, business, food industry & trade
14*	industry, law, regulatory affairs
15	NGO, law, public interest law
16*	NGO, law & biology, biotechnology policy
17*	think tank (previous government), public policy, agricultural regulatory policy

Figure 4

**Selected Distributions of Expert Scores in Three Groups of Agreement a) High, b) Moderate, and c) Low**



tion as high, moderate, or low in agreement (Figure 3, last column). In Figure 4, we provide an example of a criterion that falls into each category of agreement. High agreement was apparent in expert ranking of the “clarity of technological subject matter” (D2) as “clear” (Figure 4a). Of 17 experts, 9 ranked it between 61 and 80, with only three ranking it at 50 or below (one government and two academic experts). Also, many agree that there is little post-market monitoring (A10) built into the GEO regulatory framework. The only exceptions to this are three respondents who ranked it between 51 and 80 (one industry and two academic experts). In the moderate agreement category, empirical basis (A12) was rated slightly positive by experts (Figure 4b). However, it is interesting to note that all three industry experts rated this criterion as “strong.” Also appearing in the moderate agreement category

are 4 of the 5 outcome criteria, public confidence, research and innovation, environmental impacts, and health and safety (Figure 5). The distribution for health and safety (O26) shows outlying scores which rate the health and safety impacts as negative, one from a non-governmental organization (NGO) and another from government (Figure 5). However, the scores hover around neutral health and safety impacts (neither positive nor negative, about 50).

Criteria upon which experts disagree could indicate points of contention in the debate about GEOs oversight and about the appropriateness of the framework. Distributions from examples of these can be seen in Figure 4c and 5 (O27, distributional health impacts). Low agreement was seen for impetus, public input, and empirical basis in development; legal grounding, data requirements and stringency, treatment of uncer-

Figure 5

**Distributions for All Outcome Criteria**

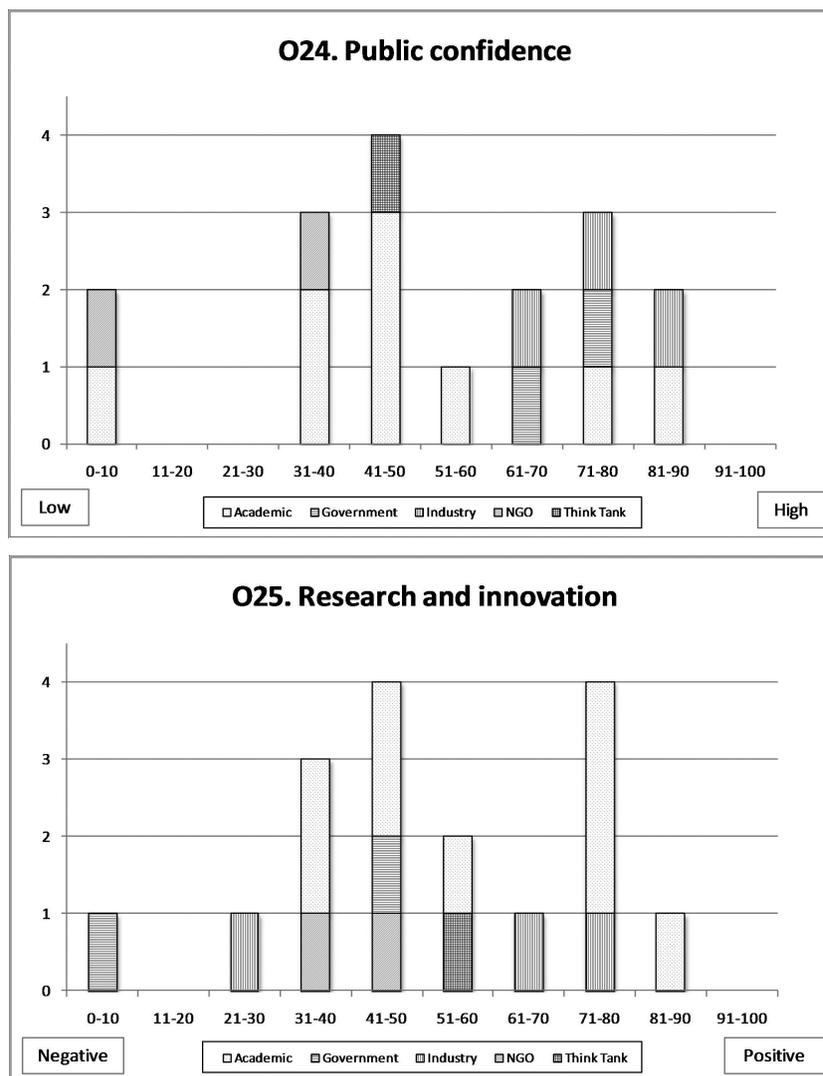
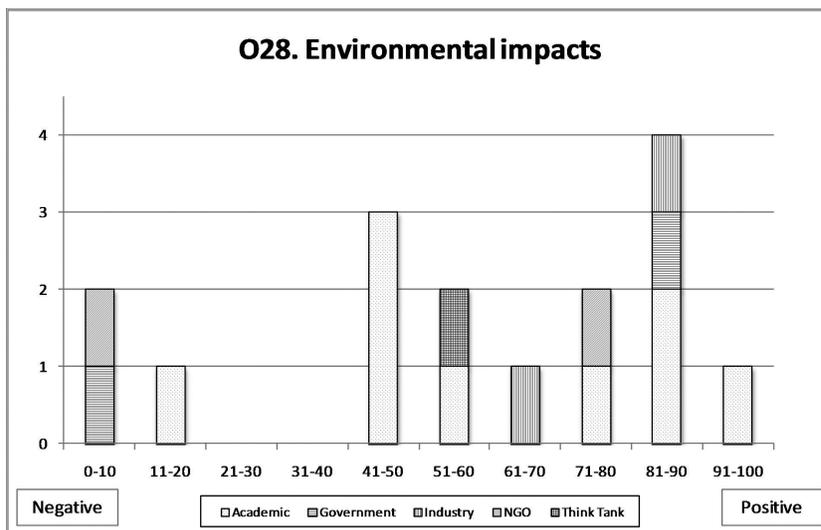
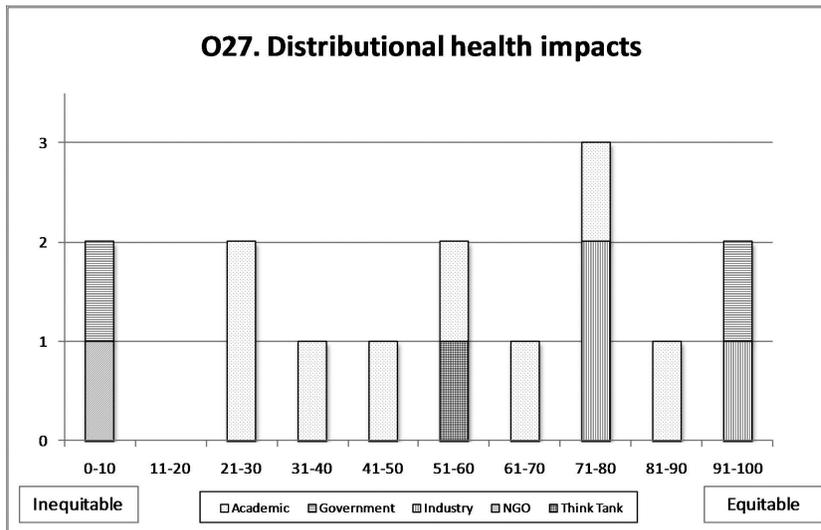
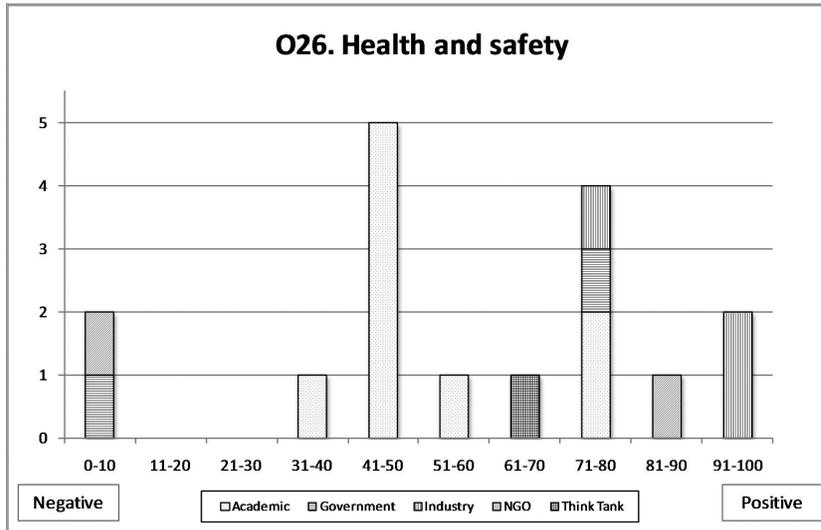


Figure 5 (continued)

**Distributions for All Outcome Criteria**



tainty, empirical basis, compliance and enforcement, and incentives in attributes; extent of change in the system; and distributional health impacts as an outcome. In some cases, a bimodal distribution where industry experts rated the criteria in one direction and NGOs rated them in another resulted. Although members of stakeholder groups are not homogeneous in their viewpoints, overall differences in ratings among the different groups were apparent in the data. These differences are important to evaluate GEOs oversight and derive lessons for nanotechnology. Ideally, an oversight system would satisfy multiple stakeholder groups.

Data requirements and stringency (A9) elicited almost a uniform distribution from the experts, with no score bin receiving more than three responses. Three industry experts ranked this criterion very high, between 80 and 100. Reasons for this pattern could include the fact that data submissions for regulatory approval are not generally shared with the public or academics.<sup>64</sup> Often only companies and regulators see the data that are required. It could also arise because the experts deal with different components of the GEOs oversight system. For example, FDA's process is voluntary and arguably no data is strictly required, although producers submit some data to the agency through the consultation process.<sup>65</sup> EPA requires extensive data through its plant-incorporated protectants rule under FIFRA,<sup>66</sup> and USDA requires some data through its environmental assessment process under FPPA.<sup>67</sup>

There was moderate agreement among the expert group that the GEOs oversight system has performed above average in health and environmental areas. Over 9 experts rated the three outcome criteria of health impacts, environmental impacts, and distributional health impacts (equitable distribution) in the most positive (60 to 100) group, although there was less agreement on the distributional health impacts (O27) by viewing the distribution and examining the SD. Generally, government, academic, and NGO representatives tended to rate the health and environmental outcomes lower (more negative), and the industry experts tended to rate them higher (more positive) (Figure 5).

There was a trend in overall scores in that on average, industry representatives rated the criteria for the GEOs system towards 100, which for most criteria would be normatively considered the most positive or desirable performance of the system (Table 2). When scores were averaged across 27 criteria (minus institutional structure) and all experts with particular affiliations, the mean score for industry experts was 71 (median=75), for NGOs experts was 31 (median=30),

for the think tank expert was 49 (median=50), for academics was 43 (median=40), and for government experts was 40 (median=40).

#### *Strengths and Weaknesses from Expert Elicitation*

In order to evaluate the performance of the GEOs oversight system, we evaluated the data to see what criteria stood out as being consistently rated in one direction or another (that is, towards low scores or high scores) by diverse experts. These outstanding ratings could point to strengths and weaknesses of the GEOs oversight system if the criteria are considered as evaluative. Means, medians, and agreement levels were taken into consideration for this question. Overall, transparency and public input were rated as "low" or "little," respectively, by this group of experts, with the exception of the development criteria of public input (D4) which had low agreement and a relatively neutral mean (=46) and median (=50). This exception might have been due to high profile events in the formation of GEOs oversight, like the Asilomar conference and congressional hearings (Figure 1), which did include the public at some level. However, there was high agreement around the lack of transparency in the development of the oversight system for GEOs (D5) with a mean of 34 and median of 30. NGO experts rated transparency in development as low (under 40), and there were only 4 scores over 60 (two from industry, one from government, and one from academe). Moderate agreement was displayed for the transparency of the operation of the oversight system (A20). Only three experts (one from industry, one from academe, and one from government) rated transparency as relatively high (over 50) (mean=41, median=35).

