

ISSUES IN THE REGULATION
of genetically engineered

plants and animals

executive summary

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Preface

Crops modified via modern biotechnology were first brought to market in 1995 and have been widely embraced by U.S. farmers. Most of these “first generation” crops were designed to help growers control weeds and agricultural pests. Today, science is poised to bring the next generation of agricultural biotechnology products to market. This next generation is likely to involve more complex genetic engineering and a wider variety of plants and animals. Some of these new products will continue to help farmers control pests and weeds, but others will have very different purposes, such as making foods with nutritional benefits and using plants and animals to manufacture valuable pharmaceutical and industrial substances.

When it developed the regulatory framework for agricultural biotechnology products in 1986, the federal government noted that regulations should be reexamined periodically to ensure that they were keeping pace with the technology. Since then, the major federal regulatory agencies governing biotechnology—the U.S. Department of Agriculture, the Food and Drug Administration, and the Environmental Protection Agency—have all issued regulations and/or guidance documents to address emerging issues. But some observers question whether the existing regulatory framework is adequate to address the issues likely to be presented by the next generation of agricultural biotechnology products. Others believe that the system is sound and has sufficient flexibility to respond to any future needs.

In light of the questions being raised by the rapid development of agricultural biotechnology, and with the lessons of 18 years of agricultural biotechnology regulation, the Pew Initiative on Food and Biotechnology (PIFB) believes it is an appropriate time to assess the regulatory framework. This report, prepared by the staff of the PIFB, is an effort to capture the current debate and the variety of perspectives that exist about the U.S. regulatory system, and to make this information available to the public and policy makers.

This report draws on a variety of sources, including the public conferences sponsored by the PIFB over the last several years and the various experts who have contributed to reports published by the organization. The report also draws on the substantial research and analysis that was carried out on behalf of the PIFB’s Stakeholder Forum on Agricultural Biotechnology, a group of stakeholders from the business, agriculture, academic, and public interest communities who met over the course of two years to discuss the U.S. regulatory system for biotechnology. This report represents solely the work of the PIFB staff, however, and does not represent the views of the experts or Forum members.

It is our hope that this report will constructively contribute to the ongoing public policy debate over agricultural biotechnology.

Michael Rodemeyer
Executive Director
April 2004

Executive Summary

Over the last quarter century, the rapid development of modern biotechnology has led to the creation of new varieties of plants and animals containing novel traits that would be difficult or impossible to achieve through traditional breeding. Biotechnology is a powerful tool that has the potential to deliver many benefits, including improved agronomic performance, food products with new consumer benefits, reduced environmental impacts, and new methods for producing valuable industrial and pharmaceutical chemicals in plants and animals. For fish and livestock, biotechnology has the potential to improve animal health, reduce the costs of production, and improve the quality of food derived from these animals.

Scientific reviews have generally found that the risks posed by biotechnology products do not differ in kind from the risks posed by their conventionally produced counterparts. In some ways, genetic engineering is more precise than conventional breeding, because scientists know what genetic material is being introduced and generally understand the functions of the expressed proteins. However, genetic engineering greatly expands the range of genetic material available for modifying plants and animals. Genetic engineering can introduce substances into food that have never been in the food supply before, and can give plants and animals new traits that have not previously been introduced into specific environments.

Concerns have therefore been raised about the potential of genetic engineering to introduce new toxins and allergens into food and to reduce essential nutrients. Concerns have also been raised about potential adverse effects on the environment from the introduction of novel genetic traits, which could inadvertently be passed on to related wild plants or animals, reducing biological diversity and disrupting ecological systems. Plants that have been engineered to express substances to repel pests have raised concerns due to their possible impact on organisms other than the targeted plant pests and the possibility that the pests may become resistant to the pesticidal substances over time.

The question of how best to regulate genetically engineered (GE) foods and other products of agricultural biotechnology has been debated for nearly as long as the technology has existed. Since 1986, biotechnology products have been regulated under a Coordinated Framework of laws administered primarily by three agencies—the Environmental Protection Agency (EPA), the Food and Drug Administration (FDA), and the U.S. Department of Agriculture (USDA). The central premise of the Coordinated Framework is that the process of biotechnology itself poses no unique risks and that products engineered by biotechnology should therefore be regulated under the same laws as conventionally produced products with similar compositions and intended uses.

