J Nanopart Res (2011) 13:1467–1476
DOI 10.1007/s11051-011-0252-z

SPECIAL FOCUS: GOVERNANCE OF NANOBIOTECHNOLOGY

Governing nanobiotechnology: lessons from agricultural biotechnology regulation

Robbin S. Johnson

Received: 15 January 2011 / Accepted: 18 January 2011 / Published online: 16 February 2011

Abstract This article uses lessons from biotechnology to help inform the design of oversight for nanobiotechnology. Those lessons suggest the following: first, oversight needs to be broadly defined, encompassing not just regulatory findings around safety and efficacy, but also public understanding and acceptance of the technology and its products. Second, the intensity of scrutiny and review should reflect not just risks but also perceptions of risk. Finally, a global marketplace argues for uniform standards or commercially practical solutions to differences in standards. One way of designing oversight to achieve these purposes is to think about it in three phases—precaution, prudence, and promotion. Precaution comes early in the technology or product's development and reflects real and perceived uncertainties. Prudence governs when risks and hazards have been identified, containment approaches established, and benefits broadly defined. Transparency and public participation rise to the fore. The promotional phase moves toward shaping public understanding and acceptance and involves marketing issues rather than safety ones. This flexible, three-phase approach to oversight would have avoided some of the early regulatory problems with agricultural biotechnology. It also would have led to a more risk-adjusted pathway to regulatory approval. Furthermore, it would avoid some of the arbitrary, disruptive marketing issues that have arisen.

Keywords Agricultural biotechnology · Nanobiotechnology · Phased oversight · Precaution · Prudence · Promotion · Governance

R. S. Johnson (✉)
Cargill Foundation, P.O. Box 5724, Minneapolis, MN 55440-4724, USA
e-mail: rjohnson3526@aol.com

The purpose of this article is to use experiences from the introduction of products of agricultural biotechnology (PABs) into commerce in the late twentieth century to help inform the design and implementation of oversight systems for products of nanobiotechnology in the early twenty-first century. Oversight for products is a narrow, but important aspect of an oversight system. It comes after basic research, which poses its own set of uncertainties and risks. It also comes before widespread adoption, where familiarity and experience often become the dominant guides of behavior. It is the fulcrum point at which science enters commerce, with its attendant clashes between private interest and public good.

In North America, that transition for PABs was guided by the Coordinated Framework for the Regulation of Biotechnology (Coordinated Framework). The Coordinated Framework defined a pathway for regulation of agricultural biotechnology that focused on the risk attributes of the products, viewing the process of genetic engineering itself as introducing no new risks compared to conventional breeding.

From the beginning, this created a potential credibility issue that can be illustrated by contrasting different types of genetic engineering. The simplest type is the use of markers to track a product, involving what most would consider as only minor genetic change. At the moderate scale, might be the use of genetic engineering to influence expression of genes naturally occurring in a product. Most people would probably still accept this as "novelty of product," not "novelty of process." The most ambitious form of genetic engineering involves inserting a gene from a foreign species. While the proponents of genetic engineering emphasized the precision of this process, the average person might be more disposed to consider this a novel process, yielding a product that could not occur in nature. Consequently, the Coordinated Framework's science-based emphasis on novelty of trait rather than of process was on shaky ground from the beginning.

The first commercial product of agricultural biotechnology to make a big splash in North America was "Roundup Ready Soybeans" (RRSBs), a product engineered to withstand harm by the Roundup Ready herbicide that kills both weeds and conventional soybeans. Shortly thereafter came Bt corn, a variety engineered to contain a pesticide to control European corn borers, again something that conventional corn could not do.

Had the first PABs been the result of marker or gene-expression techniques, the focus of attention may well have remained on the products' attributes, not the process that created them. But the patently novel products that were the vanguard of the technology understandably raised questions about the process itself. Consequently, it is not surprising that the focus evolved to what is now, as a practical matter, process-based, not risk-based. That is, as products of agricultural biotechnology move from laboratory bench to commercial sale, they are treated differently by developers and regulators than are products of conventional breeding. Once the product is approved as safe, however, there are no generic "post-approval" tracking or labeling requirements.