Public input in the operation of the oversight system (A19) showed moderate agreement among experts towards "little" public input, with 12 of 17 scores under 40, but with 5 of 17 scores over 60 (two from industry, two from academe, and one from government) (mean=40, median=35). NGO and think tank scores were 30 or under, and no scores appeared in the range of 41 to 60. This bimodal distribution of scores suggests polarized opinions about the extent of public input into decision making about GEOs oversight. The literature supports the view that certain groups of experts or stakeholders have had limited input into decisions about approving GEOs, particularly public interest groups and academic scientists who are not developers of GEOs.<sup>68</sup>

Lack of transparency and little public input in the operation of GEOs oversight are thought to be weaknesses of the system on normative grounds,<sup>69</sup> in that people have the rights to know about and participate

in decision making in a democracy like the U.S. The criterion of treatment of intellectual property and proprietary information (A15) is related to this issue. It affects how much information can be shared with stakeholders and the public. Experts rated this criterion as “closed” (mean=37, median=33) with a moderate level of agreement (Figure 3). Extensive claims of confidential business information (CBI) in regulatory submissions or other venues of public review have been identified previously as a weakness of the oversight system because it prevents disclosure of information to stakeholders.<sup>70</sup> Also, conflicts of interest (A21) in the system were rated by this group of experts as “prominent” (mean=37, median=35), although there was only moderate agreement, with two industry experts rating this criterion over 60 towards “avoided.” In the literature, several have called for the need for review by agencies and experts that are independent.<sup>71</sup>

Expert ranking of legal foundations of GEOs oversight depended on the stage of oversight. Legal grounding in the initial development of the oversight system (D3) was weighted toward “weak” (mean=39, median=30) with moderate agreement. This could reflect the ways in which existing laws were loosely interpreted to cover GEOs in the initial Coordinated Framework (see Introduction). There was less agreement surrounding legal basis in the attributes category (A8), and the mean and median were higher (=45 and =40). This shift towards a rating of stronger legal basis could stem from clearer interpretations of existing laws, publication of guidance documents, and promulgation of regulations during later phases of GEOs oversight (Figures 1b and c). For both legal grounding (D3) and legal basis (A8), industry-experts’ scores were more on the “strong” side (50 or over). Overall, legal foundations of the system seem to have improved since the development of GEOs oversight according to these experts.

Financial resources in the development of GEOs oversight (D6) and operational capacity (A18) were ranked relatively low by the experts (Figure 3). There was a high level of agreement among experts that capacity for GEOs oversight is “minimal.” Capacity is generally a positive feature of oversight; and therefore, the lack of it could be considered a weakness of the GEOs oversight system, especially if it affects abilities to promote positive outcomes and prevent negative ones.

Expert ratings of the criteria of post-market monitoring (A10) and informed consent (A22) for GEOs oversight are striking. There was a high level of agreement in our group of experts that there is very little informed consent in GEOs oversight. Twelve of the 17 experts rated this criterion as 39 or lower (mean=26,

median=20). These results are consistent with the literature documenting a lack of consumer knowledge about GEOs in the food supply<sup>72</sup> and voluntary labeling policies in the U.S.<sup>73</sup> It is also well-documented that there is a lack of post-market monitoring for GE crops that are not under the jurisdiction of the EPA.<sup>74</sup> Thirteen experts rated this criterion as 39 or under, with a mean of 27 and median of 20. Once GE products are approved and marketed, there are no formal programs or policies to require monitoring for adverse health or environmental effects.<sup>75</sup> Ecologists and health experts have raised concerns about our inability to detect long-term consequences of GE products should they arise in post-market settings.<sup>76</sup> Post-market monitoring and informed consent could be thought of as weaknesses of the GEOs oversight system, in light of their ties to ethical principles such as autonomy, beneficence, and non-maleficence.<sup>77</sup>

Experts also generally agreed that GEOs oversight is highly complex. The institutional structure of the system was rated towards “complex” with a mean of 77 and median of 80. Although the literature does not indicate whether complex regulatory systems are strengths or weaknesses of oversight, they might make the process more cumbersome and costly to developers. On the other hand, complexity might positively affect the rigor of data review. Some reports have considered simplicity as a principle of good oversight.<sup>78</sup> We discuss complexity in light of our literature search and the impacts of GEOs oversight on research and innovation below.

Several criteria that have been considered important for oversight from previous studies<sup>79</sup> were rated positively by the expert group with regard to GEOs oversight. There was a high degree of agreement that GEOs oversight is flexible (Table 1, Figure 3). Ten of 17 experts rated this criterion over 60 (mean=62, median=70). Flexibility has been previously reported as a strength of oversight systems;<sup>80</sup> however, interest and consumer groups might see a flexible system as one that could also create loopholes for industry (see Expert Interviews discussion). In our definition of flexibility, we included the ability of oversight systems to adapt to new situations (see “Genetically Engineered Organisms Expert Elicitation Survey,” available online). Adaptation was seen as a critical component of GEOs oversight by previous stakeholder groups.<sup>81</sup>

The clarity of technological subject matter during the development of GEOs oversight (D2) was rated towards “clear” (60 or over) by 14 of 17 experts (see also Figure 4a). Clear subject matter has been thought to be important for oversight,<sup>82</sup> and currently, concerns about nanotechnology oversight relate to how the technology is defined and whether regulations

capture the products.<sup>83</sup> Our expert data on this criterion supports the history of GEOs oversight in that the Coordinated Framework seemed to be explicit about which products would be covered that is, products stemming from the introduction of genes using recombinant DNA technology.

Another potential strength of GEOs oversight includes the empirical basis for making decisions about products (A12). This criterion was rated slightly on the “strong” side by our expert group (Figure 4b, mean=57, median=50). However, there was a lack of agreement in the data (Figure 4b) and scores tended to break down by affiliation as discussed above.

#### *Analysis of Outcome Criteria*

Analysis of outcomes of GEOs oversight is important for developing initial hypotheses about what constitutes “good” oversight, evaluating the GEOs system, and deriving lessons for nanotechnology. As discussed above (see Methodology), we used outcome criteria as initial dependent variables to identify other factors, such as attribute and development criteria that are positively or negatively correlated with them (see below, Correlations among Criteria).

The results of the expert data for the outcomes were interesting in that experts rated all five outcomes of public confidence, impacts on research and innovation, health and safety, distributional health impacts, and environmental impacts as neutral to slightly positive (Figure 3 and 5). From glancing at the distributions, there was moderate agreement for all but distributional health impacts (O27).

Health and environmental impacts (O26 & O28) were viewed as slightly positive by this expert group, with moderate agreement and means of 61 for both. The mean for distributional health impacts (O27) was also slightly positive at 58; however there was less agreement in the scores (Figure 5). Generally, our expert elicitation results on health and environmental impacts support the history of GEOs oversight. Despite regulatory mishaps (for example, Starlink corn in the food supply or Ht bent grass contaminating wild grasses in Oregon) and media controversy (for example, over the Monarch butterfly or Bt corn contamination in wild teosinthe in Mexico), there have not been significant reports of environmental or health damage (that is, injuries or deaths) since the marketing of GE crops. However, some groups do seem to benefit from GEOs more than others. For example, GE crops can reduce pesticide use or promote the use of safer herbicide, leading to safety and economic benefits to farmers, and sales of GE crops have benefited portions of the seed and biotechnology industry.<sup>84</sup> Consumers have not been the primary

beneficiaries from GE crops yet, although pesticide reductions from the use of some GE crops could lead to human health benefits.<sup>85</sup>

Environmental impacts associated with GE crops, such as affects from gene flow and genetic contamination of native races, impacts on non-target species like butterflies, increased weediness of relatives of GE crops, and loss of genetic diversity have been concerns since the advent of the products, although no significant impacts on ecosystems have been found. However, some argue that these impacts could be occurring but are undetectable due to a lack of post-market monitoring.<sup>86</sup>

Public confidence (O24) and positive impacts on research and innovation (O25) are considered important outcomes of good oversight systems. These outcome criteria showed moderate to low agreement in our expert scores for GEOs oversight. For public confidence, scores centered upon a mean of 54 and median of 50. Scores depended on affiliation, in that all 3 industry experts and both of the government experts rated this outcome criterion as 70 or greater, towards high public confidence (Figure 5). NGOs and most academics gave lower scores. For impacts on research and innovation (O25), there was moderate agreement around neutral scores (Figures 3 and 5). This time, however, more diversity was seen with respect to the relationship between scores and affiliation. Given the breadth of scores on these outcome criteria for judging oversight, we focused on them for a detailed review of the literature and coded for them in our qualitative analysis of the interviews (see below, Expert Interviews) in order to gather more evidence for evaluation.

#### *Impacts on Research and Innovation Literature*

As discussed above, there was less agreement in the expert scores for the impacts of GEOs oversight on research and innovation, and affiliation was not as prominent of a factor (Figure 5). Examining impacts on research and innovation of GEOs oversight would help us to evaluate the system performance and whether there are lessons for nanotechnology oversight for improving this outcome. Therefore, we chose to do a more extensive literature analysis of this outcome, focusing on quantitative data where available in order to better understand how GEO oversight has impacted research and innovation. Research in this area is not particularly abundant, and information regarding regulatory compliance costs for private companies is difficult to come by, as it is most often considered confidential. Furthermore, it is challenging to separate the pure costs of going through the regulatory approval process from those associated

with product development, as the two are often intertwined. Regardless, a sampling of the literature is discussed below. Although this article focuses on U.S. oversight, it is important to note that most companies that have developed GE crops market them globally have to go through regulatory approval in all user-countries, which adds to the costs.

According to Nicholas Kalaitzandonakes,<sup>87</sup> the compliance costs for full regulatory approval of genetically engineered crops are closely guarded by biotech companies and are therefore difficult to procure. That being said, Kalaitzandonakes<sup>88</sup> obtained a range of regulatory costs for approval of Bt and Ht maize in the U.S., which was derived from reviews and analyses of dossiers given to the regulatory bodies by major biotechnology companies. The compliance costs for Bt maize were from \$7.06 million dollars to \$15.44 million dollars, and the compliance costs for Ht maize were from \$6.18 million dollars to \$15.51 million dollars. One of our experts from the GEOs industry who was interviewed for this study stated that it costs \$8 to \$12 million dollars and takes 6 to 10 years to gain regulatory approval for a GE crop. Other estimates for the costs of regulatory approval are more modest. An appendix to a report from the National Research Council<sup>89</sup> estimates that it takes \$2.8 to \$3.8 million dollars to get a pesticide resistant crop approved.

A study conducted by Jaffe,<sup>90</sup> consisting of 62 regulatory reviews from 1995 to 2004, concluded that the amount of time required for regulatory approval has increased. For GE animals in agriculture, the time has been more extensive as the first one waits approval because of a lack of a regulatory guidance document to interpret existing laws until September 2008.<sup>91</sup> Aqua Bounty Technologies has been working on data for regulatory approval for a GE fish variety for almost a decade.<sup>92</sup>

In 1991, Michael Porter suggested that environmental regulation might have a positive effect on the performances of domestic firms, relative to their foreign competitors, by stimulating domestic innovation.<sup>93</sup> This idea became known as the Porter hypothesis. Contrary to this hypothesis, the consensus among most authors seems to be that the agricultural biotechnology industry has been stagnating over the past few years, while regulatory compliance standards are becoming tougher and more expensive. Less than three biotech crops per year had been approved by regulatory bodies from 1999-2004.<sup>94</sup> An analysis by Kalaitzandonakes<sup>95</sup> states that industry innovation and product development in agricultural biotechnology has been slowing. There has been a slowdown in the rate of deregulation (commercial approval) of new GE traits, a declining rate of research and development funds for crops with

lower market potential, and a decreased rate of newly established agricultural biotechnology firms. Some authors believe there is a correlation between slow downs in innovation, decreased product development, and the rise in regulatory compliance costs.<sup>96</sup>

Regulatory requirements can raise fixed costs and thereby limit entry into the market for smaller firms.<sup>97</sup> Limiting entry into the market can reduce competition and lower research and development expenditures for larger firms on the whole. This, in turn, can cause the orphan crop problem where certain crops are not considered research worthy because they do not generate the demand necessary to justify the high regulatory expenditures.<sup>98</sup> Rising regulatory costs seem to be assisting a trend toward a concentration of agricultural biotechnology products being attributed to a small number of large firms.<sup>99</sup> David Schimmelpennig et al.<sup>100</sup> conducted a study of the U.S. agricultural biotechnology seed industry and concluded from the empirical relationship between the number of firms doing applied GE crop research and the research output that the concentration of agricultural biotechnology firms has a negative effect on research and development.