While genetically engineered corn, cotton, and soybeans have been widely planted in the United States without evident food safety or environmental problems, the introduction of this current generation of GE crops did not occur without controversy. In Europe, the food safety crisis caused by “mad cow disease,” while unrelated to GE food, raised broad concerns among EU consumers about the safety of the food supply and the competence of government regulators, contributing to widespread consumer wariness about GE food. The resulting rejection of GE crops and market demand for non-GE varieties has become a major challenge for farmers, grain processors, grain shippers, food manufacturers, and others in industry. Incidents in the United States have also illustrated the challenge of manag-

ing GE crops. In 2000, traces of StarLink, a GE variety of corn not approved for food use, were discovered in numerous food products. While the highly publicized incident caused no documented harm to human health, product recalls and trade disruptions cost industry hundreds of millions of dollars.

Today, biotechnology developers are poised to bring the next generation of agricultural biotechnology products to market. The next generation of GE crop varieties is likely to include new agronomic traits, as well as more nutritious food and the use of GE plants to make nonfood substances such as pharmaceutical and industrial chemicals. GE animals are also on the horizon, including transgenic animals modified to produce pharmaceutical products or containing traits that improve food production. Many of these genetic modifications will be substantially more complex than the single-gene, single-trait modifications of the first generation of GE crops. The new products are expected to enter into the regulatory review process in the next two to ten years and could pose novel issues for the regulatory agencies.

When the federal agencies first proposed the Coordinated Framework nearly 20 years ago, they acknowledged the need to periodically reassess the regulatory system to ensure it is keeping pace with the technology. Given the rapid development of agricultural biotechnology, and in light of lessons learned regarding the first generation of biotechnology products, the Pew Initiative on Food and Biotechnology (PIFB) initiated an effort to assess whether the U.S. regulatory framework for biotechnology could be improved to address issues likely to be posed by the next generation of agricultural biotechnology products. This report is the final result of that effort. The overarching policy question addressed in this report is whether the existing regulatory system is “good enough” to protect public health and the environment and to maintain public trust, in light of likely future technology trends.

This report does not include policy recommendations; instead, it lays out multiple policy options and perspectives about them. The report focuses primarily on those aspects of the U.S. federal regulatory system that address food safety and environmental protection, in the context of enhancing the current system of shared agency responsibilities. The intent of the report is to provide policy makers with a better understanding of some of the current debates about the U.S. regulatory system for agricultural biotechnology and of some of the policy options that are available, should change be desired.

In developing this report, the staff of the Pew Initiative on Food and Biotechnology has drawn on a variety of sources. Over the last three years, the PIFB has published a number of reports and sponsored numerous public events that have explored various aspects of agricultural biotechnology policy. In addition, the report draws on research and analysis conducted by legal and policy experts for the Stakeholder Forum, a series of facilitated meetings that the PIFB conducted with key stakeholders between 2001 and 2003. The analysis in this report, however, represents solely the work of the staff of the PIFB; it does not represent the views of stakeholders or specific experts.

This executive summary first describes some general issues about the U.S. system being used to regulate agricultural biotechnology products. It then outlines in brief the arguments for and against modifying that system. Finally, the summary describes specific issues and policy options in three topic areas: regulating GE plants for environmental protection, regulating GE crops and foods for food safety, and regulating GE animals. These topic areas mirror the subject matter addressed in Chapters 2, 3, and 4 of the report.

General Issues

The primary purpose of any regulatory system is to protect against harm by assessing and managing the risks of potentially harmful products and activities. At the same time, a regulatory system should provide a clear pathway to the market for safe and useful products. The public trust generated by an effective and credible regulatory system has considerable significance for commerce. Regulation can provide assurance to consumers that they can rely upon the agency's independent expertise and purchase products without concern. These commercial benefits can be lost, however, if consumers lack confidence in the integrity and competence of the regulatory system.

Agricultural biotechnology products are regulated under the Coordinated Framework according to their composition and intended use, and therefore they fall under a variety of laws that contain different definitions, standards, authorities, and procedures. Evaluating the adequacy of this regulatory system to assess and manage risk involves many factors, but this report focuses on five: the clarity of each agency's overall legal authority over biotechnology products; the extent of each agency's pre-market authority; the extent of each agency's post-market authority; the clarity and transparency of the system, and the extent of opportunities for public participation; and the degree of coordination among the agencies. These general issues are summarized below.

- **Overall Responsibility and Legal Authority.** Since the laws used to regulate agricultural biotechnology do not directly address GE products, the agencies have had to interpret those laws to apply them to such products. It is not uncommon for agencies to apply laws to situations or products that were not expressly anticipated when the laws were written, and courts often give deference to agencies' interpretations of their own laws. However, agencies cannot exercise authority beyond that delegated by Congress, and actions beyond that authority can be struck down by the courts if challenged.