A second defining characteristic of the introduction of PABs was that they contained novel agronomic traits, not novel end-user traits. Had the first PABs possessed some novel trait that consumers might value (e.g., enriched omega-3), the path of public acceptance might well have been different. But the first traits were agronomic—herbicide resistance and a self-contained pesticide. These traits were well advertised to farmers by the developers of the technology. They also were quickly accepted by farmers. In fact, farmers in North America adopted this new technology faster than any previous technological breakthrough, including hybridization and chemical fertilization (Buttel 1999). Farmers saw the benefits and could translate them to their bottom lines. This was not so for consumers, however, for whom the principal benefit was a long-term gain in efficiency that they would capture through lower food prices than would otherwise prevail.

This hard-to-measure benefit contrasted with critics' claims of "frankenfoods," "super weeds," and dying butterflies. What was a no-brainer for the farmer was a source of concern for the consumer. Given the chance, American consumers would probably have resisted introduction of PABs. They were not given that chance, however, because of curious aspects of the regulatory pathway to market. First, while the Food and Drug Administration (FDA) has authority to recall a product it saw endangering human health or the environment, it could not require developers of PABs to submit their products for prior approval.

Moreover, products placed before the FDA had only two pathways to approval—"generally recognized as safe" (GRAS) status or the rigors required of food additives. Given this choice, product developers preferred GRAS, which required a finding that the novel product was "substantially equivalent" to its conventional counterpart. However compelling the scientific argument might be that RRSBs were "substantially equivalent" to regular soybeans, the fact that they could do something conventional soybeans could not do—resist a herbicide—was a plausible basis for challenging their equivalence.

Finally, the FDA process meant that, once a product was approved for marketing, it entered the marketplace unlabeled. Since manufacturers were aggressively labeling their products in seed sales to farmers, this was not an issue for them. But the products that were made from RRSBs and Bt corn were not labeled to consumers. This seemed to deny a fundamental right of consumer choice and also led organic producers to press the Department of Agriculture (USDA) to make "not genetically engineered" a defining characteristic of the organic

label. It was a marketing decision that seemed to offer the organic industry a short-term advantage. Whether it proves a wise decision in the longer run is another question.

As a result, consumers in North America have been broadly exposed to PABs without any evident harm to themselves or to the environment. Awareness of the technology and its benefits is very high among farmers and generally low among food consumers. Consumers wishing to avoid products containing bioengineered ingredients must select USDA-approved "organic" products or search labels for ingredients to which biotechnology has not been applied. In other words, products of agricultural biotechnology are widely used in North America but not necessarily widely understood.

In Western Europe, agricultural biotechnology experienced a much harsher welcome for a number of reasons. First, soybeans are not grown in the European Community. They flow into the market from abroad under a zero duty binding granted during the Dillon Round of trade agreements. This zero duty binding has been a source of contention with European farmers and officials, largely because it undercuts the Common Agricultural Policy and its goal of propping up prices for European farmers (Runge 1988). Consequently, a rejection of agricultural biotechnology would appear to do little harm to Europe's farmers while helping to slam the gate on soybean imports, at least from the United States. Some corn was grown in the European Community, and some was imported from the United States under an Article XXIV concession extracted by the United States in the wake of the enlargement of the Community to include Spain and Portugal (Kuhn and Wehrheim 2002). On balance, shutting this import door also looked more appealing than having access to the technology.

Second, the idea of going "genetically modified organism" (GMO) free appealed to one of the smaller food retailers in Europe—Iceland Foods—which thought that it would gain a competitive advantage in an otherwise very consolidated industry (Phillips and McNeill 2002). However, Greenpeace and other groups threatened boycotts to pressure the other food retailers to reject products of the technology, characterizing them as "frankenfoods" and their environmental consequences as threatening.

Third, this new technology originated from Monsanto, a U.S.-based multinational corporation at a time when fears that U.S. multinationals were "taking over Europe" were widespread and very emotional. Unfortunately, Monsanto's aggressive marketing of its product only played into these fears, creating another source of resistance (Moore 2001).

European regulators responded to this adversarial reception first by suspending approvals of bioengineered products and subsequently by imposing two standards for product marketing: a requirement that products with more than 0.9% bioengineered ingredients be labeled as "contains or may contain GMOs" and a zero tolerance for any food or feed shipment containing an unapproved biotechnology trait, even if it has been approved in the exporting jurisdiction (EC Regulation No. 1830/2003).

