Commentary: Emerging Technologies Oversight: Research, Regulation, and Commercialization

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The paper by Kuzma, Najmaie, and Larson on "Evaluating Oversight Systems for Emerging Technologies: A Case Study of Genetically Engineered Organisms" uses a collection of techniques to identify the necessary attributes of a good oversight system for new technologies. It looks at the experience in the United States with regard to genetically engineered organisms (GEOs) that have agricultural applications.

That experience had a number of dimensions that made it a usefully illustrative exercise. It began with a generalized Coordinated Framework for regulating biotechnology, whose approach was modified under stress from one that was focused on a product's novelty to one driven (more than initially intended) by the mere application of biotechnological techniques. The traits introduced — herbicide tolerance and pest resistance — required involvement of all the major regulatory laws and agencies. These agronomic traits separated the farmer adopters and beneficiaries of this new technology from the consumers who had to accept its products and accompanying risks, whatever they might be. This assured at least tension between the two and often generated controversy. And, the system that was developed to provide oversight in Western Europe proved different from that in the United States, creating additional stress points and burdens for American oversight.

The result was a framework that altered as experience with agricultural biotechnology unfolded. It created a regulatory system that was cobbled together from a patchwork of existing legal authorities and agencies and a contentious environment for market acceptance because of the separation of those benefited from those exposed to any attendant new risks, which then was complicated further by international trade tensions. In many respects this experience taught lessons by exception rather than by example. Yet, the reality is that many new technologies, including nanotechnology, likely will unfold in a similar setting: an overarching framework that must adapt to stress; a collection of regulatory laws and agencies rather than a single, well-crafted authority; and a range of attitudes toward the new technology and its products.

What lessons did the authors derive from their surveys, interviews, and analyses? First, "in a democracy such as the United States, an oversight system should respond to a range of viewpoints, values and concerns."[1] It needs to take into account consumer concerns along with scientific criteria. The challenge is: how?

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The authors moved from this general premise to a technique called "multi-criteria decision analysis" (MCDA). "MCDA relies on the notion that no simple outcome metric can capture the appropriateness or effectiveness of a system, allows for integrating heterogeneous information, and enables incorporation of expert and stakeholder judgments."[2] In other words, they looked at the attributes of oversight through several different lenses, looking for consensus. That approach defined the paper's "two primary purposes: to evaluate the oversight system for GEOs (based on previous theories of the literature) and formulate hypotheses (ground theory approach) about what criteria are important for good oversight of emerging technologies."[3]

This review will not walk through all the steps taken in the authors' paper, which are well laid out and explained there. Rather, it is enough for present purposes to note the starting and ending points of that analysis. It begins with "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)."[4] For ease of reference, let's call these: trust, benefits, costs, safety, and innovation.

Jumping to the conclusions of the authors' paper, they found "several lessons for oversight of emerging technologies":

- "the importance of reducing complexity and uncertainty in oversight for minimizing financial burdens on small product developers" (i.e., innovation);
- "consolidating multi-agency jurisdictions to avoid gaps and redundancies in safety reviews" (i.e., safety);
- "consumer benefits for advancing acceptance of GEO products" (i.e., benefits);
- "rigorous and independent pre- and post-market assessment for environmental safety" (i.e., costs);
- "early public input and transparency for ensuring public confidence" (i.e., trust);
- "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" (i.e., all of the above).[5]

In other words, the paper enumerates with increasing confidence and specificity the attributes needed in a good oversight system. It is less clear, however, what is the appropriate standard for each attribute, how to achieve each attribute in an ever-changing real world, how much of each attribute is needed, how to manage trade-offs among attributes, and what is the priority to assign different attributes and different ways of achieving them. By being comprehensive in their inventory of attributes, the authors have still left unanswered the tantalizing question of how to operationalize a good oversight system.

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This paper also will leave that question less than fully answered, in large part because it only can be fully answered in practice, not in the abstract. But it may be useful to add to the focus on an oversight system's attributes a discussion of such a system's approach. That is, when should rigor be predominant, when should conflicting concerns be weighed and balanced, and when does testing give way to education? I would like to get at this issue of a good approach to oversight from a unique effort to create a consensus oversight system for products of agricultural biotechnology.