Agencies have adopted broad and sometimes controversial interpretations of their legal authorities in order to cover biotechnology products. Should any of those interpretations be successfully challenged, some GE plants and animals could fall outside of regulatory oversight. In addition, the agencies have yet to clearly indicate how the next generation of biotechnology products will be regulated; in a number of cases, new products could plausibly fall under several laws. The choice of law under which to regulate a product has implications for the rigor and transparency of its regulatory review.

Even if a biotechnology product falls clearly within the jurisdiction of a particular agency and law, the law may give the agency authority over only a limited set of risks. In order to ensure a more complete review of the full range of potential risks, agencies in the past have coordinated their activities under their different laws. For some forthcoming biotechnology products, it is not clear whether, even with agency coordination, adequate legal authority exists for agencies to consider the full range of food safety and environmental risks that the products might present.

- **Pre-Market Authority.** How a particular GE product is classified has significant consequences for the type of regulatory review it receives. Some products are subject to a mandatory pre-market approval process in which a developer has the burden of convincing an agency—before a product can go to market—that the product is safe to eat or will not harm the environment. Other GE products can legally go to market without

agency approval, and the burden in these cases is on the agency to demonstrate that a product is unsafe before it can be removed from the market. These differences have several consequences. First, they lead to some inconsistencies, whereby products with similar risks are regulated in different ways. Second, the lack of a pre-market approval process for some biotechnology products (e.g., food) can raise a question about the adequacy of that process to ensure food safety. Third, since some forthcoming biotechnology products could be subject to more than one law, the choice of how to characterize a product will determine whether or not it is subject to pre-market approval.

- **Post-Market Authority.** Different laws provide the agencies with different authorities to monitor and respond to problems that might occur after a product has entered the marketplace. Some agencies have fairly broad powers to require monitoring and reporting once a product goes to market, while other agencies have little or no such power.
- **Clarity, Transparency, and Public Participation.** The processes by which agencies assess and manage risk have important implications for creating trust in the regulatory system. Each law used to regulate agricultural biotechnology products has its own procedures for public notice, public participation, and transparency. Some agencies operate under laws that provide for fairly open and transparent processes, while other agencies' processes are largely closed to public participation and provide only limited information to the public. Also, agencies vary in the degree of clarity provided to developers and the public regarding the procedures for review and approval of biotechnology products.
- **Coordination.** The regulatory system used to govern agricultural biotechnology—like any system that requires coordination among multiple agencies—has the potential for unnecessary duplication and lack of clarity regarding which agency has lead responsibility.

Arguments For and Against Change

The significance of the general issues noted above and of the specific issues associated with each agency (discussed in the following pages) is a matter of debate. Some argue that the current regulatory system has worked well, and that changing the system is likely to generate more problems than it would solve. They argue that the current system is sufficiently rigorous to protect against food safety and environmental risks, and they point to the lack of evidence of any harm to human health or the environment from crops that are currently on the market. They also argue that agencies have adequate authority under existing laws to adapt and respond to needs as they arise. While some legal uncertainties may exist, these observers say, as a practical matter developers are unlikely to challenge agencies' interpretations of their laws. To the extent that developers comply with agency rules, the regulatory system achieves its goal of protecting public health and the environment. With respect to concerns about the credibility of the regulatory system, some argue that the system should focus solely on its risk assessment and management responsibilities and not on public opinion or market concerns. Others acknowledge the importance of maintaining the credibility of the regulatory system but argue that a large majority of the public already has confidence in the system, and therefore it does not need to be changed.

Other observers take an opposing position and argue that the regulatory system needs improvement. In this view, changes are needed to (1) reduce the chances that a potentially

harmful product could bypass regulatory oversight or receive inadequate oversight, (2) provide a clear and predictable regulatory pathway for developers, and (3) ensure consumer confidence in the integrity of the regulatory system. While some observers harbor reservations about some current products and past agency decisions, many who support changing the system are more concerned about the next generation of agricultural biotechnology products. Future GE plants and animals are likely to introduce more complex genetic modifications and novel traits, which will raise more difficult environmental and food safety assessment and management issues. These observers argue that the current system does not provide clear legal authority to cover certain new kinds of products, nor does it give agencies adequate tools to assess risk and prevent harm or detect and respond to harm should it occur. Stretching an agency's authority through creative legal interpretations, some say, exposes the agencies to both legal risks and a loss of consumer confidence. Public trust is likely to be further eroded by processes that are not clear, transparent, nor participatory. These observers argue that an improved regulatory system could help build confidence in biotechnology products and provide insurance against any future biotechnology or food safety crisis.

