Chapter 4

Food Safety and Consumer Choice Policy

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Agricultural biotechnology has the potential to help address a wide range of public health, nutritional, agricultural, and environmental problems in developed and developing countries, as described in a wide variety of scientific (NRC 1985), government (Glickman 1999), industry (Council for Biotechnology Information n.d.), and international (Persley and Lantin 2000; FAO 2003) sources. Despite this potential, the commercialization of the first generation of crops based on these technologies has met with concern and protests from consumer and public interest groups (Consumer's Union n.d.), environmental groups (NRDC 2000), and some governments (EC 2000) and scientists (Union of Concerned Scientists n.d.). This conflict has grown to such proportions that it has resulted in the banning or slowing of the commercialization or use of these products in some countries (*Economist* 1999), disrupted the distribution of food aid in drought-stricken southern Africa (*Economist* 2002), reduced U.S. exports of major commodities (*Economist* 2000), affected the value of Wall Street stocks for major agricultural biotechnology companies (*Financial Times* 2000), and become a major issue of contention in the regulation of international trade (*Financial Times* 2003).

Many of the proponents of agricultural biotechnology have suggested that the issue should be resolved through the application of sound science (Prakash and Bruhn 2000) and that it would be unethical to ban the use of or inhibit the potential benefits associated with this technology for addressing serious problems related to public health, nutrition, poverty, and the environment (Leisinger 2000; Pinstrup-Andersen and Schioler 2000). Many of the critics have called into question the adequacy of the scientific knowledge (Wolfenbarger and Phifer 2000; Clark and Lehman 2001) about this technology, questioned its benefits and raised concerns

regarding its potential risks (PSRAST 1998), and claimed that regulatory decisions have been based more on politics than on science (Eichenwald, Kolata, and Petersen 2001; Ferrara 2001).

In contrast to the first generation of genetically modified (GM) crops, which have been designed to address production problems, the second-generation crops currently under development will include a much wider range of alterations. One set will involve changes of potential interest to consumers in developed and developing countries, such as changes in the levels and types of specific fatty acids, vitamins, minerals, phytochemicals, and antinutrients (e.g., phytate). A second set of genetic modifications will focus on agronomic, environmental, and nutritional traits relevant specifically in developing countries, such as drought and saline resistance, insect protection, antiviral and antifungal properties, and enhanced iron, zinc, folate, or pro–vitamin A content, among others. In general, the genetic, metabolic, and food compositional changes in these future crops are expected to be more complex than those of the first-generation crops and may pose more complex regulatory questions (FDA 2001; Kuiper et al. 2001).

The purpose of this chapter is to describe the food safety and consumer issues raised by GM foods, with a particular focus on the choices and trade-offs relevant to southern Africa. Although the ultimate focus of the chapter is on the choices and policy trade-offs relevant to southern Africa, it begins with a detailed analysis of how GM foods are regulated in the United States by the Food and Drug Administration (FDA). This is because FDA policies remain the authoritative position of the U.S. government as applied to the United States and, to a large extent, as projected into international and bilateral discussions and negotiations. Therefore, it is important that developing countries become very knowledgeable concerning FDA policies and their scientific, legal, and political bases so that they can engage in those discussions and negotiations on a more equal footing. In addition, an examination of how the scientific, legal, and political considerations were addressed in the U.S. context holds lessons for southern African countries as they ponder the most appropriate institutional and procedural mechanisms for them to use to reach judgments and develop policies of their own.

The second section of this chapter builds on the first by placing the scientific considerations in the southern African context. This section highlights the significant differences between the U.S. and southern African contexts, the even greater scientific uncertainties in the southern African context as compared to the U.S. context, and the implications for research and policy development. The third and final section provides a framework for discussing policy options and trade-offs under conditions of high complexity and uncertainty, such as in GM agriculture.

Sources and Methods

A large body of literature has already emerged concerning the development of agricultural biotechnology policy, most of it in the past five to eight years as a result of the intense controversy. This includes an immense volume of media reports, popular and semipopular books and magazine articles, industry and trade newsletters, reports and commentaries from a wide spectrum of critical and supportive nongovernmental organizations, special issues of or articles in scientific and social scientific journals, and academic books. Most of these sources contain verifiable factual information (e.g., dates of meetings, names of participants, topics discussed, and decisions). However, they also present selective representations and interpretations of scientific knowledge and health and safety risks, reflecting the views of the authors or the organizations.

An important feature of the methods used in this chapter is the heavy reliance on primary sources, such as documents from the *Federal Register,* reports from the National Research Council (NRC, the working arm of the National Academy of Sciences, NAS), and internal memos of the FDA. These sources are used because most of the debate concerning the regulation of GM foods is based on second- and third-hand representations and interpretations of official policy and its justifications as promulgated by the FDA. Such debate is highly prone to perpetuation of the intentional or unintentional distortions and biases of various parties, especially in light of the scientific and legal complexities and ambiguities posed by GM foods. I acknowledge that the use of primary sources and direct quotes is subject to its own methodological pitfalls, such as biased selection of quotes, misinterpretation of quotes, or presentation of them out of context. However, it has the distinct advantage of grounding the subsequent debates about such matters in the "primary data," in keeping with the established norms for deliberation in science and law.

Disclosure

It is appropriate in a chapter of this type to acknowledge and disclose the important role that the author's views and motivations have played in assembling and interpreting the information. During my roughly 20 years as an applied academic I have devoted roughly half my time to food and nutrition problems and policies of developing countries, half to the food and nutrition problems and policies of the United States. My view concerning agricultural biotechnology is that it holds many potential benefits in developed and developing countries, and I am hopeful that ways can be found to realize these benefits while permitting individuals and countries to reduce or manage the uncertainties and risks. I am acutely aware of the

extent to which agricultural biotechnology poses a distinct profile of risks and benefits in developed versus developing countries, and my strongest commitments on this issue are to ensure that individual countries can form their own informed judgments and policies.

My first reading of the FDA's 1992 policy in the summer of 2000 suggested that science and politics were poorly articulated and may have been seriously misused in this case, thus giving rise to my further investigations. My subsequent research reinforced these initial impressions. My current research and writing on this issue is motivated in large part by my view that scientific knowledge, good politics, and normative considerations all should occupy prominent and explicit roles in addressing this and similar controversies, and I articulated this view in works published before I developed my current interest in agricultural biotechnology (Pelletier et al. 1999, 2000; Pelletier 2001). As agricultural biotechnology, nutritional fortification, and other efforts to nutritionally alter national and international food supplies move forward, I now see that the ability to integrate scientific knowledge, good politics, and normative considerations into policy development, above all, will require governance mechanisms that are more open, inclusive, transparent, and accountable than they generally are today.