A Three-Phase Approach to Oversight

For roughly two years, I participated in a Stakeholder Forum on agricultural biotechnology, sponsored by the Pew Charitable Trusts. It brought together a spectrum of views — from innovators large and small (i.e., developers of agricultural biotechnology products), through handlers, processors, and manufacturers of food (i.e., users of products of agricultural biotechnology), to consumer and public interest groups (i.e., the market for products of agricultural biotechnol-

ogy). This diverse collection of people with differing experiences and values, under the guidance of trained facilitators and with broad access to governmental, academic, and private sector expertise, attempted to forge a consensus system for regulating biotechnology in the food chain.

The participants were people of good faith. Regular monthly meetings built up trust and shared knowledge. Inputs from experts drew out the history and rationale for specific laws, rules, agencies, and practices. A commitment to secrecy and non-attribution promoted candid exchange. Great progress was made, through analysis in some cases and compromise in others, in bridging differences around key issues such as standards, transparency, flexibility, rigor, public input, agency capacity, and data requirements. Yet in the end we failed to reach a regulatory consensus.

The experience, however, taught more than the elusiveness of agreement on how to oversee emerging technologies. It illustrated the importance of seeing "oversight" as performing at least three distinct and different functions: governing research, guiding regulation, and facilitating commercialization. The research phase necessarily involves the largest risks of uncertainty, the greatest sensitivity on the part of developers to confidential/proprietary information, and large distinctions among institutional players, from resource-strapped entrepreneurs, through academic researchers, to well-funded and profitable companies. The overriding issue in the research phase is risk avoidance, which leads to a preference for "precaution" (that is, requiring evidence of no risk), yet this must be pursued without disadvantaging smaller developers.

The regulatory function arises when a concept has become a product. It involves the familiar agencies — in the case of agricultural biotechnology, they are the Environmental Protection Agency (EPA), the Food and Drug Administration (FDA), and USDA's Animal and Plant Health Inspection Service (APHIS). They apply scientific methods to the assessment of health, safety, and environmental risks. In this phase, precaution gives way to "prudence" (that is, no evidence of risk), and regulatory capacity, public input, and timely decision making become critical considerations.

The commercialization function takes a product the safety of which has been affirmed and whose environmental risks have been weighed by the appropriate regulatory agencies and brings it to market. That the question of environmental risk has been settled does not mean that the issue of perceived risks has been resolved (nor the issue of unforeseen risks from prolonged exposure). Successful commercialization involves earning consumer acceptance in the marketplace, which takes effective "persuasion" (i.e., evidence of benefits exceeding costs).

While oversight involves all three functions, it does not mean that the functions occur serially, one neatly ending before the next begins. All are going on simultaneously with respect to different products, with a breakdown in one function on one product likely to feed back onto other products or phases (e.g., leakage of unapproved Starlink corn into the food/feed supply fanned doubts about the safety of approved products). All may be going on simultaneously with respect to different developers, with lax performance by one developer in one phase potentially poisoning the atmosphere for others (e.g., genetic drift of plant-based pharmaceuticals heightened concern about contamination more generally). And a slip-up by an oversight agency in one phase can taint perceptions of all agencies or phases (e.g., APHIS's weak enforcement of confinement measures gave rise to lawsuits and concerns over environmental safety).

This means that oversight must perform all three approaches well — with respect to all developers and all products. Since "well" does not, in most endeavors, mean "flawlessly," the remedies for errors also require careful attention in their design and execution. In the research phase — where precaution, meaning evidence of no risk, prevails — containment must be complete and aggressively enforced. Research must operate in a "zero-risk" environment, but a release must be followed up with credible risk assessment and minimization strategies.

In the regulatory phase — where prudence, meaning no evidence of risk, is the safety standard — the operative definition of risk is: "the probability that exposure to a hazard will lead to a negative consequence."[6] Risk assessment here is not about weighing costs and benefits. Rather, it is about probabilities of exposure, nature of hazards, and potential for harm. Similarly, risk reduction remedies are about degrees, not absolutes; regulatory risk reduction is about dosage.