Regulating GE Plants for Environmental Protection

The EPA and the USDA's Animal and Plant Health Inspection Service (APHIS) each have responsibility for reviewing the potential environmental impacts of some GE plants. The EPA reviews the environmental impacts of pesticidal substances produced in the tissues of GE plants under the authority of its general pesticide law, the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). GE pesticidal substances are known as plant-incorporated protectants, or PIPs. The EPA may also have authority, under the Toxic Substances Control Act (TSCA), over GE plants that produce industrial chemicals. To date the agency has not exercised that authority, however. APHIS reviews most GE plants under its authority to control plant pests under the Plant Protection Act (PPA) and its predecessor plant quarantine laws.

FIFRA requires that a GE plant developer receive approval from the EPA before conducting most field tests of or commercializing a PIP-containing plant. The developer has the burden of proving that the PIP will not cause "unreasonable adverse effects on the environment." FIFRA allows the EPA to take into account both benefits and risks in approving a pesticide product. The agency can impose restrictions on the use of a product, require adverse-event reporting, and "call in" additional data if problems emerge. The agency can also take action against any pesticide that lacks the required pre-market approval, without needing to show that the pesticide could cause harm.

The EPA uses TSCA authority to review new chemical substances for potential environmental harm, prior to their manufacture. The agency has asserted that it has authority under TSCA to regulate plants that have been genetically engineered to produce industrial products (called plant-made industrial products, or PMIPs). Except for GE microbes, however, for which the EPA has issued regulations under TSCA, the agency has yet to act on its TSCA authority to regulate GE plants or animals. Under Section 5 of the law, developers must notify the EPA of a new chemical substance before its manufacture, but the burden is on the agency to demonstrate that the substance would pose an unreasonable risk to the environment in order to take regulatory action.

APHIS's regulation of GE plants is based on its authority to protect plants, from diseases, viruses, insects, and other plant pests. The agency's current rules are based on the now-repealed Federal Plant Pest Act (FPPA), which gave the agency broad authority to regulate the interstate movement of plant pests to protect agriculture. The regulations presume that most GE plants are potential plant pests, because genetic sequences from plant pests (e.g., viruses and/or bacteria) are typically used in transformation processes. Under its regulations, APHIS requires GE plant developers to either (depending on the plant) notify the agency about upcoming field trials or obtain a permit to conduct them. Before a GE plant can be grown commercially, the producer typically asks APHIS to find that the plant is not, in fact, a plant pest. Once APHIS makes such a finding, the plant is declared deregulated and may be grown without restriction. The National Environmental Policy Act (NEPA) also applies to APHIS's regulatory decisions regarding GE plants. This law requires APHIS to prepare an environmental impact statement unless it finds that a proposed action will have "no significant environmental impact."

ISSUES

This report identifies the following issues regarding the regulation, under the Coordinated Framework, of the potential environmental impacts of GE plants:

- **APHIS's Authority over GE Plants.** It appears that APHIS's existing regulations may not technically cover all GE plants, as some genetic transformation processes do not use DNA from plant pests. Although developers of GE plants are complying with the regulations, APHIS may not be able to enforce its rules for some GE plants without other evidence that they are plant pests. APHIS's authority over environmental releases that are purely *intrastate* is also unclear.
- **APHIS's Authority to Consider Environmental Risks.** The FPPA has been used primarily with regard to plant pest damage to valuable agricultural crops. Nothing in the FPPA gives APHIS authority to consider broader environmental risks, such as risks to wildlife or ecosystems. APHIS must consider environmental impacts under NEPA procedures, but NEPA does not authorize the agency to make regulatory decisions on the basis of environmental impacts that go beyond plant pest risks. Further, APHIS lacks a statutory basis for weighing risks and benefits when a GE plant might pose a significant risk to the environment.
- **APHIS's Post-Market Authority.** APHIS currently has the authority to require risk mitigations, use restrictions, and monitoring for GE plants being grown under permit. In many cases, however, the last step in the regulatory process involves a decision by APHIS that a plant is not a plant pest and therefore can be deregulated. At that point, APHIS no longer has legal jurisdiction over the plant and may not be able to enforce restrictions, reporting requirements, or monitoring without new evidence that the plant is a plant pest.
- **Commercialization without Approval.** In some cases, a GE plant can be grown in commercial quantities under APHIS's notification process, which does not include public notice, a separate environmental assessment, or an affirmative decision by APHIS that the plant will not harm the environment.