Contextual Differences between the United States and Southern Africa: A Preview

Although the contextual differences between the United States and southern Africa will be addressed in greater detail in the second section of this chapter, it is important to note them explicitly at the outset so that the analysis and critique of the FDA's policies in the first section of the chapter can be interpreted in light of these differences. As shown in Table 4.1, the two contexts differ widely in the nature of their food safety concerns; the prominence of agriculture, food security, and malnutrition in the lives of their people; the nature of their dominant health concerns; and their food regulation systems. This may imply that the potential benefits as well as the potential risks of technological innovation may have a disproportionate impact in the southern African context. For instance, one of the lessons from the Green Revolution was that adoption rates for new technologies often were lower than expected among smallholders because they perceived the potential benefits and risks of new technologies differently than did agricultural scientists, and their heavy reliance on agriculture for survival caused them to be risk-averse.

Populations in the southern African context also rely heavily on a small number of staple foods for the majority of their caloric intake, may consume parts of plants considered inedible in the United States, and employ different methods for

Table 4.1 Contextual differences, United States and southern Africa

Contextual features	United States	Southern Africa
Food safety concerns	Microbiological, chemical, bioterrorism, irradiation, genetic engineering	Microbiological
Types of foods	Highly diverse, processed and prepared or cooked; social and ethnic diversity	A few major commodities; non-Western processing, preparation or cooking, and understanding of what are "edible parts"
Food insecurity	8 to 10% of population are uncertain about their future access to food	>50% of population have chronic or seasonal food shortages
Causes of food insecurity	Unemployment, low wages, high costs of living, mental or physical disability	Agroclimatic conditions, low productivity, limited economic alternatives
Food quality concerns	Taste, appearance, convenience, healthfulness, emergent social attributes (whether food is sustainable, organic, ethnic, local, GM-free, etc.)	Taste, appearance, processing, storage
Health concerns	Late-onset chronic diseases, obesity, reemergent infectious diseases, aging population	Endemic HIV, infectious diseases, under nutrition and micronutrient malnutrition, young population
Food production and supply	Industrial, national or international distribution, technology-intensive, 2% of population live on farms	Subsistence and local markets, variable technology, majority of population live on farms
Economic base	Large, diversified formal sector and wage economy	Subsistence agriculture, local-scale economies, small formal sector
Food laws and regulations	Extensive, highly developed; high potential for enforcement	Generally limited regulations and enforcement capacity
Drivers of agricultural biotechnology	Industry, government, scientific establishment	Bilateral and international agencies, transnational industry, national scientists and specialists

Source: Compiled by the author.

Note: Some of the entries in this table require modification or elaboration by regional specialists.

food processing, preparation, and cooking, all of which may have a bearing on food safety. Finally, these populations suffer from widespread malnutrition and infectious diseases, including HIV, which may cause or exacerbate food safety problems that would not exist in healthy, well-nourished populations. This may imply that southern African populations may stand to disproportionately experience the benefits and the risks of GM foods, depending on the nature of the

modifications and how they interact with the food habits and health or nutritional status of these populations.

The nature of the contextual differences just noted makes it difficult or impossible to render an overall judgment concerning the safety of GM foods in the United States or southern Africa. This is because the outcomes ultimately depend on the nature of the genetic modifications, the metabolic and compositional changes induced by those modifications, and how they interact with various contextual features, as discussed in the next section in the context of the U.S. population.

It is important to note that the terms of reference for this chapter are to examine food safety and consumer choice issues. Those terms of reference do *not* include estimating the potential benefits of GM agriculture for improving food security, nutrition, and health status. This is rather awkward because the examination of policy options and trade-offs very much requires that the risks and the benefits be examined in tandem. Thus the final section of the chapter will suggest a framework for such analysis. But the details will need to be filled in during and after the first of the planned roundtable discussions.

The FDA's Policies for GM Foods

Timeline

Table 4.2 presents a timeline of key events related to the development of agricultural biotechnology policy in general, and the FDA's policy in particular. Policy developments are shown on the left, and a variety of scientific and societal events that shaped or responded to policy development are shown on the right. The policy developments shown are described in detail in the chapter. Due to space constraints the societal developments are not addressed in detail, but these are well described in a number of other sources (Charles 2001; Hart 2002; Winston 2002). This timeline is intended to help the reader follow the policy developments described in later sections of the chapter.

Legal Framework

In 1992 the FDA published "Statement of Policy: Foods Derived from New Plant Varieties" (FDA 1992) in response to numerous requests from industry, academia, and the public to clarify its interpretation of the existing regulatory frameworks as they pertain to plant varieties produced by "the newer methods of genetic modification." The 1992 policy included a review of scientific issues relevant to public health, the regulatory status of GM foods, and labeling, along with guidance to industry concerning how they might meet the FDA's regulatory requirements

Table 4.2 Key events in the development of agricultural biotechnology policy, 1973–2002

Policy developments	Year	Societal and scientific events
Gordon Conference held on the safety of bacterial recombinant DNA (rDNA) experiments	1973	Boyer and Cohen perform gene transfer; Singer and Soll letter appears in *Science*
Asilomar Conference held; voluntary moratorium enacted	1975	
National Institutes of Health forms Recombinant-DNA Advisory Committee (RAC); safety procedures developed	1976	Citizens in Massachusetts and California protest rDNA research
Extensive research and containment procedures address safety questions	1978	rDNA bacterium produces insulin
	1979	Public protests of rDNA research subside; rDNA bacterium produces human growth hormone
Diamond v. *Chakrabarty* permits gene patents	1980	Cloned bacteria produce interferon
	1981	President Reagan initiates deregulation
Gore hearings reveal lack of scientific evidence on environmental safety	1983	Ice-minus bacterium developed; first rDNA transformation of a plant succeeds, with kanamycin resistance gene
Bayh-Dole Act allows university patents; Biotech Working Group formed	1984	Regulatory uncertainty hinders biotech research; National Research Council (NRC) issues promotional report
BSCC (Biotechnology Science Coordinating Committee) formed	1985	NRC issues promotional report
OSTP (Office of Science and Technology Policy) Coordinated Framework adopted (June); Food and Drug Administration (FDA), U.S. Department of Agriculture (USDA), and Environmental Protection Agency (EPA) clarify policies (June); Monsanto executives visit Vice President Bush (late in year)	1986	
Public questions the scope of oversight proposed by agencies; BSCC attempts to resolve oversight	1987	NRC issues promotional report; ice-minus open-air testing begins; National Academy of Science (NAS) white paper defines key principles
Regulatory uncertainties continue	1988	NAS–Food and Nutrition Board issues annual symposium report
BSCC unable to reach consensus; OSTP forwards issues to Quayle Council	1989	NRC issues report on introduction of rDNA into the environment; L-tryptophan food supplement kills two dozen people
OSTP proposes Scope of Oversight	1990	