Despite the majority of authors claiming that U.S. GEOs regulation has stifled innovation and research, there are a few that have found differing results. Overall, no consensus exists as to the cause of the slow down in research and innovation in the industry. Some authors believe that the regulatory framework is a major cause of the decrease in innovation, and they view indicators such as increasing regulatory compliance costs and increasing regulatory approval times as signs of an in-commensurate degree of stringency.<sup>101</sup> However, others believe that the relationship between regulation and research and innovation is much more ambiguous. Kalaitzandonakes<sup>102</sup> argues that evidence is inconclusive as to whether the GEOs regulatory framework is the primary cause for the decrease in research, development and innovation. Jaffe's<sup>103</sup> regression analysis indicated a positive correlation between regulatory stringency and research and development spending, but found no correlation between regulatory stringency and innovation. In our expert elicitation data, we did not find a significant ( $p < 0.0016$ ) correlation between data requirements and stringency and impacts on research and innovation, although we were able to obtain experts' perceptions of the relationships from the survey interviews (see Expert Interviews). In summary, more research is required in order to develop a better understanding of the dynamics between features of oversight and impacts on research and innovation.

### *Public Confidence Literature*

For the outcome of public confidence (O24), there was low to moderate agreement in the expert scores, and affiliation was a factor in the sense that the industry experts rated public confidence as a result of the GEOs oversight system more highly than other experts (Figures 3 and 5). As such, we chose to do an extensive literature analysis of this outcome, focusing on quantitative data where available in order to better understand how GEO oversight has affected public confidence. One difficulty with measuring public confidence in oversight is the many forms in which it can be measured, such as trust in, attitudes toward, or opinions about products, systems, or actors. Our review focused on literature from 2000 to the present regarding three public confidence dimensions related to GEOs: general U.S. public opinion of GEOs and their products; public trust in different institutions and groups for oversight of GEOs; and general public trust in regulation with regard to GEOs. Our review is not meant to be exhaustive, but deals with key publications concerning these subjects.

There have been several important studies concerning the quantitative analysis of U.S. public opinion regarding issues relating to GEOs. Several surveys have been conducted by the Pew Initiative on Food and Biotechnology (PIFB). According to one poll, 53 percent of adults somewhat or strongly disagree with the idea of GE insects; 65 percent of adults somewhat or strongly disagree with GE fish; and about 46 percent disagree with the idea of using GE plants.<sup>104</sup> Another PIFB poll indicates that Americans know relatively little about GE foods and their views are shapeable, yet they remain supportive of continued research into them.<sup>105</sup> A later PIFB poll<sup>106</sup> indicated that opposition to GE foods had softened since 2001 (from 58 percent in 2001 to 47 percent in 2004). In 2005 PIFB conducted yet another poll and found that despite continuing concerns about GE foods, U.S. consumers do not oppose new uses of the technology, but they do support an active role by regulators to ensure public safety; however, consumers do remain uncomfortable with GE animals.<sup>107</sup> A final PIFB poll was released in 2006, and the findings indicated that support for GE foods has remained consistent while opposition has declined. Americans remain mostly uncertain about the safety of GE foods, and consumers are far less comfortable with GE foods derived from animal clones than GE plants.<sup>108</sup>

Other studies support the findings of the PIFB polls. A 2003 Food Policy Institute (FPI) poll determined that Americans have very little knowledge of agricultural biotechnology and that opinion on GE foods is split. About half of Americans approve of GE

plants and about a quarter approve of animal-based GE foods, although approval increases when information about the specific benefits of GE foods are given, which shows that consumers' opinions are malleable based on additional information.<sup>109</sup>

A phone survey conducted in a study by Susanna Priest<sup>110</sup> found that 52.8 percent of respondents affirmed that genetic engineering would "improve our way of life in the next 20 years" and 30.1 percent of respondents said they believe that genetic engineering "will make things worse" over the next 20 years. According to Priest,<sup>111</sup> the numbers are only somewhat positive because this approval rate is lower than the approval rate for other technologies ranging from computers (87.8 percent) and solar energy (87.7 percent) to space exploration (62.2 percent). Only nuclear power had similar approval ratings with 43 percent expecting it to improve life and 32.4 percent expecting it to "make things worse." Harris Interactive<sup>112</sup> conducted a survey in which they found that only 38 percent of Americans polled thought that the benefits of plant-based GE foods outweighed the risks. Forty-three percent viewed the risks of plant-based GE foods as outweighing the benefits. From all the surveys, some general themes emerge: approval versus disapproval of plant-based GE foods is fairly evenly split with a slight decrease in opposition in recent years; most Americans are still uncomfortable with the idea of animal-based GE foods; and a significant proportion of Americans are unaware of GE foods.

Originally, the public's lack of knowledge about relevant scientific subjects was thought to be the main reason why public opinion became acrimonious toward certain emerging technologies. However, it is now argued that this "knowledge deficit theory" is insufficient to fully explain public perception.<sup>113</sup> Several other theories as to how the public forms its perception of emerging technologies have been proposed. Most publications concur<sup>114</sup> that public trust in institutions, such as regulators, plays an important role in how the public perceives emerging technologies like biotechnology. The degree of trust that a person has in institutions plays an important role in that person's perception of risk and acceptance of emerging technologies. Even though trust in institutions does not fully eliminate the sense of risk, it is a valuable instrument for the risk abatement.<sup>115</sup> Michael Siegrist et al.<sup>116</sup> have developed a model in which trust influences affect or feelings, which then influences perceived risks and benefits and ultimately public acceptance. John Lang and William Hallman<sup>117</sup> explain that if the public is not knowledgeable about GE foods, then they are forced to rely on academic and regulatory institutions, experts, non-governmental institutions, and industry

when forming their opinions about GE foods. They also propose that trust is a complex issue consisting of multiple components such as transparency, public input, honesty, and competency. In our work, we used transparency, opportunity for public input, and avoidance of conflicts of interest as features of oversight systems and potential components of trust to explore relationships between them and the outcome of public confidence in the system (see below, Correlations among Criteria).

The roles and trust-levels of actors in oversight systems have been studied. Priest<sup>118</sup> explains that trust in regulatory agencies (which is measured in her study by whether people believe agencies are doing well regulating biotechnology, or competency) is not high, and neither is trust in the media. Trust in the scientific community is extremely high and trust in industry is a bit lower. In the study conducted by Lang and Hallman,<sup>119</sup> the federal government, grocers and grocery stores, industry, and the media are all not well trusted by the public; however, universities, consumer advocacy organizations, medical professionals, scientists, and farmers are fairly well trusted. In the PIFB 2006 poll, biotechnology companies and news media were the two least trusted groups while scientists and academics were near the top.<sup>120</sup> Overall, it seems that government and industry are not well trusted by the public and this could affect how oversight of GEOs is viewed given the prominent roles they play. Academic experts seem to be well trusted; however, there was a limited role for them in GEOs oversight in the main regulatory agency, USDA, until recently.<sup>121</sup> Independent, expert advisory committees for the environmental release of GE crops and other oversight decisions such as food safety of GE crops were lacking, although EPA used these types of committees through its scientific advisory board committees. Our conflict of interest criterion (A21) addresses the roles of independent or conflicted parties in GEOs oversight. Conflicts of interest (COI) are likely to decrease public confidence in oversight (Jaffe<sup>122</sup>; see below, Expert Interview Results), and actors such as industry groups that have financial COIs are generally less trusted.

Another important issue is what the public thinks of the job that regulators are doing to manage GEOs. When people are asked whether current regulations are sufficient for GE foods, a majority of respondents either moderately or strongly disagreed, and the public seems supportive of regulation.<sup>123</sup> However, in a seemingly conflicting study, an Ipsos-Reid<sup>124</sup> poll discovered that a majority of the consumers surveyed were “very confident” (13 percent) or “somewhat confident” (58 percent) in the government to regulate food safety (including GE foods). Caution should be taken when

comparing the different survey results as the two studies ask different types of questions. Due to the difficulties resulting from attempting to cross-compare dissimilar opinion studies, it is difficult to make general conclusions about the extent of public confidence in GEOs and their oversight. Disagreement in the literature supports the disagreement we saw among experts in our study for the outcome of public confidence in oversight (O24) (Figure 5). From our data (Figures 3 and 5) and the literature, at best we can conclude that public confidence in the GEOs oversight system is mixed or neutral, and more comprehensive studies are needed.

#### *Correlations among Criteria*

Under the goal of deriving lessons for nanotechnology, one of the sub-goals of our work was to develop hypotheses about what features of oversight systems lead to outcomes that most would consider positive, such as beneficial health and environmental impacts, equitable distributions of health benefits, high public confidence, and promotion of research and innovation. These relationships could school the development of nanotechnology oversight by suggesting the importance of certain attributes of oversight for other attributes or outcomes. In order to probe relationships among development, attribute, and outcome criteria groups (Figure 2), we generated correlation coefficients in pair wise combinations for all possible combinations of criteria (Figure 6a and 6b; see Methodology).

From the beginning, we understood that given the limited number of experts and GEOs as the only case study, we could not suggest causal relationships among criteria. Instead, our goal was to identify correlations in order to generate testable hypotheses about oversight systems for our future work (for example, in evaluating additional historical models, or in larger, more comprehensive expert, stakeholder and public opinion studies). Given the small number of experts and stakeholders, we initially decided upon a stringent cut-off for significant correlations that would lead to p values equal to or less than 0.0016 (p critical). This translated to correlation coefficients of  $r=0.7$  and coefficients of determination of  $r^2=0.49$  or higher. Interestingly, no criteria that made this cut-off were found to be negatively correlated.

From the correlation coefficients (Figure 6a), we drafted an influence diagram to illustrate criteria pair wise relationships (Figures 6a and b). There are several types of criteria relationships (Figure 2): (1) those within a group of criteria, for example, as exhibited between public input and transparency within the development or within the attributes categories;

Figure 6

**Relationships among Criteria**

a) Influence diagram: only criteria relationships for which  $r^2 \geq 0.49$  or  $r \geq 0.7$  ( $p < 0.0016$ ) are shown to reduce complexity of the diagrams. Criteria that are absent did not show any correlation at this significance level. Boxes indicate choice or decision variables and circles indicate outcome variables. b) significant correlations between different categories criteria — although arrows point in one direction, it is possible that the influence is reversed, for example through feedback.