Consequently, the European Community's approach to regulating agricultural biotechnology has been process-, rather than risk-, based from the beginning and has involved labeling and marketing standards that are commercially difficult to meet. Collectively, these measures reinforce the notion that such products are inherently riskier than conventional foods. As a result, food manufacturers have reformulated their products to avoid use of bioengineered ingredients (Gruere et al. 2008), and European Union (EU) consumers have essentially no experience with biotech products, which prevents familiarity from easing their concerns about the technology. In addition, the stringent standards around "adventitious presence" of bioengineered ingredients have forced countries exporting products to the EU either to adopt costly separate marketing channels for biotech products or to refuse accepting the introduction of the technology into their farming systems (Hanrahan 2010).

There are several lessons that can be drawn from these contrasting experiences with "oversight." First, "oversight" of a process that involves the commercialization of science needs to be defined broadly, encompassing not just regulatory findings about the safety and efficacy of a new product from a new technology, but also public understanding and acceptance of the technology and its products. "Science-based" may not be good enough if the result is either poorly understood by the general public or, in the case of some of the early PABs, counter-intuitive.

Second, the oversight process adopted needs to vary the intensity of the scrutiny it applies to novel products of new technologies, not just with respect to risk but also with respect to certain perceptions of risk. Otherwise, market acceptance can become a struggle between developers, who are not seen as credible, and critics, who may have genuine concerns or other agendas.

Finally, sound oversight in a globalizing economy should seek to avoid conflicting standards or to find commercially practical solutions for applying different standards in different markets. Otherwise, the marketplace risks becoming balkanized in ways that may serve no one's interests in the long term.

The purpose of oversight

In a simpler time, people had either direct experience with how products were made or an intuitive grasp of what was involved. The production processes were replicable in the backyard or at the garage workbench. That is no longer the case with many technologies and certainly will not be the case with nanobiotechnology. The science underlying nanobiotechnology is very sophisticated, and the production techniques involved (or required to insure the safety of the products and the production processes) are not easily replicable. Moreover, it is a technology resulting in products that can interact with the environment in ways that are both hard to understand and potentially unpredictable. Simply put, people do not understand how nanobio works. Public perceptions can contribute to unnecessary skepticism about new technologies. People naturally want a sense of security and certainty. They also seem to become less tolerant of risks as their discretionary income rises, especially with respect to products for which they cannot control their exposure.

As the experience with PABs illustrates, this public dynamic exists particularly in the case of foods. The supply chain is long, and attributes that are valued by some links in the chain may not be valued—and may even be feared—by other links. There also is a long history of protection around agricultural practices that informs much of what occurs with respect to policies affecting farming and food. There simply is not a level playing field with respect to technologies "from abroad" or "from multinationals" as compared to locally produced products.

The dynamics with respect to medical applications can be very different, especially where one is treating serious or fatal diseases and the new technology promises a positive outcome or a lower cost not available conventionally (Hoban 1998). On the other hand, resistance in some quarters to vaccinations shows that some will manifest their desire to control an uncertain situation through resisting what "science" tells them serves their best interests.

At some point, the desire for risk avoidance clashes with the reality of the scientific process, which formulates and tests hypotheses with the implicit recognition that increasing knowledge is likely to change our understanding of risks. Advancing science can change what is thought to be safe, for example as with the finding that hydrogenated vegetable oils containing trans fat. Advancing scientific techniques also continuously lower the threshold at which an exposure can be detected. Though the scientific view may be that potential harm only arises at a dosage far above detectable levels, consumers with sufficient discretionary income may still perceive risk at any level.

This combination of increasing sensitivity in detecting exposures and changing understanding of what constitutes risk results in some people being less inclined to rely on scientific experts to assess what is safe. They want to judge for themselves, even though they may not understand the underlying technology. It also broadens the field of risk perceptions, enabling opponents of change to raise doubts about new developments. There is likely to be a complex interplay between acceptance of authoritative voices and the ability to choose to avoid a new technology. This interplay needs special attention as technologies become more exotic or distant from common experience.