In the commercialization phase, scientific risk has been favorably resolved. But perception of risk can linger (or even be played upon by opponents of a technology or product). There are many "risk perception factors," including novelty, man-made over natural, involuntary versus chosen exposure, lack of benefit versus offsetting benefit, dreadful harm versus familiar harm, personal control versus controlled by others, untrusted sources, unfamiliar risks, high levels of uncertainty, and risk to self or loved ones versus to others.[7] Here, persuasion often is needed to overcome emotionally powerful perceptions of risk and to open the door to consumer acceptance in the marketplace.

In other words, an oversight system for an emerging, unfamiliar technology is tasked with avoiding risks when harm is unknown; assessing risks, costs, and benefits when knowable; and assisting acceptance once products are approved. These are inherently contradictory tasks. They require different attributes — or at least a different balance among attributes — for each task. And they entail different remedies when or if an error occurs. So when looking at research and development activities, oversight should take a precautionary approach to risk, with a strong emphasis on avoiding public or environmental exposures, rigorous enforcement of this standard, and timely correction of errors.

Different tasks require different approaches, different remedies, and probably different actors. Necessarily, each phase will embody different emphases on various oversight attributes as well.

When a product comes before regulators for approval, the appropriate approach is prudent application of sound science. Safety is now a function of the chain from probability of exposure through likelihood of a negative consequence, with a number of control points. Managing this risk is different in kind from avoiding exposure, and remedies should reflect this.

When a product is approved, the overarching challenge is commercial acceptance. This requires persuading consumers that risk is minimal and benefit significant. Any post-approval monitoring should avoid needlessly undermining this goal.

Different tasks require different approaches, different remedies, and probably different actors. Necessarily, each phase will embody different emphases on various oversight attributes as well. Failure to think separately (although not necessarily sequentially) about each of these tasks may explain many of the conflicting opinions about an "oversight system" or confusion about priorities. For example, until a risk is known or defined, precaution is the best approach. Once a risk is defined, prudent management of it, especially where offsetting benefits are offered, is preferable to avoidance of risk. Where a threshold has been established below which there is no harm, persuasion to rebut false perceptions of risk is appropriate. And with respect to an emerging technology, all can be occurring simultaneously, which makes oversight of new, unfamiliar technologies particularly challenging.

Some Illustrative Examples

How can thinking about oversight in phases help in applying the attributes of oversight identified in the authors' paper? As a reminder, those key attributes were the following: reduced complexity to promote innovation, especially by small producers; consolidating regulation to avoid gaps; identifying consumer benefits; rigorous environmental risk assessment; transparency for public confidence; and public input into all phases of the oversight system. For ease of reference, again, these attributes are: innovation, safety, benefits, costs, trust, and all of the above.

Research and Development

At the research and development stage, the oversight approach should be precautionary. This should reassure the public that health and safety are being protected through containment requirements that are designed to prevent public release or exposure. Given these rigorous standards, there should not be pressure to release confidential or proprietary business information, which technology developers large and small will appreciate. Avoiding regulatory gaps would be facilitated by mandatory containment/exposure standards. And the issues of consumer benefits and environmental costs or risks are largely deferred at this stage.

A critical issue in this phase of oversight is the appropriate regulatory response to an unintentional release of a product under research. Since the safety standard is precaution — i.e., evidence of no risk — the standard is breeched in fact by the release. Starlink illustrated the problem that then ensues: a release leads to detectable levels of contamination, which imposes both large "clean up" costs and persistence of barely detectable levels commingled with safe products. Both the reality of risk reduction and reduced perception of risk would be aided, if the appropriate regulatory agency did an expedited review to establish a temporary safety threshold below which the contamination is determined to present the equivalent of no risk. This would help to restore normal commerce and public confidence that the danger presented by the unintentional release is being contained without relieving the offending party of clean-up costs. Such a safety standard for contamination would clearly be temporary and would not serve as any precedent for a safety judgment on the trait itself.