A

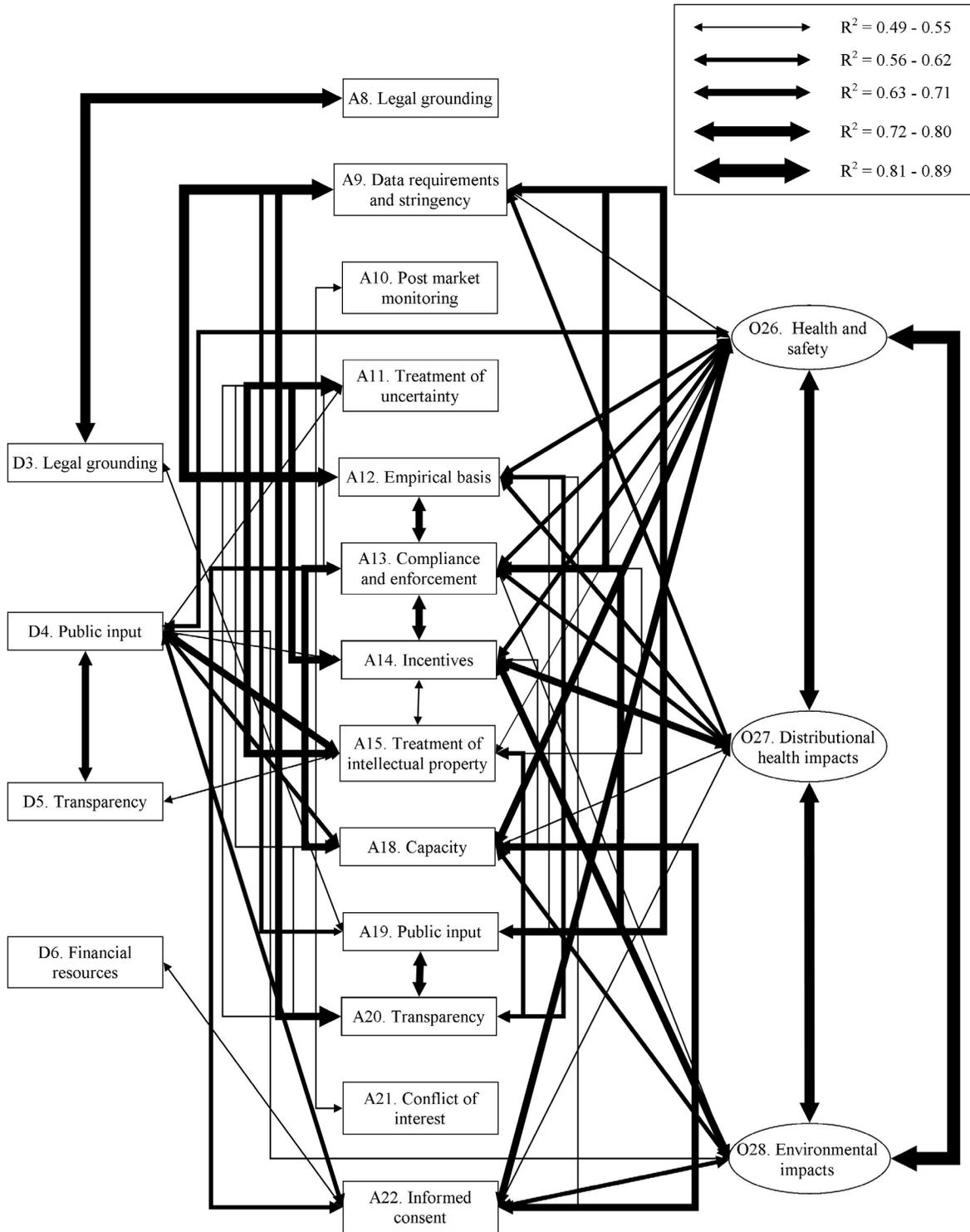
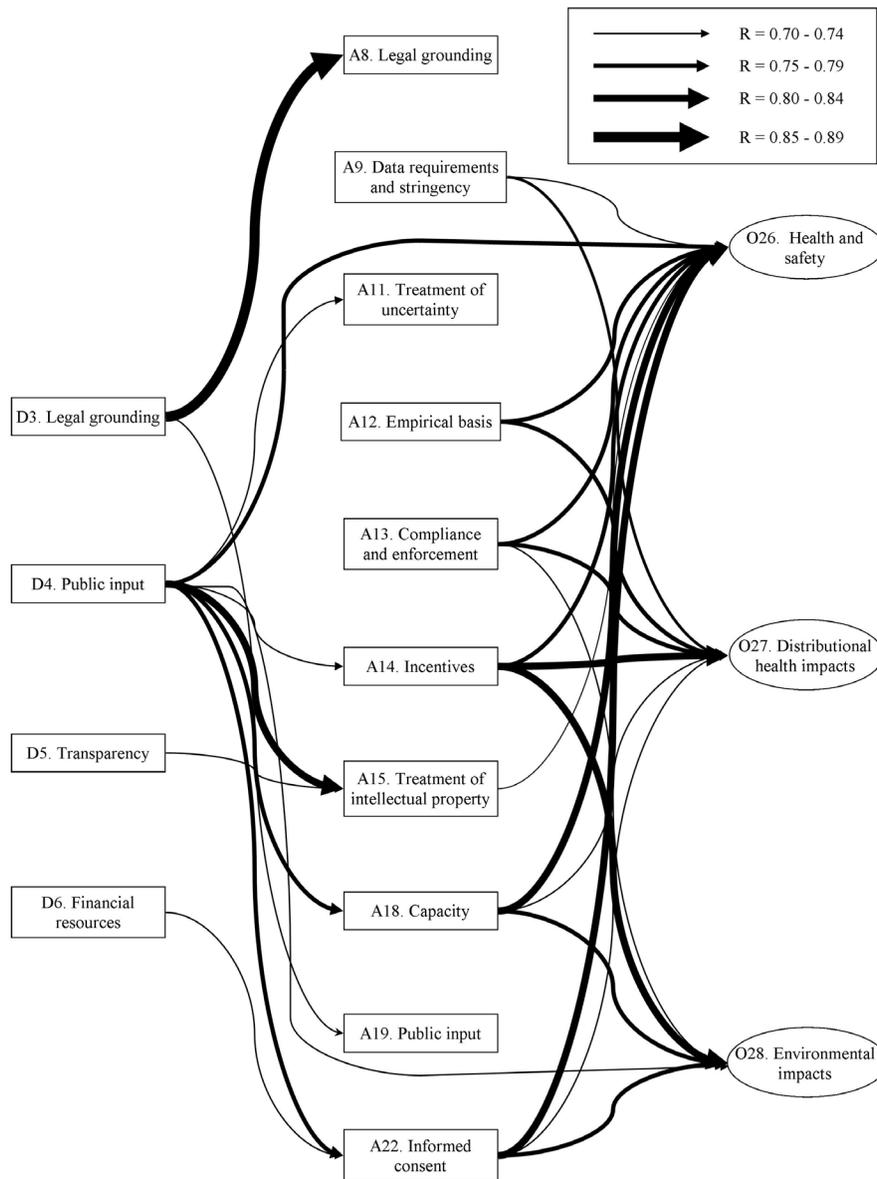


Figure 6 (continued)

**Relationships among Criteria**

**B**



(2) those between development and attributes criteria, such as the relationship between public input in development (D4) and the treatment of intellectual property (A15) in operational attributes; or (3) those between attributes or development criteria and oversight outcomes, such as the correlation between capacity in the system (A18) and health and safety outcomes (O26). The most significant correlations are discussed below.

The strongest correlations were seen within the group of outcome criteria, that is between health and safety, environmental safety, and distributional

health impacts ( $r > 0.85$ ). This is not a surprising result for two potential reasons: one, environmental safety and health and safety are closely intertwined; and two, there are limited comprehensive evaluations of these outcomes with regard to GEOs oversight in the literature, so expert biases and perceptions of risk and benefits likely come into play, causing an expert to rate the three using similar scores. The latter was seen when individual expert scores were tracked (data not shown). It is interesting to note, however, the correlation between two seemingly distinct elements of

oversight: positive (O26 and O28) and fair outcomes (O27).

It was surprising to find that no criteria were correlated with the outcomes of public confidence (O24) and impacts on research and innovation (O25) at a significance level of  $p < 0.0016$ , as much of the oversight literature hypothesizes about the structure and feature of systems and impacts on these outcomes. For example, links between regulatory issues and public confidence have been acknowledged by natural and social scientists, stakeholders, and policy makers alike, and were confirmed in our literature analysis. When GE pigs entered the human food supply without regulatory approval, even FDA, an agency that bases its decisions primarily on science and legal limits, wrote in its letter to the developer of the GE pig: "It is imperative that all safety regulations be followed scrupulously to help assure the highest level of confidence possible in the conduct of this type of research."<sup>125</sup> Another issue often cited in the literature is that FDA's review process is voluntary and thus the public is not as willing to accept GE foods (for example, PIFB<sup>126</sup>). One possibility for the lack of correlation at  $p < 0.0016$  could be that there was more disagreement among experts with regard to these outcomes (Figure 5). Our expert interview data indicate that public confidence is an important outcome and affected by other criteria or features of oversight. Therefore, we relaxed the level of significance ( $p$  critical  $< 0.05$ ) and discuss correlations between public confidence and several other criteria in the context of the qualitative analysis of the interviews (see below, Expert Interviews).

Correlations among different categories of criteria were examined (Figure 2). The development criterion that showed the greatest number of relationships to other criteria was public input (D4). Public input was positively correlated with health and safety (O26) with a strength of  $r = 0.79$  ( $p < 0.0002$ ), and with the attributes of treatment of uncertainty (A11), incentives (A14), treatment of intellectual property (A15), capacity (A18), public input (A19), and informed consent (A22). Several hypotheses could be generated based on these relationships. Research could focus on the following questions, among others: (1) Does more public input during the development of oversight systems lead to more positive health and safety impacts? and (2) Does greater public input during development affect the capacity, so that it becomes greater in the emergent oversight system due to increased public input?

The attributes criteria that emerged as most tightly correlated with the health, environmental, and distributional-health outcomes include capacity and informed consent. Informed consent (A22) was cor-

related with health and safety (O26) at  $r = 0.84$  and  $p < 0.00003$ . This relationship makes sense from a theoretical perspective, in that the more people know about what they are consuming and to what they are exposed, the more they can avoid unwanted risks. This hypothesis would need to be tested, although risk perception literature supports the importance of voluntary exposure to risks to people (informed consent) and how voluntariness impacts their views about safety.<sup>127</sup> Another hypothesis that could be explored for this positive correlation is that informed consent, or labeling in the context of GE foods, leads to better detection of health and safety outcomes.<sup>128</sup> The relationship between greater capacity and more positive health and safety outcomes could be explored in cross-comparisons among historical models, and it also makes sense from a theoretical standpoint. With more resources and knowledge, regulators are apt to make more accurate and appropriate decisions.

Weaker correlations, but still significant, were seen between health and environmental safety outcomes and data requirements and stringency, empirical basis, compliance and enforcement, treatment of intellectual property, and incentives (Figure 6). These relationships suggest the need for rigorous scientific-based risk assessment and openness about it in order to achieve good oversight. This theme was mentioned several times in the interviews with experts (see below, Expert Interviews) and is another set of hypotheses that can be tested across additional historical models.

Strong positive correlations within groups of criteria, and between similar ones, support the validity of our methodology. For example, within the attributes category, data requirements and stringency (A9) and empirical basis (A12) were highly positively correlated with a  $r = 0.88$  ( $p < 0.000002$ ). The definitions of the two relate to each other (see "Genetically Engineered Organisms Expert Elicitation Survey," available online) in that the greater the empirical basis, the more data requirements.

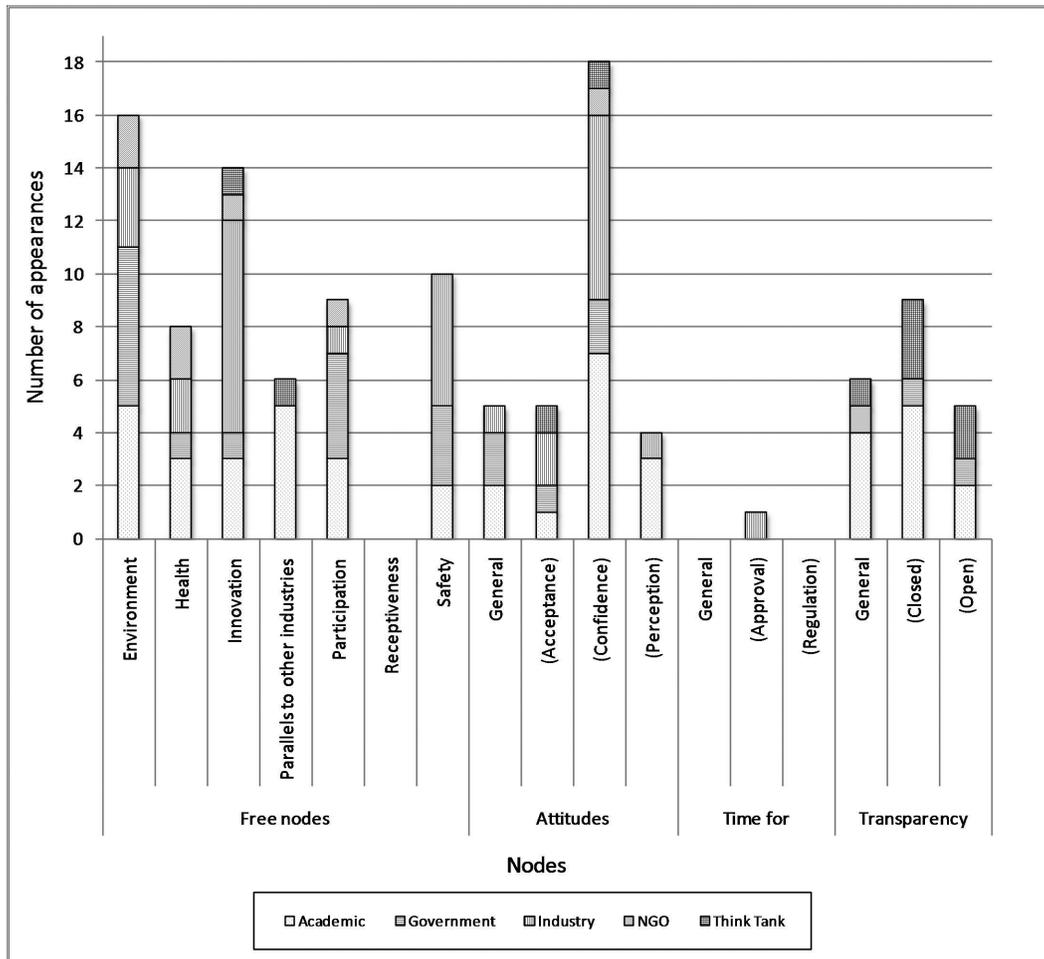
#### *Expert Interviews*

As the application of expert elicitation using multiple criteria for evaluating historical oversight systems has not been previously reported to our knowledge, we wanted to strengthen our analysis with semi-standardized expert and stakeholder interviews. The interview results were intended to help develop hypotheses and refine hypotheses generated from the quantitative data or literature. We also used the interviews to begin to explore oversight lessons for nanotechnology. Experts and stakeholders were interviewed to obtain information on the performance of GEOs oversight and how lessons from this case study relate to emerg-