- **Clarity, Transparency, and Public Participation.** While APHIS's permitting and deregulation process involves the release of some information to the public, some observers (including the National Research Council of the National Academy of Sciences) believe that APHIS could do more to provide public information and engage external scientific advice.
- **The EPA's Post-Market Authority.** Under its current FIFRA rules, the EPA cannot hold growers directly liable for violations of planting restrictions intended to prevent unwanted gene flow or the development of insect resistance. The EPA enforces the restrictions only against the entities with the pesticide approvals (the registrants) and seed companies, raising a question about the adequacy of EPA enforcement.
- **The EPA's Authority over Plant-Made Industrial Products.** The EPA has asserted a potentially broad claim to jurisdiction over genetically engineered plants under TSCA; however, there is an initial question of whether a whole living organism, such as a plant, meets the definition of chemical substance under the law. If the EPA does not have jurisdiction over whole plants, it may be able to claim authority over the genetic constructs and the chemical substances produced in the plants, much as the agency has asserted authority over the pesticidal proteins produced in some GE plants.
- **EPA Exemptions for Small-Scale Field Trials.** Current EPA rules allow experimental field trials of PIP-containing plants to be conducted without prior notification or approval, provided that the trials are less than 10 acres and meet certain conditions intended to minimize the possibility of environmental harm. While such trials are covered by APHIS's notification and permitting processes, the exemption raises an issue about the adequacy of EPA monitoring.

POLICY OPTIONS

Should policy makers decide that the above issues need to be addressed, the report sets forth the following policy options:

- **Clarify APHIS's Legal Authority over GE Plants through Administrative Rules.** In 2000, Congress consolidated the FPPA and other plant quarantine statutes into the Plant Protection Act. The PPA gives APHIS additional authority that could provide a stronger legal basis for its review of GE plants for environmental effects. APHIS has not yet issued regulations under the PPA, but if it does, the agency could regulate GE plants as potential noxious weeds as well as plant pests. A noxious weed is defined in the PPA as a plant that, among other things, has the potential to harm natural resources or the environment. This provision would give APHIS the ability to regulate GE plants on the basis of their potential harm to the environment, rather than using viral vectors and damage to plants as the jurisdictional hook. This approach does not completely solve the lack of a clear environmental decision standard, however. While the law mentions environmental harm in the definition of noxious weed, it does not provide APHIS with a substantive legal standard to use in granting or denying a permit based on broad environmental risks.
- **Clarify APHIS's Pre-Market and Post-Market Authority through Administrative Rules.** APHIS could institute a new risk-based, tiered permitting system under the PPA through which GE plant developers would obtain affirmative approval from the

agency in order to field test GE plants or grow them for commercial use. Such a permitting system would not involve deregulating plants at the final stage. Rather, APHIS would issue general release permits—either unrestricted or containing restrictions to minimize adverse environmental impacts and/or to require the reporting of adverse events. APHIS could also build into the process greater transparency and opportunities for public participation.

- **Clarify APHIS’s Authority through Legislation.** While the above changes could be implemented without changing existing law, Congress could provide greater legal certainty by altering the law to give APHIS explicit direction regarding the regulation of GE plants. In particular, a legislative change could provide APHIS with a clear environmental standard for making regulatory decisions, beyond the procedural provisions of NEPA, and clearer authority over intrastate releases. Legislation could also be more ambitious and create an explicit, mandatory pre-market permitting system for GE plants, providing an independent legal basis apart from APHIS’s plant quarantine authorities. An even more significant departure from current policy would be for Congress to direct APHIS to regulate the environmental impacts of GE and non-GE plants based on the novelty of their traits, rather than on their plant pest or noxious weed characteristics.
- **Clarify Authority Regarding Plant-Made Industrial Products.** The EPA could issue regulations under TSCA to clarify the agency’s role with respect to plants engineered to produce industrial substances. Alternatively, APHIS may be able to regulate such plants under the PPA and coordinate its review with the EPA, to ensure that plants engineered to produce industrial chemicals pose no environmental harm during all stages of development, from field trials to commercial use.
- **Provide Direct EPA Authority over Growers.** If growers’ compliance with planting restrictions for GE seeds becomes a concern, the EPA could consider administrative options for bringing those restrictions under more direct EPA oversight and enforcement.

Regulating GE Crops and Foods for Food Safety

The FDA and the EPA share responsibility for the safety of food derived from GE crops. The EPA is responsible for assessing and managing the risks of pesticidal substances produced by some GE crops, while the FDA is responsible for all other food safety issues that might be posed by food derived from GE crops.