Regulatory Review and Approval

As a concept becomes a product for which market approval is sought, the review standard should be one of prudence rather than precaution — a requirement of no evidence of risk. This is the stage when trust, safety, and costs come to the fore. While it also is important to have approval processes that are not onerous for innovators, this must be balanced against the above attributes. Benefits are of secondary importance here but become more important as a product approaches the commercialization stage.

The experience with products of agricultural biotechnology revealed several problems with current FDA authorities affecting trust and safety. One was that FDA, while it had authority to require a product be recalled, did not have authority to mandate premarket approval. While technology developers saw FDA review and approval as mandatory in fact, if not in law (to avoid the devastating effect of a recall), some elements of the public did not find this an adequate assurance. Some means — preferably administrative, but legislative if necessary — may be needed to close this perceived safety gap in order to ensure broad public trust of and confidence in the system.

As problematic as labeling in the post-approval monitoring process is the question of traceability.

Another problem with FDA authority over food uses was that there were only two routes to approval: (1) "generally recognized as safe" (GRAS); or (2) food additive status. This led product developers to seek GRAS status for products that may have been "as safe as" their conventional counterparts, but that were still clearly different. The "food additive" alternative was too lengthy, costly, and restrictive for many of the novel products being brought to the FDA for review.

These extremes established an unnecessary appearance of a trade-off between safety and commercial interests. It was here in particular where discussions under the Pew Stakeholders Forum showed that a middle ground could have been developed with safety standards, testing protocols, scope for public comment, and timetables to a final decision that would have been acceptable to industry and the public alike. U.S. consumer and public interest groups were willing to accept less rigor than European precaution, and product developers were willing to accept biotechnology-based (i.e., process-based) standards that imposed a higher hurdle than that imposed on products of conventional breeding (even though they felt the risks were not higher and, indeed, were often lower).

Another sticking point in the regulatory review process involves post-approval marketing requirements. Food processors, handlers, and manufacturers would not accept mandated, generic labeling requirements like those in Europe (e.g., "contains" or "may contain" GMOs). Consumer and public interest groups acknowledged that such an approach to labeling risked becoming a de facto ban on the technology (as manufacturers reformulated their products to avoid the label) but also felt that consumers had a "right to know" what was contained in food products.

An uneasy truce has grown up around the decision that "organic" would mean, among other things, free from biotechnology. Consumers wishing to avoid GMOs can buy organic products. This, however, is an unhappy compromise all around. It lacks precision for consumers, yet it may unfairly burden organic products long term, if the benefits of future generations of biotechnology products become compelling.

Related to this is the problem of thresholds. Unlike the case above where I advocated setting a temporary threshold for contamination by an unapproved product inadvertently released into the market, the problem here is not one of assessing safety. Rather, it is a question of developing commercially viable systems for keeping genetically engineered and non-genetically engineered commodity streams separate. The more commercially viable it is to maintain separate streams at reasonable cost, the more actual choice there will be for consumers.

The European threshold for "adventitious presence" of GMOs at 0.9 percent is not commercially realistic. It is vulnerable to sampling error, and the remedy (rejection of the cargo) is too costly. A threshold of 5 or 10 percent avoids unduly punishing inadvertent errors, and permitting normal commercial practices like mixing or blending of lots to comply with the threshold makes the outcome even more predictable. This kind of commercial realism is more likely to offer consumers real choices and to give them an opportunity to experience the new technology, rather than be uninformed or unexposed.

A commercially viable threshold and normal commercial practices for compliance also would help avoid the imposition of generic labels. This would open the door not only to a more real consumer experience with products of new technologies, but also to labeling regimes that voluntarily assert the benefits of the

new technologies incorporated into a specific product. Such a labeling regime would help replace generic "warnings" with attribute-specific information about new products, thus facilitating consumer judgments.

As problematic as labeling in the post-approval monitoring process is the question of traceability. Here it is important to distinguish the ability to trace individual lots of a product (for the purposes of facilitating recalls, for example) from the ability to evaluate whether a type of genetic modification is giving rise to unforeseen longer-term risks or whether practices recommended to avoid dangers like pest resistance (e.g., through use of refuges) or genetic drift (e.g., through spacing or timing techniques) are actually being followed. The latter concerns are prudent ones to monitor with respect to new technologies, but that monitoring can be done less obtrusively and at much less cost than through the traceability requirements imposed by the European Community, for example. Under those, identification and control at every stage of the marketing chain is required, at unnecessary cost and with discriminatory effects on imports.