(*continued*)

Table 4.2 (continued)

Policy developments	Year	Societal and scientific events
Quayle Council shapes oversight policy; FDA begins review of FlavrSavr tomato	1991	Gulf War
OSTP issues final Scope of Oversight; FDA issues Statement of Policy; USDA issues proposed rules	1992	Biotech industry rejoices in FDA policy, though some object to political influence in its development; 4,000 citizens request labeling
USDA finalizes its rules	1993	Recombinant bovine somatotropin (rBST) approved by FDA, public protests ensue; Monsanto adopts aggressive strategies under new CEO (Shapiro)
FDA approves FlavrSavr tomato	1994	rBST protests subside
EPA approves *Bacillus thuringiensi* (*Bt*) corn	1995	U.K. and EU approve Roundup Ready soybeans
	1996	GM maize and soybeans commercialized in U.S.; U.K. acknowledges bovine spongiform encephalopathy (BSE) in human deaths
FDA clarifies its consultation policy; USDA eases its regulations; EPA finalizes its regulations	1997	Public protests begin in Europe
EPA approves Starlink maize for animal feed	1998	Pustzai conducts disputed GM potato studies; Bio-Integrity sues FDA
GM foods become U.S.-EU trade issue; FDA holds three public meetings in response to the conflict and receives 35,000 public comments thereafter	1999	European retailers reject GM food; U.K. imposes three-year ban on new GM crops; EU mandates labeling for GM foods; UN biosafety protocol blocked by U.S.+4; Lossey conducts disputed monarch butterfly study; Seattle citizens protest World Trade Organization, transnational corporations, GM foods, etc.; Golden Rice announced and denounced.
NRC issues report on health and environmental safety of pest-protected plants; Bio-Integrity's suit of FDA dismissed	2000	UN biosafety protocol adopted; Starlink maize detected in human food supply
FDA proposes mandatory premarket notification for new GM foods	2001	Starlink removed from human food supply
NRC issues report on environmental effects of transgenic plants; Institute of Medicine initiates report on assessing the unintended health effects of GE food	2002	Chapela and Quist conduct disputed Mexican maize study; southern African drought and GM food aid debates held; NRC issues report on safety of animal biotechnologies; conflict arises between biopharmers and food farmers; pharm-maize contaminates soybean field

Source: Compiled by the author.

before marketing GM foods. The guidance to industry consisted of five decision trees and accompanying text detailing the types of considerations and safety tests that might be performed under various circumstances. The FDA's 1992 policy statement represented an interpretation of how existing regulations were to be applied to GM foods, reflecting the FDA's view that the "newer techniques of plant breeding" (using recombinant DNA or rDNA) did not pose any fundamentally new risks that might require new regulations.

The FDA asserted that it has sufficient authority to regulate GM foods either under the adulteration clause (section 402(a)(1) of the federal Food, Drug and Cosmetic Act),[1] which normally governs whole foods, or under the food additives clause (section 409), which normally governs chemical substances added to foods to achieve an intended effect. GM foods pose a challenge to this binary choice because they are whole foods and have been altered to achieve an intended effect through the "addition" of new segments of DNA and the intended expression product(s). In resolving this issue the FDA had to proceed carefully because the choice would have profound implications for the level and type of premarket testing required, the strictness of the legal safety standard, labeling, the burden of proof placed on various parties, the administrative burden on the FDA, and the pace with which GM foods would enter the marketplace. As noted in the timeline, these policies were being developed throughout the 1980s and the early 1990s, when deregulation was a dominant theme in federal politics and policymaking.

The food additive clause mandates that producers file a food additive petition with the FDA before marketing foods containing an additive, and usually requires that producers perform extensive safety testing to demonstrate that there is "reasonable certainty of no harm" when the additive is used as intended. If successful, this petition results in an affirmative statement from the FDA, in a letter to the producer, stating that the food additive has been approved. All approved food additives must be listed in the ingredients section of the food label. Some added substances can be exempted from the food additive petition process under the GRAS (generally regarded as safe) clause if they have a long history of safe use (e.g., spices, vinegar, and natural flavors) or have been determined to be GRAS in the judgment of qualified experts.

The adulteration clause of the Food, Drug and Cosmetic Act is the authority under which the FDA normally regulates (and recalls) whole foods to guard against microbiological, chemical, or physical contamination. The 1992 policy states: "Section 402(a)(1) of the Act will be applied to any substance that occurs unexpectedly in the food at a level that may be injurious to health. . . . It is the responsibility of the producer of a new food to evaluate the safety of the food and assure that the safety requirement of section 401(a)(1) is met" (FDA 1992, p. 22990).

Under this clause the FDA typically defines enforcement guidelines known as "action levels" for various contaminants when the identity of those contaminants is known. The prospect of adverse publicity and the threat of legal action normally creates the incentive for industry to adhere to these guidelines and associated good manufacturing practices. However, unlike the food additive clause, the guidelines bear no mandate for premarket testing or for ex ante demonstration that the food meets the higher safety standard of "reasonable certainty of no harm" that applies to food additives. Instead, because these substances occur unexpectedly by definition, a problem with the food typically might be revealed through marketing testing, surveillance, adverse event reports, or outbreaks of illness. In the case of new substances or substances for which action levels have not been defined previously, the food would be considered adulterated "if, by virtue of the added substance, there is a 'reasonable possibility' that consumption of the food will be injurious to health" (FDA 1992, p. 22989).

Thus the food additive clause generally provides greater ex ante assurance of safety for new substances but is more burdensome for producers and for the FDA, while the adulteration clause generally relies upon good manufacturing practices, marketing detection, and recall authority to protect public health.

In its 1992 policy the FDA avoided exclusive use of either the food additive clause or the adulteration clause, and instead sought a type of middle ground. Specifically, (a) there was no mandate for premarket testing or approval; (b) GM foods, as in the case of other whole foods, were presumed to be GRAS unless the details of a specific case suggested otherwise; (c) developers of GM foods, as in the case of developers of other whole foods, were allowed to independently judge whether the new variety was GRAS; (d) developers could voluntarily follow a set of decision trees provided by the FDA to guide their GRAS determination and testing on a case-by-case basis; (e) developers were urged to voluntarily consult with the FDA at the beginning of this process when deciding the protocols they would follow and again at the end to review their findings; and (f) if successful, this process would result not in an affirmative approval letter from the FDA, as in the case of food additives, but rather in a letter that simply reiterated the conclusions the developer had drawn and stated, "FDA has no further questions."