The FDA’s responsibility for the safety of food from GE crops comes from the federal Food, Drug, and Cosmetic Act (FDCA). In 1992, the FDA issued a policy statement indicating that new proteins introduced by genetic engineering that are substantially equivalent to proteins already found in food are likely to be generally recognized as safe (GRAS), and therefore would not require mandatory pre-market approval. (Food additives that are not GRAS, by contrast, do require the FDA’s pre-market approval). A GRAS determination for GE foods focuses on whether the food is “as safe as” its non-GE counterpart.

The FDA encouraged biotechnology developers to voluntarily consult with the agency, however, before bringing GE products to market. In this consultation process, the FDA reviews summaries of safety testing conducted by the manufacturer and, if satisfied, pro-

vides the manufacturer with a letter stating that the agency has “no further questions” and reminding the manufacturer that safety is the manufacturer’s responsibility. In 2001, the FDA proposed making this pre-market consultation mandatory, but it has not acted to finalize that proposal. The FDA believes that it has reviewed, under the voluntary process, all GE foods currently on the market. The FDA has the authority to remove foods from the market if they are adulterated—that is, if they have an added substance that “may render the food injurious to health” or if the food contains an unapproved food additive.

Under the FDCA, the EPA is responsible for setting an allowable level, or tolerance, for the residue of a pesticide in food, or for exempting the pesticide from the need for tolerance. This tolerance is set at a level to ensure a “reasonable certainty of no harm.” Under the law, a food that contains pesticide residues that exceed the EPA’s tolerance is illegally adulterated. The agency can take a food off the market by showing that it contains residues that exceed the tolerance, without having to show that such levels will cause actual harm.

ISSUES

The report identifies the following issues concerning the regulatory system governing the food safety of GE crops:

- **The FDA’s Pre-Market Authority.** Foods from GE crops, like foods from other new varieties of conventionally bred crops, may legally go directly to market without pre-market approval from the FDA unless they are food additives. The FDA has no monitoring program in place nor any practical way of knowing what products are being introduced into the marketplace. The FDA can use its post-market enforcement authorities to take harmful products off the market, but in most cases the burden is on the agency to prove that a product contains an unapproved food additive. Some believe that a mandatory pre-market approval process is needed to ensure the safety of future GE foods, instill consumer confidence, and provide a legal “safe harbor” for food companies. Others believe that the current system has worked well to ensure food safety, and that it enables the FDA to oversee GE foods without unnecessary and costly pre-market approvals.
- **Food Safety Issues Posed by the Adventitious Presence of Unreviewed Substances.** APHIS regulates field trials of GE crops to minimize the possibility of the adventitious presence of low levels of unreviewed genetic material mixing with non-GE food crops. Neither APHIS nor the FDA has clear responsibility, however, for assessing the potential food safety risks of experimental or nonfood-use (e.g., PMIP-containing) crops being grown at the field trial stage. (The EPA does have authority to consider the food safety of PIPs at the field trial stage.)
- **Transparency and Public Participation.** The EPA’s process for approving tolerances, or exemptions for tolerances, for pesticide residues in food is fairly transparent and includes opportunities for public comment prior to an agency decision. The FDA’s food additive approval process is similarly open. To date, however, nearly all GE foods have been reviewed by the FDA in the voluntary consultation process, which lacks transparency and provides essentially no opportunity for public participation. After each consultation, the FDA makes available a summary of the manufacturer’s analysis that provides the basis for the manufacturer’s belief that the food is “as safe as” a comparable conventional food.

POLICY OPTIONS

Should policy makers determine that changes are needed to address the issues discussed above, the report lays out the following policy options:

- **Make Pre-Market Notification Mandatory through Administrative Rules.** The FDA could require product developers to notify the agency before bringing a food derived from a GE plant to market. This would provide the FDA with greater assurance that it is reviewing all GE foods for possible food safety issues before they go to market. It is not clear, however, that the FDA has the authority to impose any sanctions on developers who fail to notify the agency.
- **Add an Affirmative Finding of Safety by the FDA (with or without mandatory notification) through Administrative Rules.** The FDA could make affirmative findings of safety regarding GE crops undergoing the voluntary consultation process. The agency could strengthen the language in the letter to developers to confirm the adequacy of the basis for a developer's conclusion of safety, or it could go further and express its own, independent finding of safety. An FDA finding of safety would provide consumer assurance and a legal "safe harbor" for food companies, but would likely require the submission of more data and additional FDA resources. The FDA probably does not have the authority to combine such a finding with a mandatory pre-market notification requirement. In other words, it would still be lawful to go to market without such an FDA letter.
- **Develop Food Additive Approaches through Administrative Rules or Guidance.** The FDA could choose to apply the food additive approval provisions to GE foods, thereby requiring that each GE food be proven to pose a "reasonable certainty of no harm" before being marketed. The food additive approval process provides for greater transparency and public participation. However, the process is costly and time-consuming. In addition, the FDA would need a justification for reversing decisions it made in 1992 and reaffirmed in 2001 that most genetic modifications are likely to be GRAS, and thus not food additives. Alternatively, the FDA could provide clearer guidance about what GE crops could presumptively be considered as containing food additives, by establishing criteria or listing categories of foods.
- **Coordinate Agency Regulation to Achieve Mandatory Pre-Market Food Safety Review.** Under this option, the FDA would coordinate its food safety review with APHIS's pre-market approval process under the PPA. APHIS would withhold its approval of a food product until it was notified by the FDA that that agency had satisfactorily concluded the food safety consultation process for that product. Because a crop typically is not commercialized without APHIS's approval, this option would in effect create a "mandatory" food safety system. However, APHIS's legal authority to deny a permit or bring an enforcement action on the basis of food safety concerns is uncertain.
- **Provide the FDA with Pre-Market Approval Authority through Legislation.** Congress could amend the FDCA to provide the FDA with a specific grant of authority to create a mandatory pre-market approval process for foods derived from GE crops. This legislative approach could be tailored to create an appropriate approval process that includes all the desired elements. However, legislation would represent a change to established food law and could create new uncertainties and delay the approval of

products. Also, there is a danger that the law could be amended in ways that do not achieve the desired outcomes.

- **Clarify Authority for Early Food Safety Reviews, to Minimize Risks from the Adventitious Presence of Unreviewed Crops.** The FDA has a number of options by which it could conduct early-stage reviews of experimental or nonfood-use GE crops to assess potential food safety concerns relating to their adventitious presence in the food supply. The FDA could encourage early, voluntary consultation with developers. It could conceivably use its food additive authority to consider the likely mixing of experimental genetic material as an indirect food additive requiring proof of safety; it could also provide guidance to establish action levels that would warrant a food safety concern. The FDA could also use its authority to regulate the manufacture of human and animal drugs to impose requirements on field trials of plants engineered to produce pharmaceuticals, for the purpose of keeping them out of the food supply. The EPA could use its authority under TSCA to regulate field trials of plants that produce industrial chemicals; it already exercises this kind of authority under FIFRA for PIP-containing plants. Alternatively, if desired, legislation could be drafted to provide clear authority for the FDA and the EPA to conduct such reviews.

Regulating GE Animals

Like GE plants, GE animals can raise food safety and environmental issues. The genetic modification of animals also raises unique issues associated with animal welfare.

Federal agencies have provided little guidance on how or even whether they intend to regulate genetically engineered animals. A number of laws may have relevance, but their application remains speculative. The FDA may have authority to require a mandatory pre-market approval for all GE animals under its authority to regulate new animal drugs. (The FDA has stated that it is using this authority to review an application for a genetically engineered, faster-growing salmon.) Alternatively, the FDA could use its general food safety laws to simply ensure that food derived from GE animals is safe to eat. The USDA's Food Safety and Inspection Service is responsible under current law for inspecting meat in the slaughtering process; it could have the authority to keep GE animals out of the food supply if they have not been approved as safe for consumption. APHIS may also have some legal authority to address some GE animals under several laws, including the Animal Health Protection Act (AHPA), used to control animal pests and diseases; the Animal Damage Control Act (ADCA), intended to protect crops and livestock from injurious wildlife species; and the Animal Welfare Act (AWA), intended to ensure the humane treatment of research animals. Finally, APHIS could use the PPA to regulate some animals that are "plant pests." However, the agency has not indicated whether or how any of these statutory authorities might be used to regulate GE animals.

The FDCA defines a new animal drug as any article intended to "affect the structure or function" of an animal; thus, a genetic construct inserted into an animal, as well as its expressed protein, could arguably be considered a new animal drug. Under the law, the FDA must approve any new animal drug as being both "safe" and "effective" before it can be marketed. If these provisions were applied to GE animals, developers of GE animals could conduct research under investigational new animal drug exemptions. When a GE

animal is ready to go to market, the developer would apply for FDA approval of a new animal drug. The burden would be on the developer to show safety. The FDA has interpreted the law to require proof that food from the animal is safe for humans to eat and that the animal poses no environmental health risk to humans or animals.