In other words, at the regulatory phase, a prudent approach to standards, protocols, and follow-up can gain public trust, protect public health, and permit private innovation and commercialization. By contrast, extending the precautionary approach into the regulatory phase errs on the side of risk avoidance, while an excessively promotional approach would likely undermine public confidence and, ultimately, commercial success.

Commercialization

Once a product has been approved for marketing, the oversight system should help persuade the public to accept products of the new technology. This has at least three important implications for the oversight system. First, products of an emerging technology should not be burdened with generic labeling or warning requirements not imposed on conventional products that are not safer. There are better ways to inform and educate consumers.

Second, there is an affirmative role to be played in helping the public better understand the emerging technology. Technology developers are suspect in their claims because of their self-interest. The "risk perception factors" that critics of the technology can play upon are particularly powerful with respect to emerging technologies, which are almost by definition unfamiliar, often come from "untrusted" sources, may be embedded in products that consumers feel they cannot control or avoid, and are vulnerable to alarming characterizations.

The benefits of emerging technologies may be small in the initial stages or structured in ways that understate their value, so that conjectural risks may seem to outweigh them. Part of building public confidence is resolving doubts about safety, but part also should be in reinforcing awareness of benefits that may be hard to measure or understand in their full implications. More important, recent research at Yale shows that people tend to react to a new area — like nanotechnology — based on their own cultural conditioning and values. As David Rajeski, Director of the Project on Emerging Nanotechnologies concluded, "How information about nanotechnology is presented to the vast majority of the public who still know little about it can either make or break this technology....this research shows that diverse audiences and groups react to the same information very differently."[8]

This means that it not only is important to communicate positively and proactively about products of new technologies found to be safe, but that the message has to be pitched differently to different audiences. Doubts that some would try to resolve just by understanding the facts will only be removed by more persuasive approaches for those inclined to be skeptical.

Third, there needs to be feedback from this third phase of successful commercialization back into the regulatory review process. Often, market acceptance turns on more than removing concerns about safety or environmental risks, and more than touting a product's benefits. There may be ethical concerns, as with cloning of animals, or environmental uncertainties, as with the risk of genetically altered fish escaping from production ponds and overwhelming their wild counterparts, or contamination worries, as with pharmaceutical traits drifting into the food supply.

An affirmative regulatory finding of no harm is not enough to resolve such doubts. Technology developers, especially smaller ones with limited financial resources, may press marketing efforts ahead in the face of such doubts, jeopardizing public comfort levels with the technology. Food manufacturers may be pressured by interest groups to declare their refusal to use such inputs in their products, cutting short the opportunity to develop consumer experience with the technology. The result can be the rejection of a safe, beneficial development simply because the market was inadequately prepared for it.

In such circumstances, it may make sense to slow official approval until such doubts have been aired and resolved, or until consumers, industry, or both are agreed on a strategy that keeps open prospects for market acceptance. Then, once the persuasion phase has proceeded far enough, the regulatory release can be made with better prospects for public confidence

and market acceptance. A premature release, by contrast, can both blunt commercialization prospects and damage public confidence in the regulatory process.

Summary

As an emerging technology migrates from concept to product to market acceptance, a well-functioning oversight system will shape its approach differently for each phase. With research and development being the most fraught with unknowns, the approach should be precautionary in the science but limited in public participation. As a product enters the regulatory phase, prudent scientific scrutiny, accompanied by a large role for public input, is likely to be the most appropriate. Once a product enters the market, public involvement in its acceptance should be aided by credible persuasion.

The attributes identified by the authors need to run through all three phases, but their relative roles shift with each phase, and the remedies for correcting mistakes or preserving options change in ways that should protect the integrity of the system while minimizing the costs and disruptions. An oversight system that modulates as a product moves through it will not resolve all questions or doubts, but it stands the best chance of getting the mix of attributes attuned to the full range of society's interests.

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