Figure 7

### Interview Coded Themes and Frequency

The X axis contains themes identified by the literature and nodes used to search interview text in Nvivo. Y axis indicates the number of times that theme appeared in the interview text. Expert affiliation associated with each appearance is depicted in the graph.



ing nanotechnology oversight systems. Eleven experts (including stakeholders) were interviewed using a broad set of questions from which conversation flowed (see Methodology) (Table 2). Questions were purposefully broad, and did not solely relate to the criteria, in order to obtain more contextual information than the quantitative expert elicitation survey.

We read through the interview notes and used the information throughout our analysis of GEOs oversight. In addition, formal content analysis was used to analyze the interview notes. Seventeen conceptual clusters were used for coding,<sup>129</sup> which were based on the oversight literature and our set of criteria. Words were used to represent the concepts, and text relating to the concepts (either containing the exact word or not) was included in the analysis. The concepts were organized into free or tree nodes (see Methodology),

and the number of appearances of the nodes in the interview notes was tracked (Figure 7). Nodes mentioned six or more times by the 11 interviewees were concepts relating to the “Environment,” “Confidence,” “Innovation,” “Safety,” “Health,” “Transparency,” and “Participation.” The prominence of these concepts in the interviews supports our use of them in our criteria, such as health and safety, research and innovation, public confidence, public input and transparency (Table 1).

Expert and stakeholder comments largely reinforced the historical literature on GEOs concerning outcomes and processes of oversight (Appendix 1). Direct responses to the questions are summarized in appendix 1. For concepts relating to the “environment” node, interview data suggested the lack of confidence in the GEOs oversight system to handle environmen-

tal risks either pre- or post-market. Several experts mentioned the need for more rigorous environmental assessments in pre- and post-market settings. It was noted by one expert that there has been no evidence of damage from GEOs to date; however several others mentioned the shortcomings of USDA-APHIS's environmental review processes and the documented gene flow from GE crops into wild relative plants (for example, Ht creeping bentgrass in Oregon or Bt corn in Mexico). "Health" concepts from the interviews focused on pharmaceutical proteins engineered into GE crops entering the human food supply unintentionally and causing human health risks. Historically, there have been incidents of cross-contamination, including GE corn engineered with a pharmaceutical protein that was a contaminant in soybeans destined for human food (Figure 1b and 1c). Comments about FDA's process were mixed. Some felt that it was not stringent enough for GE foods, given its voluntary nature, but a few comments noted how long it has taken for FDA to consider and develop a policy for GE animals. Some noted that FDA's process is transparent for GE plant-based foods, but others noted that it is not transparent for GE animals.

Interviewee statements about "innovation" support the mixed results of our literature analysis on impacts of oversight on research and innovation. Several interviewees thought that GEOs regulation was stifling innovation, while others thought that the regulatory system supported industry innovation through "lack of vigor in the framework." Others indicated that small companies and university developers do not have the resources to comply with the system, supporting the arguments in the literature for the orphan crop and industry consolidation problems. Another expressed the view that "sometimes halting innovation is a good idea." This statement would suggest that growth in research and innovation might not always be a positive outcome of good oversight.

In the area of public attitudes (tree node, parent), acceptance, confidence, and perception (tree nodes, children), experts disagreed. This disagreement is supported by the somewhat mixed results of public perception and attitudes studies (see above, Public Confidence Literature). Some experts stated that the U.S. public is pro-technology, not concerned about GEOs, or apathetic, while others believed that public confidence in GEOs and oversight of them are lacking. These mixed comments also support the quantitative results as manifested by the wide distribution in expert scores for the outcome criterion of public confidence (Figure 5). It was mentioned several times by experts in the interviews that mandatory and independent regulation, as well as transparency, promote public

acceptance of or confidence in technology. In light of these comments, we reanalyzed the quantitative data for relationships to the outcome of public confidence (O24) using a different cutoff of significance ( $p < 0.05$ ) for the correlation coefficients. Positive correlations at this significance level were seen between the outcome of public confidence and public input, data requirements, and incentives (Figure 8). These relationships support several statements from the interviews and help to generate hypotheses that are congruent with previous public perception studies.<sup>130</sup> For example, one could hypothesize that greater public input into an oversight system (D5 or A19) engenders trust, resulting in greater public confidence (O24). Another hypothesis could link stronger data requirements (A9) as a feature of mandatory oversight systems, to increased public confidence (O24). Experts made such connections in the interviews. Finally, increased incentives for compliance (A14; "Genetically Engineered Organisms Expert Elicitation Survey," available online) could increase public confidence by reducing mistrust of industry that might stem from the perception that industry does not always fully comply with oversight processes. Mistrust of industry and problems with conflicts of interest have been reported in other studies<sup>131</sup> and were stressed by several of our experts in the interviews.

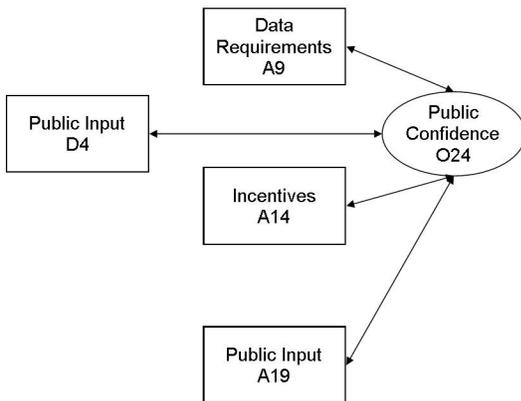
Interestingly, significant correlations between transparency and outcomes of oversight, such as public confidence, were not seen in our quantitative data, despite the importance of transparency in the interview data (20 appearances, counting the parent and child nodes) (Figure 7). Several experts stated in the interviews that GEOs oversight was not transparent overall, although there were elements of transparency. The more transparent elements mentioned were USDA's website on approvals, environmental assessments, and findings of no significant impact (see [www.isb.vt.edu](http://www.isb.vt.edu)) and EPA's dockets for FIFRA approvals. A few experts suggested a link between transparency and the treatment of intellectual property. For example, confidential business information is removed from public versions of regulatory dockets to protect intellectual property.<sup>132</sup> Several experts noted that it was difficult to assess the effectiveness of GEOs oversight because of insufficient public information on products. Links in the interviews were made between mandatory, independent regulation that is free from COI and greater public confidence.

A few experts mentioned the importance of consumer benefits for increasing public acceptance of and confidence in GEO products and oversight. The first products of GEOs largely benefited agribusinesses and farmers. Previous studies support the hypothesis that consumer

Figure 8

### Influence Diagram for Relationships of Criteria to the Public Confidence Outcome

Using a weaker correlation significance cutoff ( $p < 0.05$ ), positive correlations of several criteria with the outcome of public confidence were seen.



benefits are important for public acceptance of emerging technologies. For example, Michael Siegrist<sup>133</sup> found that perceived benefits and risks are affected by trust and that both influence public acceptance of biotechnology. In our study, we combined the risks and benefits into the “health and safety” outcome, and saw significant relationships in expert scores between this outcome criterion and attribute criteria of informed consent, public input, and treatment of intellectual property (Figure 6). It would be interesting to test whether these features of oversight affect public trust, perhaps through increased consumer health and safety benefits. Future studies are needed to survey the public and stakeholders to explore the complex relationships between public trust and confidence; oversight attributes of public input, treatment of IP, and informed consent; and perceived or real consumer benefits.

Another theme that arose in the interviews, but was not directly covered in the criteria, was interagency relationships and political systems of oversight. Several comments from the interviewees focused on the lack of interagency cooperation, controversies over political territory, and inadequate sharing of information between agencies. These problems can impact outcomes of oversight according to our expert group. The Coordinated Framework primarily involves FDA, EPA, and USDA and focuses on GE plants and microorganisms. Some products, like GE plants containing pesticidal proteins (plant-incorporated protectants) are overseen by all three agencies. Several other federal agencies, such as the Fish and Wildlife Service of the Department of Interior and the National Marine Fisheries Service of the Department of Commerce, could be involved for more emergent GE products

such as GE fish and insects, depending on the gene, the use of the GEO, and location of release.<sup>134</sup> Over and under coverage of risks and lack of coordination are important issues highlighted by the literature.<sup>135</sup> Several of the experts interviewed in this study highlighted problems with interagency coordination and their adverse effects on health and safety, public confidence, and research and innovation. Related to these comments are our experts’ scoring of institutional structure as highly complex (Figure 3). Complexity could negatively affect coordination among regulatory bodies, which in turn could decrease public confidence and reduce other positive outcomes of oversight such as health and safety.

### Discussion

We have demonstrated a methodology that uses three types of evidence to evaluate oversight for a set of technological products, GEOs in food and agriculture. Our integrated oversight assessment approach<sup>136</sup> was based upon diverse perspectives and multi-disciplinary criteria in a policy analysis framework. Through evaluation in three different ways (interviews, quantitative expert elicitation, and historical literature analysis), we were able to critically examine GEOs oversight and more broadly generate hypotheses about relationships among features and outcomes of oversight. There were weaknesses in each of our evidence gathering approaches, and hypotheses will need to be tested across other historical models. However, the use of three data gathering approaches, and cross-comparing the results from each one, strengthens the analysis. Although none of the components of the overall methodology is brand new, we cannot find any published work that uses a blend of expert elicitation, MCDA, interviews, and normative and literature analysis to evaluate oversight systems from multi-disciplinary perspectives.

Our first line of evidence, quantitative expert elicitation, had its shortcomings, both in the limited sample of experts and biases which could affect the accuracy of the results. Motivational biases relate to incentives for experts to report scores that do not truly represent their beliefs, and they may be conscious or subconscious.<sup>137</sup> Again, members of a stakeholder group do not necessarily have uniform views about GEOs oversight, but differences between groups as a whole were seen. We saw a difference in scores from industry experts (mean=75) and experts with other affiliations (means=31 to 49). This could be due to motivational biases or true beliefs about the GEOs system based on different experiences with it (for example, data submission processes) or more positive judgments about its features and outcomes. On the flip side, certain mem-

bers of NGOs may also have scored GEOs oversight lower for motivational reasons, because of different experiences with the system (for example, adversarial interactions with other organizations, such as through legal petitions), or more negative perceptions. Academics and government scores were more moderate overall. For many elements of GEOs oversight, there was significant disagreement in the expert scores, often breaking down by affiliation. Our expert data reflect the polarization in the debate about GEOs as portrayed by the media and captured in the literature. If motivational biases were not the predominant factor in expert and stakeholder scoring, the differences suggest that the GEOs oversight system satisfied industry stakeholders more than consumer or environmental groups. We believe that an ideal oversight system would be positively rated by both stakeholder groups. Further research should explore what attributes and outcomes of oversight are most important to different stakeholder groups, as we did not specifically collect or analyze the data to address this question.