There are, however, ways to assuage these attitudes. One is the ability to weigh new benefits against new costs or risks. Farmers, for example, quickly perceived the benefits of pest-resistant and herbicide-tolerant bioengineered seeds in terms of less work, better yields, and lower costs. Food consumers, on the other hand, did not experience these benefits, and their gain—lower food costs over time—was incremental and hard to detect. So, while farmers accepted agricultural biotechnology at a

more rapid rate than any earlier technological innovation, consumers, especially European consumers, saw little to offset the potential risks the technology was alleged to have. Consequently, for benefits to potentially offset costs or risks, they must be real, they must be felt or at least understood, and they must relate to the person's specific interests.

On this latter point, there is some evidence that European consumers are bothered that their resistance to PABs is denying access to such technology to poor developing countries who cannot afford to maintain separate marketing channels but whose agricultural systems would benefit from the capabilities of genetic engineering (SeedQuest 2007). This suggests that not all benefits must be personal, but there must be a fact-based process for weighing costs and benefits. In that process, technology developers carry very low credibility. For example, the claims of technology developers promoting "golden rice" often get unnecessarily discredited by the European public. As a result, other informed observers with fewer vested interests need to weigh in on the debate.

A second potential solution to skepticism around a new technology is transparency. Products developed or approved in secret are certain to encounter more skepticism than those exposed to public scrutiny. The traditional vehicle for increased transparency is public participation in the regulatory approval process. Knowing that doubts were raised and answered is an important confidence-building step in oversight. Transparency, however, must be balanced against the legitimate needs of technology developers for confidentiality around business and research data.

Skepticism also can be assuaged through informed choice. A person free to avoid a product about which she has doubts is likely to be more tolerant of that product being marketed to others than one who has no means to avoid exposure. Moreover, the side-by-side comparison of attributes and price can pave the way for overcoming doubts if the benefits become more tangible and the feared costs do not come to pass. The problem here is one of providing information without assigning stigma. The EU GMO labeling regime ultimately functioned as a ban on agricultural biotechnology. The "contains GMO" label was understandably perceived as a warning. This impression was reinforced by individual lot tracking requirements more typically used for a product recall regime than for a product monitoring system. As a result, food manufacturers reformulated their products to avoid the label, and European consumers ended up with the choice made for them rather than by them.

On the other hand, the North American approach enabled agricultural biotechnology to achieve rapid market penetration in some products (e.g., corn and soybeans going largely to animal feeding or industrial uses) where the modified trait was not seen as reaching human consumers. By contrast, agricultural biotechnology has not yet been accepted in other markets (e.g., wheat and rice used largely for human consumption). This suggests that oversight needs to facilitate understanding, not just usage, if it is to result in acceptance.

The widespread adoption of biotechnology in corn and soybeans and its virtual absence in wheat and rice create problems at several levels. Consumers of wheat and rice are not gaining the benefits that extension of the technology to those products would provide. At the same time, farmers are being denied the benefits that would flow to them, causing them to shift their cropping decisions away from wheat and rice and toward corn and soybeans. As a result, inter-commodity distortions are arising that, if left to grow over time, could become serious problems for the global food system.

All of this argues for a broad view of oversight. It is not just about a science-based regulatory finding that a product is safe and efficacious. Public experience with shifting risks, increasing sensitivity in detecting exposure, and a heightened preference for avoiding risk mean that both the scientific community and industrial commerce need an oversight system that also delivers public understanding and acceptance of new technologies and the products they make possible. A tangible connection to the technology's benefits, transparency at key stages in the oversight process, and informed choice in using or avoiding products of the technology are key tools in delivering that understanding and market acceptance.

A three-phase process of oversight

One way of designing an oversight system that delivers not just science-based findings of safety and efficacy, but also public understanding and market acceptance is to think about oversight in three

phases—precaution, prudence, and promotion. The phases of oversight should vary in their intensity of scrutiny depending on at least four factors: the degree of scientific uncertainty that exists around risk; the potential scale of the hazard that could be presented; the likelihood that exposure could be controlled to minimize or eliminate the hazard; and the size and distribution of the benefits to be achieved. These four factors can help define each of the three phases of an oversight system designed to deliver safety, efficacy, public understanding, and market acceptance.