In effect, these guidelines allowed most foods to avoid the higher requirements of the food additive petition process but provided for a greater degree of (voluntary) consultation between the FDA and developers than is the case for non-GE whole foods. In practice, the FDA believes all new varieties marketed to date have gone through the consultation process, but the details on the testing protocols and consultations are not readily available to the public. The FDA's logic and the decision trees achieve this middle ground, in effect, by treating the intended expression

products of the transgene (as well as metabolically related nutrients, known toxicants, and known allergens) as the primary focus of premarket assessment and GRAS determination by developers, and treating any unexpected (e.g., pleiotropic or insertional mutagenic) effects of the transformed variety as subject to the marketing adulteration clause (FDLI 1996, p. 94).

As revealed in subsequent sections of this chapter, this approach responded to two powerful considerations: (a) the high-level political mandate to minimize the regulatory interference with this industry and (b) the enormous gaps in scientific knowledge, evidence, and testing methods concerning the unintended consequences of transgenic breeding of food crops, which made it difficult or impossible to produce affirmative evidence of the presence or absence of unintended harmful changes in the new variety.

The profound lack of evidence and testing methods related to the unintended effects of genetic engineering (GE) is a critically important consideration for interpreting the conflicting and contradictory claims related to GM foods. It means that statements from government, industry, and other groups to the effect that "there is no evidence that any of the GM foods currently on the market have caused harm or are unsafe to eat" is primarily a statement about the lack of evidence rather than an affirmative statement regarding safety. It also means that statements from consumer or public interest groups about the dangers or risks of GM foods are primarily statements about the potential for harm rather than about demonstrated harmful effects.

The manner in which the FDA's 1992 policy statement addressed these issues is analyzed in the next section.

Scientific Issues in the FDA's Statement of Policy

In its 1992 policy the FDA notes that a spectrum of techniques exists for genetic modification, including traditional breeding, mutagenesis, somaclonal variation, wide-cross hybridization, protoplast fusion, and the more recently developed rDNA techniques. The FDA notes that all of these techniques have the potential to introduce extraneous genetic material and undesirable traits, and thus they require extensive backcrossing with the parent line to achieve the desired results. Moreover, it asserts that rDNA techniques are superior in this regard: "In theory, essentially any trait whose gene can be identified can be introduced into virtually any plant, and can be introduced without any extraneous material. Since these techniques are more precise [than other forms of genetic modification], they increase the potential for safe, better-characterized and more predictable food" (FDA 1992, p. 22986). This logic forms the basis for the FDA's oft-repeated position that rDNA techniques are simply an extension of genetic modification that has been used by humans

for thousands of years, that it creates no fundamentally new risks, and is more precise and predictable than traditional plant breeding.

Although rDNA techniques may be more precise with respect to the genetic material being transferred, this is not the only relevant consideration. Specifically, as the FDA notes, there are scientific reasons why the insertion of the material and the phenotypic effects are not entirely predictable:

> DNA segments introduced using the new techniques insert semi-randomly into the chromosome, frequently in tandem multiple copies, and sometimes in more than one site on the chromosome. Both the number of copies of the gene and its location in the chromosome can affect its level of expression, as well as the expression of other genes in the plant. . . . Additionally, as with other breeding techniques, the phenotypic effects of a trait may not always be completely predictable in the new genetic background of the host. (FDA 1992, p. 22986)

Since this statement was written, these possibilities have come to be referred to as insertional mutagenesis.

The FDA's policy statement notes that a limited number of backcrosses often are performed to enhance the stability of the line and the ability to cross the trait into other lines, but it does not indicate whether this procedure eliminates the unexpected phenotypic effects referred to previously. Moreover, it states that all breeding or genetic modification techniques have the potential to create unexpected effects, but that "plant breeders using well-established practices have successfully identified and eliminated plants that exhibit unexpected, adverse traits prior to commercial use" (FDA 1992, p. 22987).

This statement of reassurance, which appears several places in the statement of policy, does not describe these practices and their efficacy, but some indications are provided in one passage that states: "The established practices that plant breeders employ in selecting and developing new varieties of plants, such as chemical analyses, taste testing and visual analyses, rely primarily on observations of quality, wholesomeness and agronomic characteristics. Historically these practices have proven reliable for ensuring food safety" (FDA 1992, p. 22988). Thus, while stronger methods are available to assess the safety of the intended expression products from the transgene (described below), the statement of policy seems to imply, but does not actually state, that these traditional plant-breeding methods might be sufficient to reduce the likelihood of unintended toxicologic, allergenic, or compositional effects arising from insertional mutagenesis and pleiotropy. We will now examine some excerpts of the policy statement dealing specifically with toxicants and allergens.

Toxicants. One class of potential unintended effects from genetic modification relates to toxicants. The FDA lists several known toxicants found in specific foods (e.g., protease inhibitors in some cereals, lectins and cyanogenic glycosides in some legumes, cucurbiticin in squash and cucumbers, and lathyrogens in chickpeas) and notes that many of these occur at levels that do not cause acute toxicity, while others may cause severe illness or death if foods are not properly prepared.

To guard against inadvertent elevation of known toxicants when creating new varieties, a critical portion of the FDA's guidance to industry states:

> It is not possible to establish a complete list of all toxicants that should be considered for each plant species. In general, the toxicants that are of highest concern are those that have been documented to cause harm in normal or animal diets, or have been found at unsafe levels in some lines or varieties of that species or related species. In many cases, characteristic properties (such as bitter taste associated with alkaloids) are known to accompany elevated levels of specific natural toxicants. If such characteristics provide an assurance that these toxicants have not been elevated to unsafe levels, analytical or toxicological tests may not be necessary. (FDA 1992, p. 22996)

In those cases in which more detailed analytical tests seem warranted, the FDA notes that the interpretation of such tests is complicated by the great variation in levels of naturally occurring toxicants within and between varieties and that great uncertainty exists concerning safe ranges. Thus it states: "In some cases, analytical methods alone may not be available, practical or sufficient for all toxicants whose levels are needed to be assessed. In such situations comparative toxicological tests on new and parental varieties may provide assurance that the new variety is safe. FDA encourages producers of new plant varieties to consult informally with the agency on testing protocols for whole foods when appropriate" (FDA 1992, p. 22996).