From the expert elicitation data, correlation coefficients among criteria in four groups (development, attributes, evolution, or outcomes) were examined to explore relationships between features of oversight and outcomes. We found significant positive correlations between features of oversight such as public input, informed consent, capacity, data requirements and stringency, and compliance and enforcement and outcomes of environmental impacts, health and safety, and distributional health impacts. As discussed previously, these correlations do not confirm causation; however, they are useful for formulating hypotheses. Hypotheses such as the following could be tested across other historical models of oversight: greater public input during development of oversight increases positive health and safety outcomes; greater informed consent during operation of oversight systems increases positive health and safety outcomes; greater capacity during operation increases positive health and safety outcomes; and more incentives for compliance with oversight increases positive environmental impacts.

Additional hypotheses and strengths and weaknesses of GEOs oversight were suggested from our analysis. GEOs oversight had low transparency, little public input, prominent conflicts of interest, little informed consent, closed approach to protecting intellectual property, little post-market monitoring, and few financial resources to develop according to the average ratings of this group of experts. The legal grounding during the development of the system was also considered weak by this group of experts. In the words of one expert, the historical approach to GEOs oversight was “cobbled together” using existing laws

and agencies, which led to either the reality or perception that the legal hooks for regulation were not that strong. In addition, the FDA’s process has remained voluntary although the agency published and solicited comments on a mandatory process in 2001.<sup>138</sup> Public confidence suffered as a result of the patchwork system and FDA’s voluntary process, as mentioned by several experts. The literature<sup>139</sup> and the positive correlation between data requirements and stringency as an oversight attribute and public confidence as an outcome (Figure 8) support the link between mandatory oversight and public confidence that was made during the interviews. As the three lines of evidence converge on this hypothesis, it is ideal for additional testing across other historical models. Furthermore, future policy options for emerging technologies oversight should consider whether a mandatory system is more likely to promote public confidence.

Insufficient oversight for environmental safety is a weakness that emerged from both the literature and interview data, although environmental safety as an outcome was rated somewhat positively on average in the quantitative expert elicitation (Figure 3). Several interviewees criticized USDA-APHIS’s environmental assessment processes, and there have been notable court challenges to the agency, as discussed previously. Some interviewees indicated that there has been no detectable harm from GE crops to the environment and humans to date. However, others noted prominent cross-contamination events through gene flow or product mixing, which can be of human health (Starlink, pharmaceuticals in GE crops), cultural (Bt corn in Mexico), or ecological concern (Ht creeping bentgrass in OR) (see Introduction and Figure 1) and the lack of post-market monitoring to detect impacts should they occur. As discussed previously, USDA-APHIS has been challenged and lost in federal court over complaints about the rigor of the agency’s review processes.

The GEOs oversight system was rated by the experts as highly complex. Complexity in oversight may impact research, innovation, and product development. In the interviews, several experts attributed decreased innovation to the complex system for oversight, as well as public concerns over risk and societal issues. Genetically engineered animals have been stalled for approval for over eight years, and approvals of GE plants for marketing are also on a downturn (<http://www.isb.vt.edu>). However, we did not see significant correlations between any attribute criteria and the outcome of impacts on research and innovation. Some of the literature cited the effect of high oversight costs on prohibiting research and innovation. In the interviews, a few experts suggested that, as a consequence of a complex regulatory system, it takes a substan-

tial investment to get a GEO product approved (see *Impacts on Research and Innovation*). Complexity and cost seem to give advantage to larger companies over smaller ones, and smaller companies who are dealing with orphan GE products that might ultimately have broad social value may not survive. However, from the quantitative data, we did not see any significant correlations between institutional structure (complex or simple) and other attributes or outcomes of oversight.

An important goal of our work was to derive hypotheses and evidence-based lessons for the oversight of other emerging technologies, such as nanotechnology. Nanotechnology involves a broad set of methods, products, and applications at a very small scale — about the size of several atoms or a biological molecule like a protein. Nanotechnology products are rapidly entering the marketplace, and there has been significant debate in the literature about how these products should be overseen.<sup>140</sup> At the nanoscale, materials have been shown to take on novel electrical and other properties, such as higher reactivity and penetrability, and questions arise as to whether there should be special consideration of nanotechnology products in oversight systems. Nanotechnology differs from genetic engineering in that it does not always involve biological material. However, it can, and products of nanotechnology that relate to GEOs in food and agriculture include the delivery of genetic material to plants and animals using nanotechnology, and more broadly, engineered nanomaterials used in food and agriculture.<sup>141</sup>

Interview data was collected on how lessons from GEO oversight can inform the debate about nanotechnology oversight (see *Methodology*). Experts in this study generally had more experience with GEOs but were cognizant of emerging products of nanotechnology and issues associated with them. They recommended several elements for nanotechnology oversight that stem from their views on GEOs oversight:

- regulations tailored specifically to nanotechnology;
- conscientious consideration of public perceptions from the outset;
- fostering public confidence with greater transparency;
- expecting the unexpected;
- having solid risk-assessment programs;
- a proactive approach on the part of industry to deal with the regulatory system as well as consideration for safety first;
- a need for meaningful upstream public engagement;
- clarity in agency authorities;
- opening up safety studies to the public;

- significant resources to the government agencies involved in oversight;
- careful and transparent upfront thought about regulation;
- concerted education efforts about emerging nanotechnologies;
- inclusive development of the regulatory systems;
- consumer or social benefits as a priority in the technological products;
- widely distributed post-market monitoring; and
- clear and rigorous standards.

A few interviewees indicated the importance of science-based risk assessment for nanotechnology product reviews and did not think that social and economic impacts should be considered in the review process. This viewpoint contrasted with several other interviewees that stated the need for upstream public engagement<sup>142</sup> and consideration of public values.

In the interviews, one expert stated that nanotechnology oversight should be as clear and coherent as possible for companies, particularly small ones, and that although oversight should be rigorous, it needs to promote innovation, not stifle it as might have been the case with GEOs. GEOs oversight was rated as highly clear in its subject matter according to this group of experts (Figure 3). Clarity in subject matter could be considered a strength of the GEOs oversight system — one that could be a lesson for other emerging technologies. For example, nanotechnology oversight has been seen as difficult because of a lack of a common definition and understanding of what nanotechnology is and what products would be included in nanotechnology oversight.

GEOs oversight was also rated as highly flexible (Figure 3). Flexibility was mentioned as an important attribute of oversight by some of interviewees, as it helps to provide for adaptation in light of the quick evolution of technology. This was a lesson from GEOs oversight in that the system was developed for a certain and limited set of products in 1986, and did not anticipate pharmaceutical product in GE crops, GE insects, and GE animals until recently. The regulatory system has struggled with each of these new types of GEOs<sup>143</sup> (Figure 1). It is difficult to anticipate what products might emerge from nanotechnology 20 years or more from now. On the other hand, flexibility was considered by some of the interviewees as an attribute that could provide opportunities for less rigorous review. Nanotechnology oversight should consider a balance between flexibility that promotes adaptation and anticipation versus flexibility that might decrease rigor and public confidence in oversight.

Currently, no special data is generated for products of nanotechnology in most agencies, like the FDA.<sup>144</sup> EPA's has a voluntary stewardship program,<sup>145</sup> but many nanoproducts are on the market without premarket testing.<sup>146</sup> For GEOs, at least some data needed to be generated for market approval (that is, planting and interstate movement), and no commercial products for environmental release were on the market prior to the Coordinated Framework. From a comparative perspective, a proactive impetus was also a strength of GEOs oversight, and experts rated this criterion in the development of GEOs as slightly positive (low agreement however). Several experts from the interviews indicated that with nanotechnology, oversight has been much more reactive, as the products are in the marketplace without a federal oversight strategy for them.

Other recommendations for nanotechnology oversight emerged from the interviews. Standards for nanotechnology were seen by some of the experts as a positive requirement for industry so that the U.S. can compete in the global market. For GE crops, the contention between the EU and U.S. was in part due to different standards and labeling of products with more than 0.9 percent GE ingredients. Common international standards can promote trade, research, development, and deployment.

It was also recommended that independent experts (free of COI), especially in environmental science, be consulted early in product development and before oversight decisions are made. Many experts agreed that oversight should be informed by those who are not conflicted. For example, for GEOs, USDA has a dual mandate to both promote U.S. agriculture and protect plant and environmental health. Another looming issue is CBI and how it prevents public access to data and information about products and their safety (see Strengths and Weaknesses). Several experts mentioned this as a challenge for both GEOs and nanotechnology oversight. For oversight of emerging technologies, mandatory, transparent, and independent processes with opportunities for public input seem desirable.

One broad suggestion to address the uncertainty and complexity of many aspects of nanotechnology and oversight was to focus on general oversight principles instead of specific mechanisms (for example, transparency, informed consent, public input, independent reviews). A move towards "principle-based" oversight could avoid the rigidity of systems and increase public confidence at the same time. However, more work would need to be done to see what institutional and legal frameworks would be necessary to support such an approach. Criteria and lessons described herein could form the initial basis of "principle-based oversight"; however, they would first

need to be vetted by additional experts, the public, and stakeholders; and their deployment in systems would need to be carefully considered.

In summary, our analysis suggests several lessons for oversight of emerging technologies:

- the importance of reducing complexity and uncertainty in oversight for minimizing financial burdens on small product developers;
- consolidating multi-agency jurisdictions to avoid gaps and redundancies in safety reviews;
- consumer benefits for advancing acceptance of products;
- rigorous and independent pre- and post-market assessment for environmental safety;
- early public input and transparency for ensuring public confidence; and
- the positive role of public input in system development, informed consent, capacity, compliance, incentives, and data requirements and stringency in promoting health and environmental safety outcomes, as well as the equitable distribution of health impacts.

The approach used herein is instructive for more comprehensive analyses of oversight systems, developing hypotheses for how features of oversight systems affect outcomes, and formulating policy options for oversight of future technological products. From a broader perspective, our approach can address the difficulties with judging oversight from multiple disciplines and perspectives and help to develop common principles of "good oversight."

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## Appendix I

**Semi-standardized Interview Comments Organized by Question**

Each row indicates one thematic statement by an interviewee.