Precaution

The precautionary phase typically comes early in the attempt to commercialize the technology into specific products. This phase comes during the time when scientific uncertainty about the nature and scale of risk is at its greatest and when cautionary steps are most justified. It is a time when public protection should be an overriding concern. It also is a time when confidential business and research data deserve the most respect and protection, as both the developer and the regulator have good reason to want to maintain tight controls over the development process and what is known about it. Developers are anxious to preserve any potential competitive advantage, and they want to be free to abandon a project without harm to their reputation. Little is to be gained from such factors being widely discussed.

Precaution at this early stage does present a problem for early developers. The first developers to bring products to the regulatory process may encounter more questions and slower responses than those who come later. This may have been an important factor in Monsanto's approach to the marketplace. Knowing that they had an edge on other substantial competitors may have created a "rush to market" that contributed to decisions that ended up undermining European and food grain acceptance of biotechnology.

It is unrealistic to expect product developers to weigh these broader and longer-term industry considerations. That deliberative approach must come from the overseer. In fact, both technology providers and food handlers and manufacturers have encouraged regulators not to approve engineered wheat varieties (and marketing of the grandchildren of cloned animals) in the absence of indications of acceptance from key customers or marketing channels. This is awkward if the regulator is seen as only judging safety and efficacy; it would be a more normal activity for an overseer also concerned with market acceptance.

On the other hand, innovation cannot be held captive to the last adopter. Product approvals should not be delayed simply because one or a few markets are reluctant. To identify this careful balancing act is not to say that it always will be easy, but the alternative of trying to force a technology onto an unwilling market can do long-term damage to the technology's commercial potential.

This also is a time when regulators and developers should be exploring the best means to contain or control any risks or hazards that might emerge. Once one or more of these control and containment options is selected, public discussion is well-justified, but it is likely to create more confusion than comfort to explore a theoretical range of options publicly. An example from agricultural biotechnology concerns a type of soybean rendered more nutritious through the addition of a gene from the Brazil nut. The technology developer conducted allergy studies, which revealed immune responses in individuals with allergies to Brazil nuts. As a result, the technology developer abandoned the project, but the legacy of allergenicity concerns has endured (Nestle 1996). Similarly, critics of agricultural biotechnology forced developers to abandon use of so-called "terminator" genes that prevented second-generation seeds from germinating. They did so to protect the right of farmers to save seeds for planting next year rather than being dependent on buying new seed each year (Weintraub 2003). This has not prevented biotechnology companies from enforcing their rights, but it has removed a potentially useful technology from the tool kit for preventing unwanted spread of gene attributes.

Regulators and developers also should be encouraged to discuss confidentially both the potential benefit of the contemplated product and ways in which those benefits might be distributed most equitably. A frank exchange at an early stage could defuse acceptance issues down the road. Even if it does not change the product mix being brought to market, it can raise both the regulator and the technology provider's sensitivity to the issue of "who benefits." The result might be to reduce the

time it takes for a technology to become available to poorer countries or poorer farmers, or it might accelerate research into traits that would benefit smaller or less commercially rewarding markets as part of a broader, more orchestrated effort to strengthen acceptance of the technology.

Prudence

In the prudential phase of oversight, risks and hazards have been identified, control or containment systems selected, and potential benefits and their distribution broadly defined. The pathway to regulatory decision now needs to be shaped in a way that insures that transparency becomes a prominent concern. This is a time when safety and efficacy are judged and costs and benefits are weighed. Public questions and doubts must get built into the review in a participatory and interactive way. Some of the veil of confidentiality of data also must be pierced in this phase.

At the same time that product developers are being asked to be more open, they also deserve more certainty about the pathway to a regulatory decision. Included should be both the hurdles to be cleared and the timelines to be expected, so that there is a proper balance between caution and innovation. Greater predictability around the approval process' obligations and schedules is a critical factor for product developers.

Properly constructed, this phase of oversight could change the way the unspoken incentives work in the regulatory process. Activists often complain that regulators are captured by the industries they regulate, a charge that gains credence whenever a former regulator moves to a job in industry. The process also attracts criticism because experts consulted by the regulator have ties to industry, even though it often is difficult to find knowledgeable people who do not have such ties. An uninformed regulator, however, should be as unwanted as a predisposed one.