As noted, the 1992 policy suggests that the new variety should be compared to parental varieties or to untransformed varieties as a screen for potentially significant changes. The policy states that this is consistent with the concept of substantial equivalence, as developed by the Organization for Economic Cooperation and Development, and with principles discussed in a joint Food and Agriculture Organization–World Health Organization report (FAO-WHO 1991). The FDA's 1992 policy states that comparisons should be made of the following: (a) toxicants and allergens known to occur in the host or donor species, (b) the concentration and bioavailability of important nutrients for which a crop is ordinarily consumed, (c) the safety and nutritional value of newly introduced proteins, and (d) the identity, composition, and nutritional value of modified carbohydrates, fats, or oils.

The concept of substantial equivalence has been further explicated, defended, and critiqued since that time (Millstone et al. 1999; FAO-WHO 2000; IFT 2000) and is one of the subjects currently under study by an NRC committee (NRC n.d.). It suffers from ambiguity concerning what constitutes a meaningful difference in composition, how much statistical power should be present to detect such differences, and whether the new variety should be compared only to the parental variety grown under identical conditions or to the range of values for all untransformed varieties grown under varying conditions. Moreover, it would not, as originally recommended by the FDA, permit identification of unexpected toxicants, allergens, or nutrition-relevant changes because techniques for broad-spectrum profiling gene expression, metabolic intermediaries, and proteins were not available at that time and still are not widely applied for this purpose (Kuiper et al. 2001).

It is noteworthy that a recent Government Accounting Office report (GAO 2002) stated that techniques for broad-spectrum profiling now are becoming available, which would allow for a significantly expanded application of the substantial equivalence concept, including screening for unexpected changes. However, FDA officials and some of the scientists from industry and academia interviewed by the GAO questioned the utility of these techniques because the functional or health consequences of any observed differences may not be known. This logic, if followed in the future, suggests that as more powerful screening methods become available for demonstrating compositional nonequivalence in some plant varieties, the FDA may abandon "compositional substantial equivalence" as the relevant standard in favor of "functional substantial equivalence." It is unclear whether the burden of proof for ascertaining functional equivalence would fall on the manufacturer, on the FDA, on consumer groups, or on the scientific community at large. Nor is it clear whether the new variety would continue to have "presumptive GRAS status" unless or until such adverse consequences were demonstrated.

As reflected in this section and in the decision trees provided by the FDA, the existence of large knowledge gaps, scientific uncertainties, and practical constraints resulted in an FDA policy that requires a high degree of judgment and discretion on the part of producers when deciding how to demonstrate the GRAS status of novel varieties. Since that policy was issued, the FDA has elaborated upon its "evolving approach" to GRAS determinations, with much greater emphasis on independent determinations by producers, much greater reliance on the "common knowledge" component rather than on direct evidence from testing, and a more limited role for the FDA (FDA 1997). As noted, granting discretion to producers was purposely designed into the 1992 policy because GM foods do not fit neatly into either the food additive or the adulteration category. Most of the branches in FDA's decision trees end in the advice that producers "consult FDA," as in the previous excerpt.

This provides flexibility for industry and the FDA but creates problems related to transparency in the regulatory agencies. The NRC (2000) committee stated: "The details of these consultations are not readily available for public scrutiny. If the public wants to obtain documents containing information and data submitted to FDA for consultation, they must request the documents from FDA through the Freedom of Information Act (FOIA). Processing and fulfilling FOIA requests can take a long time" (NRC 2000, p. 175).

In addition to concerns related to known toxicants, the FDA's policy statement notes the potential for creating new toxicants through plant breeding:

> Plants, like other organisms, have metabolic pathways that no longer function due to mutations that occurred during evolution. Products or intermediates of some such pathways may include toxicants. In rare cases, such silent pathways may be activated by mutations, chromosomal rearrangements or new regulatory regions introduced during breeding, and toxicants hitherto not associated with a plant species may thereby be produced. Similarly, toxicants normally produced at low levels in a plant may be produced at high levels in a new variety as a result of such occurrences. (FDA 1992, p. 22987)

The statement of policy goes on to say that the likelihood of this occurring is "considered extremely low in food plants with a long history of use that have never exhibited production of unknown or unexpected toxins" (FDA 1992, p. 22987).

Accordingly, as noted earlier, the decision trees provided as guidance for industry do not require or suggest any methods for screening for such new toxicants. This despite the FDA's clear acknowledgment (quoted earlier) of the scientific reasons why unexpected effects could result not only from reactivation of "silent pathways" but also from pleiotropic effects of the transgene, from insertional mutagenesis, and from differences arising from the functioning of the gene in a new genomic background.

Allergens. The FDA's policy statement says: "FDA's principal concern regarding allergenicity is that proteins transferred from one food source to another, as is possible with rDNA and protoplast fusion techniques, might confer on food from the host plant the allergenic properties of food from the donor plant" (FDA 1992, p. 22987). It notes that while all known allergens are proteins, only a small fraction of the thousands of proteins in the diet have been found to be allergenic, the most common of which are milk, eggs, fish, crustacea, mollusks, tree nuts, wheat, and legumes (notably peanuts and soybeans). In some cases the specific protein in an

allergenic food is known, and in other cases it is not yet known. In either case, the FDA states: "Appropriate in vitro and in vivo allergenicity testing may reveal whether the new variety elicits an allergenic response in the potentially sensitive population" (FDA 1992, p. 22987).

In other words, the FDA claims that in vivo and in vitro methods may be capable of testing new varieties for allergenicity in those cases in which the foods or their allergenic proteins are already known, and the FDA's decision trees guide producers in ascertaining which new varieties may warrant such testing. If new varieties are found to be allergenic, such foods could be labeled as such or steps could be taken to eliminate the allergenicity through more refined breeding. However, one of the limitations of allergen testing, even when the identity of the protein is known, is that indirect tests are the only feasible methods, and each has weaknesses. For instance, the amino acid sequences (epitopes) that might signal allergenicity are not known with precision; the in vito digestibility tests may be conducted at nonphysiologic pH levels; tests often are conducted on proteins isolated from bacteria rather than on a food itself, potentially overlooking translational modifications, as in the *Bacillus thuringiensis* (*Bt*) protoxin versus the active endotoxin (NRC 2000); and samples of human sera from sensitive individuals are not sufficiently abundant to permit widespread use of that test (GAO 2002).