ISSUES

The report identifies the following issues regarding the potential application of existing laws to the regulation of GE animals:

- **The FDA's New Animal Drug Approval Authority.** If applied to GE animals, the FDCA's new drug approval authority would require a mandatory pre-market review of the safety and efficacy of each genetic alteration, including an assessment of the safety of food derived from the GE animal. Defining a permanent, inheritable genetic alteration as a drug marks an expansion of the scope of the law, however, and raises questions about how well it "fits" with GE animals. Assuming the new animal drug provisions apply, they give the FDA only limited power to look at potential environmental impacts; the agency has acknowledged that the law does not provide it with authority to look at environmental impacts that do not have health consequences. In the case of GE animals, one concern is that they could escape and mate with wild relatives, spreading new genetic traits throughout wild populations. It is unclear whether the FDA could properly consider this type of environmental impact under the new animal drug approval process. In addition, the FDA may not have authority over environmental releases that take place in early-stage research, before developers file for investigational new drug exemptions. Finally, by law, the new animal drug approval process is confidential; there is little transparency and no opportunity for public comment prior to the agency's approval of a new animal drug.
- **The FDA's Food Safety Authority.** The FDA could decide not to regulate genetic constructs and expression products as new animal drugs, and instead consider only the food safety issues for animals intended for the food supply under its general food safety authority. While this approach would provide consistency with the GRAS/food additive approach used for foods derived from GE plants, some of the same concerns regarding the regulation of GE plants would apply to GE animals. In particular, the lack of a mandatory pre-market safety approval would be a point of contention. This approach would also leave environmental and animal safety issues up to some other agency to address.
- **USDA Authorities.** The USDA lacks clear statutory authority to administer a program for permitting the release of most GE animals and managing potential environmental, food safety, and animal welfare concerns. APHIS administers a number of laws that could, in theory, partly apply to the regulation of GE animals for environmental and animal welfare issues. The AHPA gives APHIS broad authority to control livestock pests and diseases, but whether it would apply to many GE animals is unclear. Similarly, the application of the ADCA and the PPA to GE animals is very uncertain, although each might have some limited uses.

POLICY OPTIONS

Should policy makers determine that changes are needed to address the issues noted above, the report lays out the following policy options:

- **Clarify the FDA's Authority over GE Animals.** As noted previously, the FDA could regulate GE animals under two different approaches: a food-safety-only approach using food safety law, or a new animal drug approval approach. The approaches involve very different regulatory processes. Under the new animal drug process, genetic constructs and their expression products would require pre-market approval by the FDA for safety and efficacy, while under the food-safety-only approach food derived from GE animals would likely not require pre-market safety approval. Under either scenario, the FDA could provide guidance on how it intends to proceed. While guidance regarding the new animal drug approval process would provide needed clarity, the FDA's authority to address the full range of environmental issues under that rubric would still be constrained, and the approval process would remain closed to public input. Addressing such issues would require legislation. As with any option involving legislation, there are concerns that the law as passed could include undesirable changes, create new uncertainties, and slow down the approval process in the short term.
- **Clarify USDA Authority.** The USDA could provide guidance or issue regulations to implement authorities under the AHPA, the ADCA, the AWA, the PPA, and/or the meat inspection laws to address environmental and animal health and welfare issues. None of these laws provides clear legal authority, however, to establish a system to regulate the environmental release of GE animals similar to APHIS's regulation of GE plants. Should policy makers determine that APHIS is the appropriate agency to regulate those aspects of GE animals, the agency would require additional legislative authority. Policy makers could also consider whether the USDA should be given authority to establish a tracking and identification system to keep GE animals not approved for food use out of the food supply.

Conclusion

In the coming years, new applications of genetic engineering technology to agriculture will continue to be developed and introduced. Marketplace acceptance of the resulting products will largely depend on the ability of the Coordinated Framework to safeguard public health and the environment and ensure public confidence in the regulatory system. The development and market introduction of these products will also be affected by how clearly and efficiently regulatory agencies apply their authorities. This report identifies a number of key issues that have been raised regarding the regulatory system for agricultural biotechnology products, as well as policy options that could be used to address those issues, should change be desired. Interested parties hold a wide array of opinions on whether these issues amount to a compelling need for change, and on whether specific changes would be desirable and beneficial. By compiling these issues and policy options in one place, the Pew Initiative on Food and Biotechnology hopes to provide a constructive addition to the policy debate and a useful reference for policy makers and interested parties.