The other risk is perhaps more subtle, but of growing industry concern. In this view, regulators are only vulnerable to criticism from Congress or the public when products they approve result in problems. The incentive for the regulator, consequently, is to err on the side of caution, as she is seldom if ever praised for speeding a new benefit or product to market.

The twin tasks of increasing transparency and public participation while making the timeline and pathway to a decision more certain and predictable could come together in a way that constructively modifies the regulator's role in the prudential phase of oversight. He may become less of a judge and more of a facilitator of constructive dialog among technology developers, public representatives, and outside experts. Timelines force questions and objections to be raised in a timely fashion rather than as a never-ending series of added concerns. Public participation broadens the sense of responsibility to be not just cautious but also sensitive to the potential benefits of an innovation, while the developer gains more insight into the reactions to her offering.

Prudence also means flexibility in adjusting the level of scrutiny to the scale of risk or the degree of uncertainty. Crossing new frontiers demands closer oversight than reviewing new models of established technologies. New scientific understandings should modify review processes and intensities. Oversight, in other words, must adapt to changing risk, knowledge, or public concern.

The two aspects of regulatory approval that seemed most troubling to critics of agricultural biotechnology were that FDA review was not mandatory and that too many products moved through the easy GRAS door to approval. It was not a satisfying answer to critics that FDA's recall authority made prior review and approval of PABs mandatory in fact if not in law. In addition, product developers saw little lost and much to be gained by making review legally mandatory. They did not want to open up the whole law to get there. A practical solution ought to be available here.

The forced choice between GRAS and food additive status underlines the need for a risk-based, tiered approach to review and approval. Calling PABs substantially equivalent to conventional products seemed to abuse the common meaning of those words in the minds of many. At the same time, most people, including industry critics, could acknowledge that not all PABs needed the scrutiny entailed in the food additive process. A similar debate seems to be underway with respect to medical devices. A range of options makes more sense with respect to technologies whose risks are modified by scientific advance, manufacturing experience, and lessons from application.

Promotion

In the promotional phase of oversight, the questions around safety and efficacy largely have been

answered and the costs and benefits weighed. Now, public understanding needs to be deepened, and support must be brought to bear on market acceptance. This is a marketing question rather than a safety issue. Government's role should be neither to label the product (with the risks of branding the product less safe or fit) nor to disregard the "public's right to know" and desire to choose. Rather, it is to design the rules of marketing to insure that communications are fact-based, accurate, clear, and not misleading. It lays out "fair play" rules for marketing rather than content rules for labels.

In many respects, this may be the most controversial role of the overseer and the most difficult to execute. The regulatory model of oversight makes advocacy on behalf of a technology or product that one has reviewed appear unseemly and inappropriate. Yet, a broader understanding of oversight reveals how apt it is for the government to discount false or misleading criticisms. It is done regularly, for example with respect to fears that arise in connection with vaccinations. Similarly, the Federal Trade Commission issues rulings on fair versus misleading product claims, as it did in the case of dairy producers claiming health benefits from dairy products free of bovine somatotropin (BST), a bioengineered dairy cow growth hormone.

The core idea is to encourage the use of information in a manner that is fact-based and not misleading in order to help educate consumers to make more informed choices. The core risk is to avoid letting a regime designed to govern marketing practices veer into the realm of making or implying judgments about safety. The absence of information to the North American consuming public about PABs makes their acceptance in the marketplace limited and potentially fragile. The mandatory labeling and tracking regimes adopted in Western Europe inflated concerns and tended to validate unsubstantiated criticisms of bioengineered products.

The goal of informed consumer choice must advance both objectives. It must insure that the information available to the public is well-grounded, which can at times require public officials to debunk or clarify misleading claims. It also must insure choice. Consumers should be able to follow their own dictates, if they are prepared to pay the extra costs those might entail. They should not, however, have the choice made for them or, in what amounts to the same, have the costs of less-informed choices eliminated.

The public sector also necessarily defines acceptable thresholds for defining a product's profile and the potential remedies available for breeching such a threshold (i.e., a "contamination" or "adventitious presence" incident). Those rules and remedies, however, should be as commercially practical as possible. Commercially practical thresholds, compliance standards, and remedies for contamination are the means most likely to result in side-by-side comparisons, which is the ultimate goal of consumer choice.