Although the FDA's statement of policy is primarily concerned with the eight food types that account for 90 percent of known allergens, it is known that the remaining 10 percent of known allergens are distributed across at least 160 foods (Clydesdale 1996), and many more may exist but not yet have been documented. Allergic reactions are estimated to occur in 1 to 2 percent of adults and in 5 to 8 percent of children (NRC 1998, p. 58). Inasmuch as transgenic techniques are uniquely capable of creating new varieties from vastly different genera of plants (and animals), this widespread distribution of allergens introduces far greater uncertainties and the potential for introducing new allergens, compared to other breeding methods. This would not be a serious concern if producers could test for new allergens. However, as the FDA notes: "[In contrast to the case of known allergens,] a separate issue is whether any new protein in food has the potential to be allergenic to a segment of the population. At this time, FDA is unaware of any practical method to predict or assess the potential for new proteins in food to induce allergenicity and requests comments on this issue" (FDA 1992).

Because of this gap in knowledge, the decision trees offered as guidance to industry do not suggest any direct methods for testing for novel allergens, but instead suggest that producers "consult FDA on protocols for allergenicity testing and/or labeling." It is unclear what further guidance the FDA could provide through those consultations beyond what it provides in the policy statement itself.

Summary

These sections of the FDA's policy statement regarding toxicants and allergens reveal that efforts to ensure the safety of new plant varieties are severely constrained by uncertainties, gaps in knowledge and methods, contextual factors, and practical considerations. These include the following:

- The list of potentially toxic substances in specific varieties of food crops, whose levels may be affected by rDNA insertions, is not known.

- Levels of known toxicants in foods vary widely for genetic and environmental reasons, and the "safe" or acceptable ranges are not known for most of them.

- The sensitivity and specificity of "taste tests" and other indirect tests for predicting the level or safety of toxicants in food is unknown, yet such tests are suggested as a possible screen for toxicants.

- Food allergens are known to be distributed across many foods, far beyond the eight most common ones, and to affect a significant proportion of adults (1 to 2 percent) and children (5 to 8 percent). Inasmuch as rDNA techniques are uniquely capable of transferring genes across vastly different genera and no practical methods exist for testing for new allergens, this appears to create a plausible risk from new allergens but one whose extent and seriousness is largely unknown and for which no tests are presently available.

- The FDA policy assumes that the nature, extent, and frequency of metabolic disruptions, activation, or over-expression of target and nontarget genes resulting from the (semi-random, tandem, and multiple-copy) insertion of new regulatory regions and structural genes is comparable to that from traditional breeding.

Based on this analysis of the 1992 FDA policy, Table 4.3 represents a judgment concerning the effectiveness of the FDA's guidance to industry with respect to various categories of concerns. For the reasons identified earlier, this guidance is likely to be partially effective with respect to known allergens and known toxicants. However, it is ineffective for detecting and preventing exposure to unknown allergens and toxicants and to known allergens and toxicants that arise from various genetic or metabolic disruptions. These patterns are obscured in the policy statement, however, by frequent reference to (a) well-accepted methods that plant breeders use (such as backcrossing and gross morphological inspection) to eliminate undesired traits, (b) the claim that many or all of the unexpected effects are

Table 4.3 The effectiveness of FDA regulations in addressing various categories of concerns in transgenic plants

Categories of concerns	Known[a] toxicants	Unknown toxicants	Known[a] allergens	Unknown allergens
Intended effects of the transgene	E	NE	E	NE
Transcription modification	PE	NE	PE	NE
Pleiotropic[b] effects of the transgene	NE	NE	NE	NE
Insertional effects of the transgene (location, multiple copies)	NE	NE	NE	NE
Effects of regulatory regions (overexpression, activation)	NE	NE	NE	NE
Effects of the genomic background	NE	NE	NE	NE

Source: Author's judgments.

Notes: E = effective; PE = partially effective; NE = not effective.

[a] *Known* refers to knowledge that a given substance or food source is toxic or allergenic; knowledge of effective testing methods; the "safe" or acceptable ranges, if any; and effects of processing methods.

[b] *Pleiotropic* refers to pleiotropy, the common genetic property in which a single gene can influence multiple phenotypic traits and, in this context, may have multiple effects on the chemical composition of plants due to the complexity of metabolic pathways as well as gene-gene interactions.

just as likely with other methods of plant breeding (which has not been demonstrated), (c) "practical constraints" (which actually reflect large gaps in knowledge and methods) that make it difficult or impossible to test for unexpected effects, (d) the implication that the long history of use of the donor and host plants ensures the safety of transgenic varieties, and (e) the suggestion that many or all of these unexpected effects are considered rare. Several of these claims are amenable to testing through scientific procedures, but no such evidence is provided in the policy statement.

It is noteworthy that these uncertainties, knowledge gaps, and potentials for unintended effects were of considerable concern to some of the scientists and scientific administrators who commented on earlier drafts of the 1992 policy statement, as revealed in internal memos made public through a lawsuit brought against the FDA by a coalition of nonprofit organizations (*Alliance for Bio-Integrity* v. *Shalala* 1998). They also were noted by a committee formed by the NRC to examine the pest-protected crops on the market in the mid- to late 1990s (NRC 2000), which was able to identify only one direct feeding study in a peer-reviewed journal, the disputed and highly controversial study of GM potatoes using rats (Ewen and Pustzai 1999). A search of the food safety literature on Medline, by Domingo (2000), documented a total of 101 food safety papers with the phrase

"genetically engineered foods," including 67 papers with the phrase "adverse effects of transgenic foods" and 44 papers with the phrase "toxicity of transgenic foods." Of these, only 8 papers reported findings from original experimental studies of the safety of GE products, all with rodents. Most of the remaining papers offered opinions and commentaries on the safety of GE foods, but without offering supportive data. A similar analysis of research funded by the U.S. Department of Agriculture (USDA) since 1981 confirms a paucity of research on the safety of GE foods (Pelletier 2005).

This paucity of research is in sharp contrast to the rather strong assurances of safety provided by the FDA and proponents of GE foods. It suggests that the phrase "no evidence of harm" so commonly used by the FDA and others is true in the sense that there is little evidence in one direction or the other. This is quite different from the evidentiary standard of "reasonable certainty of no harm" that would have been required if the FDA had chosen to regulate GE foods under the food additive clause of the Food, Drug and Cosmetic Act. As demonstrated in the next section, considering general scientific knowledge concerning insertional mutagenesis, pleiotropy, and other aspects of molecular biology could easily have led the FDA to adopt a more precautionary stance in the 1992 policy statement.