<b>I) How do the development and characteristics of the GEO oversight system affect outcomes such as: consumer or public confidence, health and environmental impacts, and innovation and economic development?</b>
<input type="checkbox"/> USDA APHIS (Animal Plant Health Inspection Service) evolved its system in light of NAS/NRC reports, by hiring more ecologists, banning canola for pharmaceutical (production), and imposing greater(field trial) isolation distances.
<input type="checkbox"/> FDA oversight, which is voluntary(for GE food safety) seems very weak, but it is transparent and few complaints.
<input type="checkbox"/> USDA (review process) has some levels of transparency – like the website and FONSI ( Finding of no significant impacts) documents. However, CBI(confidential business information) issues don't make sense, as the 2002 NRC committee petitioned for USDA documents, and they were slow and uncooperative. It seemed intentional.
<input type="checkbox"/> Now, with the creeping bentgrass, field trials there has been intentional slowness. Will transgenes be kept under control with (USDA's field trial) notification process? (There is) 13 miles of wind pollination and contamination from this grass. Scots and Monsanto are in a compliance violation with the trials. Field trial applicant should not be allowed to let genes "establish" in wild relatives. Their (the companies producing the grass) argument is living hybrid seeds are not established. Now they are trying to kill the grasses that have the transgene. Public confidence in this situation is LOW.
<input type="checkbox"/> (USDA) APHIS regulator has stated on the record that "a good regulatory never denies an application".
<input type="checkbox"/> (USDA) APHIS culture is a history of arrogance, until very recently.
<input type="checkbox"/> They stretched existing authority. This did not build great confidence in oversight.
<input type="checkbox"/> Because the system was cobbled together for GEOs it alienated a significant chunk of the population. This affected public confidence. However, sometimes there is an advantage to having multiple agencies, however, in this case it was cobbled together to make the system. (This) stretched existing authority.
<input type="checkbox"/> Lack of transparency did not build great confidence in oversight.
<input type="checkbox"/> Most decisions other than Starlink were appropriate.
<input type="checkbox"/> (National Environmental Protection Act) NEPA is not effective for assessing environmental effects.
<input type="checkbox"/> Regulation of agricultural biotechnology has been frustrating. EU and US have different safety approaches leading to serious market problems. Different timings of approval. Recalcitrant market controlled pace as a result.
<input type="checkbox"/> For pharmaceutical production in crops – U.S. depends more on voluntary compliance.
<input type="checkbox"/> Consumer/ public confidence is not as high as it should. However, people don't seem to care that they (GEOs) aren't regulated well. Seems to be apathy until there is a crisis. People cared about Starlink corn for a couple days. GEO crop plants were never really regulated. It should affect consumer confidence more than it is. There were stupid, not scientific arguments (against regulation) that became scientific when stated by scientists. At one point in time, things that were genetically engineered into plants didn't need risk assessment when they would have if sprayed on plants.
<input type="checkbox"/> Environment (advocacy) groups are funny with respect to what issues they choose to pursue. What they choose to cover has a large effect on the oversight system.
<input type="checkbox"/> Health and environmental effects are affected enormously by GEOs oversight. The environmental assessments and Environmental Impact Statements (done by USDA APHIS) were totally "hokey" [poorly completed]. There was such a lack of studying the ecological effects of these plants. Major issues with respect to food safety. We did some sort of experiment on the American public. Things such as the current (media) story of plants becoming resistant to pesticide are interesting because, well duh, we knew that.
<input type="checkbox"/> In the U.S. oversight generally improves consumer confidence as people have the philosophy that oversight can be representational and knowledgeable.
<input type="checkbox"/> For Environmental Health and Safety, unknowns and uncertainty are not well understood. Oversight favors most conservative social norm.
<input type="checkbox"/> Large industry doesn't necessarily worry about oversight as long as it is evenly applied and anticipated.
<input type="checkbox"/> International oversight is problematic in light of world trade, and there is a need for uniformity.
<input type="checkbox"/> Consumer confidence has had a major effect on GEOs development. U.S. consumers are accustomed to oversight for safety and this helps make people confident with regulators. However, this is not enough by itself because consumer attitudes have shifted. They are demanding that their considerations be taken into account and demanding more empowerment.

<input type="checkbox"/>	Health and Environment outcomes are where the standard is set for oversight concerning what is necessary from a risk perspective, although sometimes people will disagree. It seems balanced if some people like it and some people do not.
<input type="checkbox"/>	Current GEOs regulations are commensurate with the risk involved. There must be clear standards and one must guard against risk with a responsible development process.
<input type="checkbox"/>	When the situation is disproportionate on one side or the other, then it hurts economic development. Furthermore, if regulations are too lenient then consumers will not be accepting of the product and that will hurt economic development. In other words, we need balanced regulation.
<input type="checkbox"/>	Costs a lot of money to get a decision through, which favors large companies.
<input type="checkbox"/>	High degree of regulatory uncertainty in animal biotech has disadvantaged smaller companies.
<input type="checkbox"/>	Unclear jurisdiction between EPA/FDA and USDA causes people to sense "confusion" — affects public perception.
<input type="checkbox"/>	Narrow interpretation of authorities is the biggest predictor of impacts over time.
<input type="checkbox"/>	Resources, financial and personnel, are important for outcomes.
<input type="checkbox"/>	Compliance and enforcement require resources.
<input type="checkbox"/>	Transparency is important.
<input type="checkbox"/>	Small start-ups and universities lack resources for compliance.
<input type="checkbox"/>	EU discouraged developed countries from adopting GE crops. Narrowed the market and had some affect on innovation, probably.
<input type="checkbox"/>	Pure out of pocket cost of approval not as much as an issue as length of time.
<input type="checkbox"/>	U.S. approach inspires consumer confidence. EU politicized approach means less consumer confidence.
<input type="checkbox"/>	If a person really felt that GEOs weren't needed and bad, they wouldn't fit well into USDA.
<input type="checkbox"/>	Sometimes halting innovation and development is a good idea. Stupid, useless, environmentally dangerous research should be stifled.
<input type="checkbox"/>	The oversight process has been out of public view: done through the OSTP (Office of Science and Technology Policy) during the Reagan years. People didn't know what was going on in the initial development of GEOs oversight; it only appeared in the federal Register which is generally not observed by the public.
<input type="checkbox"/>	This is also not a transparent process. We would have gotten to the same place with transparency as well.
<input type="checkbox"/>	It has been an interesting ride. In the beginning there was a lot of fear mongering toward research, field experiments, and GEO introduction in to commerce.
<input type="checkbox"/>	The consumer has not seen any adverse effects, so they have increased confidence in the system.
<input type="checkbox"/>	Consumers seem to be comfortable with how labeling has played out with GEOs. This is one area that has been negatively affected.
<input type="checkbox"/>	In general, people who raise concerns are part of interest groups.
<input type="checkbox"/>	Our regulatory system creates a situation in which, as a company, you realize that you will be reviewed so that creates an additional incentive to weed out any products that may cause regulatory concerns.
<input type="checkbox"/>	The regulatory system has also helped to coerce companies into weeding out products that are risks due to concerns over liability.
<input type="checkbox"/>	Many products have been in commerce for ten years and there hasn't been a single case of health or environmental harm.
<input type="checkbox"/>	There could be some economic harm from GE plants if the genes contaminate wild genes and the farmer is unable to sell his crop to discriminating consumers.
<input type="checkbox"/>	When you have this type of regulatory review process small companies will have a tough time putting out products.
<input type="checkbox"/>	The regulatory review process has developed so that all the plants on the market are major commodity crops because they are the only crops that are grown on such a large scale as to justify the regulatory costs. Minor crops have become cost prohibitive. Academics are also concerned with this.
<input type="checkbox"/>	The regulatory process also impacts companies economically because litigation is an added expense.
<input type="checkbox"/>	The process was no help to public confidence because it is complicated, decentralized, and confusing (who is responsible for what?). Agencies end up passing the buck which led to regulatory gaps.
<input type="checkbox"/>	In the beginning there was some relief, so initially public confidence was good ; then over time public confidence was lost.
<input type="checkbox"/>	Health effects were negative also due to the process being decentralized, complicated, and confusing.

<input type="checkbox"/> Things went wrong, such as open air pollination that causes gene contamination with wild stock.
<input type="checkbox"/> The framework facilitated innovation and economic development due to the lack of vigor in the framework, which helped industry
<input type="checkbox"/> The government has been more of a cheerleader than a regulator.
<input type="checkbox"/> Often agencies take information from industry as “gold cloth” and uses industry information in their assessment.
<b>2) How, generally, did the criteria capture your experiences with oversight for Genetically Engineered Organisms? What elements of oversight that you consider important were missing or not adequately addressed by the listed criteria? What criteria would you choose to supplement the list with? Were there any important areas of oversight that you felt the specific methodology of using criteria did not capture?</b>
<input type="checkbox"/> This is a reasonably complete representation of experience with oversight for GEOs.
<input type="checkbox"/> This is an especially good representation of policy and social aspects of regulation for GEOs. Categories such as medical and microbial should be broken apart, although. This is admittedly hard to do.
<input type="checkbox"/> Members of the public should be solicited for their views about regulation of GEOs.
<input type="checkbox"/> Public perception not stressed, but citizen acceptance was.
<input type="checkbox"/> Agnostic about criteria on technical aspects — don’t know much here.
<input type="checkbox"/> Good criteria.
<input type="checkbox"/> Harder to capture lack of transparency and flexibility.
<input type="checkbox"/> Relationships and trade-offs among criteria are important.
<input type="checkbox"/> Covered it well, but just as a suggestion: Although it may be implicit in it, the sense of checks and balances by different units (administration, judiciary, legislative) is not explicit via the criteria. From a political science point of view. Within the institutional criteria, oversight is constructed as a process as opposed to a structure.
<input type="checkbox"/> Don’t remember specifics of criteria, but seemed fine.
<input type="checkbox"/> I think you covered the waterfront. However, I did not feel comfortable with some of the specific criteria on regulatory requirements — I don’t have good knowledge of what actually occurs for regulatory approval – haven’t experienced it directly. There are huge differences between people like myself and those with personal experiences with the system).
<input type="checkbox"/> No, they are comprehensive and covered waterfront.
<input type="checkbox"/> Product specific attributes of system were not covered. Such as GE fish and release into the environment.
<input type="checkbox"/> They captured oversight well, the areas I thought were specifically important were areas such as: Legal, public input very important. Post-market monitoring Incentives for compliance; Intellectual Property and CBI; Extent of change of system. A good system would be flexible.
<input type="checkbox"/> When does the public get involved.
<input type="checkbox"/> When each product comes online, an environmental assessment should take place.
<input type="checkbox"/> You mean this to be a question about the method design phase. It seems as though you went further in this method design phase. Normally based on other’s work, but you went one step beyond, that is great.
<input type="checkbox"/> The criteria captured the experience reasonably well.
<input type="checkbox"/> Some of the questions were tough to answer.
<input type="checkbox"/> The criteria should have been supplemented. This is because there are three different agencies that regulate GEO products. We should have provided for three different possible answers, one for EPA, one for USDA, and one for FDA because the answers are often different for each one.
<input type="checkbox"/> Should have added the element of litigation because agencies are also influenced by litigation.
<input type="checkbox"/> The criteria list was thorough.
<input type="checkbox"/> Perhaps work on separating agencies, although there is doubt as to how helpful this would be.

<b>3) Any other comments on GEO oversight?</b>
<input type="checkbox"/> The regulation of (GE) animals is based on the end product which does not necessarily mean that the right experts get involved. This is especially insufficient for regulation of environmental safety; they must go out of government and bring in the appropriate experts.
<input type="checkbox"/> Confidence in regulation is not high and public also has low confidence in regulations. This is because the process is not transparent.
<input type="checkbox"/> Flexibility of coordinated framework is a strength.
<input type="checkbox"/> Lack of transparency about authorities and ultimate decision that gets made. Also voluntary components.
<input type="checkbox"/> FIFRA is transparent, but EUP (Experimental Use Permits for field studies under FIFRA) — where is the site — only flaw.
<input type="checkbox"/> FDA notification for NAD (New Animal Drugs for GE animals) — not transparent.
<input type="checkbox"/> USDA-APHIS is improving.
<input type="checkbox"/> GE alfalfa decision with USDA-APHIS was pro-industry.
<input type="checkbox"/> The EU (European Union) is still not embracing technology.
<input type="checkbox"/> Was using pre-existing structures a good thing? Product versus process, BUT novel processes can create novel products.
<input type="checkbox"/> FDA is OK at some level for cloned meat, but USDA should be brought in (this is an example of a situation in which the appropriate experts have not been consulted).
<input type="checkbox"/> We confuse media opinion with public opinion — need to uncouple these. For rBST (recombinant Bovine Somatotropin), the original concern was about the family farmer and putting smaller dairy farms out of business.
<input type="checkbox"/> No reports or studies that say that as a result of regulations there were inadequacies in the products.
<input type="checkbox"/> Regulations were not meant to address social and economic issues, only safety issues.
<input type="checkbox"/> The U.S. framework is adequate.
<input type="checkbox"/> Couldn't say enough how stupid the oversight system was. Totally untrustworthy, with any other industry this would not have been allowed.
<input type="checkbox"/> Clinton administration OSTP papers: Couldn't publish one of the papers they produced, because the EU would realize that the regulatory system was screwed up. Trade trumps all other consideration.
<input type="checkbox"/> GE mosquitoes, the fact we spent any money on R&D is amazing. There are so many barriers to getting that to work it is amazing.
<input type="checkbox"/> There are fungi that can break down lignin, yet these new, expensive, risky GE technologies are pursued because they bring in the research funding. It is the economic influences that make money go places.
<input type="checkbox"/> When government first started dealing with the problem of GEO oversight there were two competing views. One side was advocating a halt to research until all the questions were answered. The other side was advocating for no regulation. The government ended up coming down in the middle and deciding that they would regulate GEOs, but they will regulate them the same as non-GEO products. This was a good choice. The government is using the precautionary principle and the Europeans have actually distorted the principle.
<input type="checkbox"/> Problems with the Coordinated Framework, including: Regulating the product, not process — which was scientifically sound, but inconsistent with public perception. FDA dichotomy between GRAS or food additive was too stringent — need for middle-tier approaches. Benefit-cost calculation did not match up with risk perception calculation. More attention needed to the distinctions between research, pilot, and commercialization. Needed greater recognition of the two roles of "oversight": regulation and market acceptance. Lack of attention to the dose and remedy issues around releases of GE crops that cannot be totally controlled.