The European Community's 0.9% adventitious presence threshold was not commercially viable. It was within the margin of sampling error, which meant that a cargo that tested "GMO-free" on export could test "contains GMOs" on import. The remedy was rejection of the cargo, when blending of separate lots to achieve the threshold was the normal commercial practice with respect to other "contaminants." And, of course, there was no scientific basis for that threshold, which made it function as a trade barrier.

The same was true of the "zero tolerance" for unapproved varieties, even if they had been approved in the exporting country. There was no scientific foundation for zero, and there clearly was no commercially reasonable way to guarantee zero. Again, the cost of failure was rejection of the cargo. Such a scenario was also experienced in the United States under the so-called Delaney Clause amendment to the Food, Drug, and Cosmetic Act, a zero risk standard that prohibits approval of food additives, including pesticides, found to induce cancer in humans or animals. In 1992, a court overturned EPA's policy of regulating pesticide residues constituting a negligible risk under this zero risk standard (Les v. Reilly, 968 F.2d 985 (1992)), and in 1996 legislation removed pesticide residue tolerances from the Delaney Clause altogether, given the scientific and commercial irrelevance of zero in today's world of sensitive detection.

For products whose ingredients are found to be safe, there is room for tolerance levels that respect a consumer's wish to avoid exposure while conforming to commercially attainable standards. Mixing and blending are reasonable tools to have available to remedy breeches of the standard, in the absence of any showing of harm.

The government also can play an important role in international efforts to harmonize standards and remedies and to extend the benefits of new products and technologies to underserved groups. In the case of agricultural biotechnology, the United States and the European Community waged an unseemly campaign to enlist poor developing countries on their respective sides in the battle over PABs. It would have been a better use of resources to identify whether and how the technology might serve the interests of particular developing countries and to find ways to encourage such developments where they would be helpful.

Finally, the government should find efficient ways to monitor post-approval product performance to provide the public assurance that unanticipated developments do not arise that would qualify the initial safety finding; this can usually be accomplished well short of product-tracking systems that convey a suspicion of potential harm. This seems to be particularly important for products like those that come from agricultural biotechnology and will come from nanobiotechnology. These products are biologically active, which raises some uncertainties about their long-term effects on people and the environment. Perhaps more importantly, post-approval monitoring eliminates the sense of finality that surrounds current product approvals and replaces it with a sense that concerns that have been legitimately raised are not resolved but will be watched. Admittedly, some potential harms could be hard to reverse, but a process of post-approval monitoring can go a long way to replacing strident opposition with watchful vigilance.

The flexible, three-phased approach to oversight laid forth in this paper would offer several improvements over the experience of agricultural biotechnology. The precautionary phase would have helped avoid some of the incidents of release or contamination that occurred in early product-development stages. Mandatory oversight and control is appropriate at this stage of novelty, as are conversations between regulators and developers that can help guide or steer product development away from pitfalls and toward approvable benefits and uses.

The prudential phase would have permitted a more risk-adjusted pathway to regulatory approval than the two avenues under the FDA's "generally-recognized-as-safe" (seen as too easy) or "food additive" (seen as too hard) options. It also would have allowed more public participation and debate around potential environmental risks and containment measures. Furthermore, it would have facilitated public recognition of the potential benefits of agricultural biotechnology while also encouraging developers to broaden the base of beneficiaries beyond large commercial farmers in developed countries.

The promotional phase could well have introduced some of the most substantial changes. It would have militated against both mandatory labeling in the European Union and no labeling in the United States by setting rules for customer communications that divorce marketing initiatives from safety issues. It likely would have avoided "zero" threshold or tolerance levels that discouraged experimentation and commerce. It could have laid a firmer foundation for harmonized standards and practices, again by separating safety from acceptance issues. It could have strengthened public confidence through post-approval monitoring rather than costly labeling and tracking regimes. It also might have accelerated the extension of the benefits of agricultural biotechnology to poorer production regions and less commercialized crops that are now just beginning in earnest.