The FDA's 2001 Proposed Rules

As a result of the intense public controversy over GM foods in the late 1990s the FDA held three public meetings in different parts of the United States in 1999, requested written comments on specific questions (and received over 35,000 comments), and subsequently issued proposed rules requiring premarket notification for bioengineered (GM) foods (FDA 2001). The extensive preamble to the proposed rules reveals that the FDA had reconsidered several of its positions articulated in the 1992 policy:

> FDA recognizes that because breeders utilizing rDNA technology can introduce genetic material from a much wider range of sources than previously possible, there is a greater likelihood that the modified food will contain substances that are significantly different from, or are present in food at a significantly higher level than, counterpart substances historically consumed in food. In such circumstances, the new substances may not be GRAS and may require regulation as food additives. (FDA 2001, p. 4709)

> FDA believes that in the future, plant breeders will use rDNA techniques to achieve more complicated compositional changes to food, sometimes introducing multiple genes residing on multiple vectors to generate

> new metabolic pathways. FDA expects that with the increased introduction of multiple genes, unintended effects may become more common. For example, rice modified to express pro–vitamin A was shown to exhibit increased concentrations of xanthophylls . . . and rice modified to reduce the concentration of a specific protein was found to exhibit an increased concentration of prolamine. (FDA 2001, p. 4710)
>
> There is substantial basis to conclude, however, that there is greater potential for breeders, using rDNA technology, to develop and commercialize foods that are more likely to present legal status issues and thus require greater FDA scrutiny than those developed using traditional or other breeding techniques. (FDA 2001, p. 4711)
>
> Intended changes to the composition or characteristics of the food also could raise safety questions about the food. For example, it is possible that a developer could modify corn so that the corn becomes a significant dietary source of the nutrient folic acid. Folic acid is used to fortify many foods, including breakfast cereals, because of the relationship [with] neural tube defects. However, excess folic acid in the diet can mask the signs of vitamin B12 deficiency. [In addition] it is possible that a modification would be intended to decrease the level of a substance that is considered undesirable, such as the phytate that naturally occurs in soybeans . . . or the fat content of a food. (FDA 2001, p. 4721)

One of the reasons these paragraphs, and the proposed premarket notification in general, are significant is that they overturn two of the fundamental principles expressed in the 1992 policy, namely (a) that there is no difference between GM foods and foods produced through traditional breeding and (b) that the characteristics of the product, not the process, should determine the level of oversight. These principles were used in 1992 to argue that there was no scientific basis for specific regulations for GM foods, but the rules proposed in 2001 would reverse this position. Although the FDA indicates that greater oversight is now required due to the greater scope and complexity of the genetic changes, the 1992 policy statement (and numerous NRC reports in the 1980s) clearly demonstrate that such changes were envisioned prior to the issuance of the 1992 policy. A more plausible reason for FDA's reversal of its earlier position relates to the intense public controversy that arose in the late 1990s.

The rules proposed in 2001 suggest that the FDA could have marshaled a scientific argument for creating specific regulations for GM foods in 1992, but, as described elsewhere (Eichenwald, Kolata, and Petersen 2001), was responding to

political pressures from industry and the White House in choosing not to do so at that time. In addition, the previous quotes from the proposed rules highlight the likelihood that nutritionally altered foods may involve more complex genetic and compositional changes than those addressed in the 1992 policy statement. Such changes may require greater oversight, as noted by the FDA, and an enhanced role for nutrition science and professional communities as described in the final section quoted earlier.

The concern over potential unintended compositional changes in GM foods, which was intensified as a result of the public debate in the late 1990s, has generated a small but growing number of studies in the scientific literature directly examining this possibility. Table 4.4 lists all those available at the time of a review conducted in 2001 by Kuiper et al. (2001). These studies confirm that unintended effects can occur as a result of genetic modification, although they do not address whether the frequency and magnitude of differences are different from those of conventional breeding methods or the functional consequences of the observed changes.

Table 4.4 Unintended effects of genetic engineering breeding as of 2001

Host plant	Trait	Unintended effect
Canola	Overexpression of phytoene-synthase	Multiple metabolic changes (tocopherol, chlorophyll, fatty acids, phytoene)
Potato	Expression of yeast invertase	Reduced glycoalkaloid content (–37 to –48%)
	Expression of soybean glycinin	Increased glycoalkaloid content (+16 to +88%)
	Expression of bacterial levansucrase	Adverse tuber tissue perturbations; impaired carbohydrate transport in the phloem
Rice	Expression of soybean glycinin	Increased vitamin B6 content (+50%)
	Expression of pro–vitamin A biosynthetic pathway	Formation of unexpected carotenoid derivatives (beta carotene, lutein, zeaxanthin)
Soybean	Expression of glyphosphate (EPSPS) resistance	Higher lignin content (20%) at normal soil temperatures (20°C); splitting stems and yield reduction (up to 40%) at high soil temperatures (45°C)
Wheat	Expression of glucose oxidase	Phytotoxicity
	Expression of phosphatidyl serine synthase	Necrotic lesions

Source: Modified from Kuiper et al. 2001.

Note: Data are from publicly available reports.

Conclusions Regarding the FDA's GM Foods Policies

This chapter's examination of the FDA's 1992 policy statement on GM foods holds several lessons concerning the roles and uses of science in policy development. These lessons pertain most directly to the first generation of GM foods, but also have relevance to the forthcoming varieties under development.

Many of the potential unintended consequences in the case of GM foods were amenable to scientific investigation to characterize their plausibility and likelihood, frequency, severity, or mitigation, but research on these issues appears to have been sorely neglected, even in the USDA-funded research portfolio. From a science policy perspective, developing the mechanistic knowledge, methods, and tools for investigation of unintended consequences may be a uniquely public-sector responsibility, because the private sector has insufficient incentive to do so. However, the behavior revealed in this case suggests that the prevailing incentives did not favor the investigation of unintended consequences.

The resulting gaps and biases in public research agendas resulted in scientific uncertainties that had a direct and profound impact on the FDA's decision to adopt policies that appeared inadequate to some consumer groups, to some FDA scientists and administrators, to independent scientists, and to governments in other countries. Specifically, this decision

- permitted the default assumption that unintended consequences appear no more likely in GM foods as compared to conventional foods;

- limited the tools and methods available for premarket testing of individual products, and therefore limited the types of tests the FDA could require of developers;

- virtually required the FDA to use only its market authority under the adulteration clause rather than its authority to require premarket testing under the food additive clause; and

- made it possible for the FDA to claim, in the absence of positive evidence of unintended compositional changes and functional consequences, that there was no legal basis for mandating the labeling of GM foods.