<input type="checkbox"/> Mandatory regulation is positively related to public confidence. Mandatory with outdated regulations might stifle innovation however.
<input type="checkbox"/> Both the technical aspects of regulation and what is believed to be true by the public and stakeholders.
<input type="checkbox"/> Trust and public perception are big factors in outcomes.
<input type="checkbox"/> We must look at whether regulations are: 1.) Risk and science based 2.) Proportional to the risk presented 3.) Receiving the adequate resources to enforce them and 4.) there must be a political will to make the decision.
<input type="checkbox"/> Mandatory system raises confidence. Regulation is currently narrowly focused on safety and leaves the market for efficacy and cost effectiveness.
<input type="checkbox"/> Safety 1st. Need for post-market monitoring.
<input type="checkbox"/> Need open scientific discourse.
<input type="checkbox"/> Need to pick right people to participate to get the right scientific answer.
<input type="checkbox"/> Need one agency. If you have subfactors between agency it will adversely affect outcomes. You need coherent system run by one group, open scientific discourse, and serious NEPA documents. An agency gets better at writing NEPA document then. People weren't as interested when it (oversight) first was getting started.
<input type="checkbox"/> APHIS had different CBI policy than EPA, and because of that they often don't share information well. Agency territory is a problem. You would want to have one agency to organize such an effort, otherwise it is too difficult.
<input type="checkbox"/> Before GE plant concerns such as taste and health effects could be dealt with, the biotech people had to think about the agronomic aspects of growing it. So the biggest predictors are the results of greenhouse tests and then field tests.
<b>5) Please explain the most important lessons from the history of the GEO oversight system for the oversight of nanotechnology products (recognizing nanotechnology products will fall into many categories of products)?</b>
<input type="checkbox"/> Principles for oversight of nanomaterials: 1.) precautionary foundation 2.) mandatory regulation 3.) health and safety of public and workers as paramount 4.) environmental protection 5.) transparency 6.) public participation 7.) inclusion of broader impacts such as socio-economic factors 8.) manufacturer liability.
<input type="checkbox"/> One of the most important lessons learned is to promote public confidence. In order to do this the rationale must be explained.
<input type="checkbox"/> The regulations must be based on new regulations or relevant existing ones.
<input type="checkbox"/> Regulators must also expect the unexpected, in other words avoid mistakes before they happen. Avoid the things that happened with Biotechnology.
<input type="checkbox"/> Regulators should have a risk assessment program for nanotechnology.
<input type="checkbox"/> Companies should be proactive, do their own risk work, have their own regulatory liaisons offices, and should consider safety their first concern.
<input type="checkbox"/> Important lesson is to uncouple media and public opinion. People are positive. If there is an adverse event in health or environment then people are going to be concerned. Generally we are a pro-technology society (in U.S.), however, manipulation of DNA makes people uncomfortable — distinct from nanotechnology. GEOs were special in that regard.
<input type="checkbox"/> Need for meaningful upstream engagement.
<input type="checkbox"/> Need for labor and economic stability — for GEOs this disappeared behind other issues like transparency and cultural reactions.
<input type="checkbox"/> Economic issues with nanotechnology will be more visible.
<input type="checkbox"/> Make it clear who is going to regulate what — see that the system is functional and sound. FDA is not as tuned into food and not sure if people connect "food" with FDA. However, FDA is generally viewed as competent (despite Vioxx, et al.).
<input type="checkbox"/> Take public perception into account. With nanotechnology we seem to be doing a better job.
<input type="checkbox"/> Parallels lessons for nanotechnology: with agricultural biotechnology, agencies had a lot of time before explosive growth. However, there was one subset of products initially for GE plants. They had blinders on for others. For nanotechnology, oversight should look to the future.
<input type="checkbox"/> Be aggressive about knowing about lab R&D.
<input type="checkbox"/> Be as transparent as possible related to safety.
<input type="checkbox"/> Nanotechnology would be remiss to keep safety studies secret.

<input type="checkbox"/> Take a Monarch Butterfly approach — look for future Environmental Health and Safety issues and invest more.
<input type="checkbox"/> Get smart people to identify appropriate funding level for EHS.
<input type="checkbox"/> There will be a liability perspective from the food industry.
<input type="checkbox"/> Upstream public engagement is needed.
<input type="checkbox"/> Increase resources to FDA, USDA, and EPA.
<input type="checkbox"/> Assumption of downstream participation by US and EU lead to incredible conflict that might not have been. Need to anticipate, and promote upstream participation. With US, trying to change existing systems of governance to fit GEOs caused a real strain, when some careful thought up front may have prevented that.
<input type="checkbox"/> Was using pre-existing structures a good thing? Product versus process, BUT novel processes can create novel products. Think about this for nanotechnology.
<input type="checkbox"/> Public education is important. GEO and mad cow disease got confused.
<input type="checkbox"/> Development of system should be more inclusive. Coordinated Framework was a closed door process. Need to involve public, not just industry. No people who were thoughtfully critical were at the table.
<input type="checkbox"/> So many missteps with GEOs — pharmaceutical crops and genes in food supply, Bt corn cross-pollinating wild relatives in Mexico — how come developers never thought about these upfront? Do so with nanotechnology.
<input type="checkbox"/> Cultural context — two way education is important — industry and scientists should be informed about biosafety.
<input type="checkbox"/> As R&D development is going on, do more consumer education, people have time to get comfortable with products.
<input type="checkbox"/> First products will shape perceptions. Consumer benefits thought of first and will be a positive for acceptance.
<input type="checkbox"/> Post-market monitoring is important, should be widely distributed.
<input type="checkbox"/> Consumer benefits should be thought of upfront in first products that enter the marketplace. Do not “shove things down people’s throat that they don’t want”. Standards are key to industry SUCCESS, not detrimental. We have a naive view of regulation. Recent administrations are anti-regulation, however, historically, regulation promotes industry. One example is the standards for cellular phones. Motorola almost went out of business because they did not meet EU standards — there was resistance in the U.S. to standards, so the EU developed them first. Now U.S. industry has to comply by EU standards in global economy. In Japan, there are bar codes that tell you where your food comes from. U.S. industry has resisted this and now is lagging behind for food tracking in the global market.
<input type="checkbox"/> There should be early and broad stakeholder engagement. Stakeholders should be defined very broadly meaning: public, NGOs, federal regulators, industry, academia, etc. This will allow regulators to identify areas of major concerns presented.
<input type="checkbox"/> For people to be more likely to accept the products of an emerging technology, the first products pursued should be those that specifically need the novel technology, and that are socially good products. GE papaya in Hawaii is an example, because non-GE didn’t work and the GE variety saved the industry.
<input type="checkbox"/> Nanotechnology has started out differently from biotechnology because there is no pre-market review; many products are already out on the market. This is odd because the lessons from biotechnology should have been to start strict and test early, but this is not the case with nanotechnology.
<input type="checkbox"/> People should insist on a regulatory system based on sound science.
<input type="checkbox"/> Risk assessment should be based on sound science. The regulatory process should not be distorted into a socioeconomic process at the risk assessment stage. Those are political questions.
<input type="checkbox"/> The public should be involved early and often in the process.
<input type="checkbox"/> There is a dichotomy between hype and reality. Nanotechnology is following the same path. This is relevant when talking about cost-benefit analysis.
<input type="checkbox"/> When dealing with emerging technology it is more important to follow precautionary principles. We have hubris. Nature will find a way. There are many unforeseen consequences.
<input type="checkbox"/> We need a new framework that deals accounts for these new substances. Our existing framework will become less relevant and applicable.

<input type="checkbox"/> <i>The manifestations of biotechnology have been profitable for industry. With nanotechnology they promise much public good, but actually industry benefits most. Only the most lucrative uses come to the top like biotechnology.</i>
<b>6) Any other comments on nanotechnology oversight?</b>
<input type="checkbox"/> <i>Nanotechnology oversight is currently not well informed. This is because it is an emerging technology.</i>
<input type="checkbox"/> <i>Like Biotechnology, nanotechnology is a potentially life changing technology. Most applications are beneficial, but a few are not good.</i>
<input type="checkbox"/> <i>Overall, regulators should learn from their experiences with biotechnology.</i>
<input type="checkbox"/> <i>For nanotechnology, we seem to be doing better than GEOs with EHS work. However, job displacement will be Achilles heel – what are the impacts on job opportunities?</i>
<input type="checkbox"/> <i>Agencies seem more open to regulating, not like in the 80s with GEOs.</i>
<input type="checkbox"/> <i>Food industry is now more of a watchdog and does not want to repeat experience with ag biotech.</i>
<input type="checkbox"/> <i>Nanotechnology will have a messy path towards regulation however due do Generally Regarded as Safe (GRAS) and TSCA.</i>
<input type="checkbox"/> <i>USDA Food Safety and Inspective Service hasn't even looked at authorities for nanotechnology.</i>
<input type="checkbox"/> <i>If people really understood it people would be more scared than with biotechnology.</i>
<input type="checkbox"/> <i>Just on the little about nanotechnology, it is a stumper, with the whole definition and with change of material. What does it mean for predictability? Not totally the same as GEO. Nanotechnology is both beyond what we new before of what was natural and beyond our understanding of new properties. So the problem for human society in thinking about it, seeing it, and not knowing what happens. It is difficult to know what is possible through oversight. So, in general, you see a return to general principles. Precautionary principle, transparency, etc, yet you still don't know how well oversight is going to respond and interact with the technology.</i>
<input type="checkbox"/> <i>Nanotechnology seems even further behind than GEOs regulation was. It's in the market and no standards. Swiss Re will not insure nanotechnology efforts. It seems more reactive from an oversight development perspective with nanotechnology than GEOs even.</i>
<input type="checkbox"/> <i>Technology companies for GEOs did not have effective communication with market chain: there is a "rammed down our throats" perception. Take this into consideration for nanotechnology. CBI — Is a serious problem. How do you regulate when you have no access to the necessary information?</i>
<input type="checkbox"/> <i>Totally mistrust science community :the science community should not decide how much regulation it should be subjected to. Sooner or later you are going to have stakeholders involved, so it might as well be sooner. Can't make good regulatory system without broad input from stakeholders and other "independent" people. For example, the mining industry doesn't decide its own oversight system. Need to get outside of influence. When your friends are doing stuff you trust them, and that is a problem with oversight. You need people that are regular people and environmental risk experts.</i>
<input type="checkbox"/> <i>Public engagement: Danish structured version, like consensus conferences. Outside of external influences.</i>
<input type="checkbox"/> <i>"They won't understand it" excuse is bogus as environmental risk is understandable. People can understand the likely impacts of release new technology x, y, and z into environment. Those types of public discussions have to take place. They need to be consistent.</i>
<input type="checkbox"/> <i>No confidence that universities regulate their safety very well for preventing accidental environment release. When desiring release to the environment, need to minimize negative environmental exposure and do it right. Study the basic environmental risks beforehand so that the field trials can be used to study them on a large scale. The lab stuff is kind of understood. Environment is different. Many uncertainties.</i>
<input type="checkbox"/> <i>Ask universities: how careful are these experiments being completed? Planning for field test? (many incorrect assumptions in planning). Field tests for GE trees were designed to see if trees work, not to see what the risks are. Too often products are field tested first to find if it works and how well it works, and then only as an afterthought to try and prove that it is safe.</i>
<input type="checkbox"/> <i>GE pharmaceutical products developed in corn with concerns raised about drug corn crosses with food corn. "Don't want drugs in corn pancakes." Why in corn? We put it there because that is the agricultural crop we knew most about. When you are thinking about product. This whole field is so depressing. Didn't tell where these experiments taking place.</i>
<input type="checkbox"/> <i>Proportion of resources devoted to risk studies in nanotechnology is too small.</i>

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