Shared industry and science interests

At one level, scientific interests in the advancement of human knowledge might be seen as distinguishable from industry interests in commercializing that knowledge. For any sustainable technological development, however, this is a false and shortsighted distinction. If new scientific advances are not commercialized, their benefits are not realized. Furthermore, the failure to commercialize scientific knowledge eventually erodes the funding base for advancement. As a result, it is fair and reasonable to see science and industry interests as fundamentally aligned in the long run, even if they may diverge in some settings.

From this perspective, science and industry share three fundamental interests with respect to the performance of an oversight system. First, both want predictability around the pathway from lab bench to product approval for use. Any individual product developer may like to see that pathway be quicker and less cluttered, but most firms and scientists

recognize that a higher speed to market increases risks of mistakes or public rejection. Thus, a predictable pathway that avoids surprises, unanticipated costs, or excessive delays would enable both scientists and business people to make more informed decisions in allocating scarce financial and human capital.

Second, science and industry share an interest in maintaining a healthy pace in the growth of knowledge about and application of particular technologies. As these technologies become more sophisticated, both the unforeseeable risks that the precautionary phase of oversight addresses and the public resistance that the promotional phase addresses become more important. It also may be difficult to get the right balance of rigor and public participation in the prudential phase, but that issue has been perhaps the most widely explored and discussed. Science and industry want clarity in all three phases, but the most innovative thinking may be needed in the two end points—early development of products and market acceptance of them.

Finally, industry and science share a deep and abiding interest in avoiding post-approval surprises or encumbrances. As to the former, an unpleasant surprise can badly damage the reputation of a company or research community. Post-approval monitoring should be able to provide this safeguard without cumbersome tracking logistics. As to the latter, unjustified public resistance can delay or block benefits that could be both significant and widely shared. Rules around marketing claims will serve this end better than content or process labeling.

For all of these reasons, oversight should be conceived in a broad manner, and the oversight process should be designed as a series of phases that modulate flexibly as a novel item moves from idea to market reality. Otherwise, new technologies and products may find their safety validated but their market acceptance encumbered.

Acknowledgments Preparation of this article was supported by National Science Foundation (NSF) grant #0608791, "NIRT: Evaluating Oversight Models for Active Nanostructures and Nanosystems: Learning from Past Technologies in a Societal Context" (Principle Investigator: S. M. Wolf; Co-PIs: E. Kokkoli, J. Kuzma, J. Paradise, and G. Ramachandran). The views expressed are those of the author and do not necessarily reflect the views of NSF.

References

Buttel F (1999) Agricultural biotechnology: its recent evolution and implications for agrofood political economy. Sociolog Res Online 4. http://www.socresonline.org.uk/socresonline/4/3/buttel.html. Accessed 24 Nov 2010

Gruere GP, Carter CA, Farzin YH (2008) What labelling policy for consumer choice? The case of genetically modified food in Canada and Europe. Can J Econ 41:1472–1497

Hanrahan CE (2010) Agricultural biotechnology: the U.S.–EU dispute. Congressional Research Service, Washington

Hoban TJ (1998) Trends in consumer attitudes about agricultural biotechnology. AgBioForum 1:3–7

Kuhn A, Wehrheim P (2002) A quantitative analysis of EU eastern enlargement. Institute of Agricultural Policy. Market Research and Economic Sociology, Bonn

Moore JA (2001) Frankenfood or doubly green revolution: Europe v. America on the GMO debate. In: Teich AH, Nelson SD, McEnaney C, Lita SJ (eds) AAAS Science and Technology policy yearbook 2001. AAAS, Washington

Nestle M (1996) Allergies to transgenic foods—questions of policy. N Engl J Med 334:726–728

Phillips PWB, McNeill H (2002) Labelling for GM foods: theory and practice. In: Santaniello V, Evenson RE, Zilberman D (eds) Market development for genetically modified foods. CABI Publishing, New York

Runge CF (1988) The assault on agricultural protectionism in the multilateral trade negotiations. Staff paper series, Institute of Agriculture Forestry and Home Economics. University of Minnesota, Minneapolis

SeedQuest (2007) European GM regulations impede the improvement of crops in the developing world. http://www.seedquest.com/News/releases/2007/february/18520.htm. Accessed 24 Nov 2010

Weintraub A (2003) The outcry over "Terminator" genes in food. Bloomberg Businessweek. http://www.businessweek.com/magazine/content/03_28/b3841091.htm. Accessed 24 Nov 2010