Despite the existence of critical gaps and uncertainties in scientific knowledge concerning unintended consequences, key scientific organizations (notably the various committees of the NAS and the NRC, as seen here) displayed overwhelming support for and promotion of biotechnology in general, including GM foods, while

devoting little or no concerted effort to investigation of potential food safety risks. Moreover, the NAS and the NRC increasingly have been asked to render scientific judgments on issues with enormous implications for the regulation of GM foods, which has strained their ability to separate the scientific questions from the profound policy implications that have loomed over the members of these committees. This is seen most clearly in the white paper from the five-member committee of the NAS Council (NAS 1987) and the report analyzed in detail in this chapter (NRC 2000).

The FDA's decisions were highly circumscribed by some of its statutes, as well as by high-level political pressure to minimize regulatory interference with this new industry. Within this larger political and legal context, the lack of an empirical database on the actual nature and extent of compositional changes potentially arising from pleiotropic effects or insertional mutagenesis in individual cases, along with the absence of any organized expression of concern from the scientific community, is what permitted the FDA to exercise its discretion in favor of less stringent regulations. In short, while the findings of individual scientists can be rigorous, objective, and neutral, the collective effort and collective knowledge base from the overall scientific enterprise can encompass gross imbalances with respect to risks versus benefits. This, in turn, can have an enormous impact on the policies adopted and, ultimately, on health and nutritional outcomes.

The Southern African Context

While the accounts given earlier in this chapter reveal a number of weaknesses in the FDA's GM food policies for the U.S. population, a number of contextual factors in southern Africa raise additional questions that are not well addressed by the FDA policy. Three of these reviewed in this section relate to cultural differences in food selection and preparation, special issues related to staple foods, and the health and nutritional status of populations in the region.

Cultural Food Selection and Processing Practices

One category of concerns relates to practices for food selection (definitions of edible versus nonedible portions of a plant), processing (storage, soaking, drying), preparation (cooking), and consumption, which can vary widely across cultures and are not well addressed in the FDA's policy statement. For instance, the statement relies heavily on culture-bound terms such as "proper methods of processing," "long history of use," and "normal diets," with an apparent Euro-American referent in mind. This is illustrated in the following quotations:

> Plants are known to produce naturally a number of toxicants and antinutritional factors, such as protease inhibitors, hemolytic agents, and neurotoxins, which often serve the plant as natural defense compounds against pests or pathogens [e.g., protease inhibitors in cereals, lectins in legumes, cyanoglycosides in cassava, glucosinolates in cruciferae, cucurbiticin in squash, lathyrogens in chickpeas]. Many of these toxicants are present in today's foods at levels that do not cause acute toxicity. Others, such as cassava and some legumes, are high enough to cause severe illness and death if the foods are not properly prepared. FDA seeks to assure that new plant varieties do not have significantly higher levels of toxicants than present in other edible varieties of the same species. (FDA 1992, p. 22987)

> This guidance section is primarily designed for the development of new varieties of currently consumed food plants *whose safety has been established by a history of use*. If *exotic species* are used as hosts, testing may be needed to assure the safety and wholesomeness of food. (FDA 1992, p. 22996; emphasis added)

> Processing (cooking) may affect the safety of a substance. This is particularly important in safety assessment of proteins transferred from one food source to another. For example, lectins, which are inactivated by cooking, would raise a safety concern if transferred from a kidney bean, which are eaten cooked, to tomatoes, which may be eaten raw. *The effects of any potential differences in food processing* between the donor and the new plant variety should be carefully considered at each stage in the safety assessment. (FDA 1992, p. 22994; emphasis added)

While some of the italicized sections of these quotes reveal that the FDA is aware of the importance of food processing methods for the safety of conventional and GM foods, its 1992 policy statement does not explore the implications of this for GM foods created in developed countries and exported to developing countries through commercial or food aid channels.

The NRC report (2000) revealed a greater awareness of the cultural differences in food preparation that could affect the safety of novel foods, but did not explore its food safety implications when GM foods are moved across national and cultural boundaries:

> Depending on the protein, a plant modified to express high concentration of inhibitors in edible tissues can cause adverse health effects if the plant is consumed raw, and such a risk can be reduced by designing transgenes that are expressed only in nonedible plant parts. (NRC 2000, p. 57)

> The "edible" portion of a plant varies with the species and the consumer in question. In the human diet, the part eaten can also vary with the cultural background of the consumer. (p. 72)

In summary, the FDA policy statement reveals a predominant focus on factors that may affect the safety of GM foods when consumed by the U.S. population, and it does not appear that those writing it considered the wide variety of food habits and practices in other cultural contexts that could have a bearing on the safety of the same food. *This suggests that blanket assurances concerning the safety of new varieties may not be appropriate in some cases in which they have been offered, without detailed knowledge of the contextual factors that may affect the safety of a specific product in a distinctive context.* This may not be a major factor at the present time because of the limited number of GM crops on the market, but may become a very important factor in the future as the variety of GM products increases and they come to be marketed and consumed in diverse countries and cultures. It also is relevant to the development and safety testing of GM varieties within developing countries.

Special Considerations for Staple Foods

Perhaps the most significant "cultural oversight" in FDA's policy is revealed in the section headed "Issues Specific to Animal Feeds," which states: "Unlike a food in the human diet, an animal feed derived from a single plant may constitute a significant portion of the animal diet. For instance, 50 to 75 percent of the diet of most domestic animals consists of field corn. *Therefore, a change in nutrient or toxicant composition that is considered insignificant for human consumption may be a very significant change in the animal diet*" (FDA 1992, p. 22988; emphasis added).

Although this passage claims that "the human diet" does not rely heavily on a single crop, the reality is that the majority of people in developing countries, especially the poor, do subsist on diets with 50 to 75 percent of the calories coming from a single staple food (FAO 1999). In addition, these staple foods in developing countries undergo quite different food processing methods than those used in the United States and other developed countries. It is well known that processing methods and the physiological state of the consumer can greatly affect the stability of potentially allergenic proteins and toxins during processing and after ingestion (Taylor and Lehrer 1996). *The net effect of these differences is that the effective dose of potential allergens (or toxins) to which southern African consumers may be exposed may be many times higher than that assumed for the U.S. population.*

To illustrate the magnitude of the differences between the U.S. diet and diets in southern Africa, it is instructive to examine some of the key conclusions drawn

from evaluation of the Starlink maize contamination that occurred in the United States. Starlink maize is one of the *Bt* varieties of genetically modified maize, and in 1998 it was approved by the U.S. Environmental Protection Agency (EPA) for use in animal feed. (The EPA is responsible for reviewing the safety of such products because the transgenic protein (CRY9C) is classified as a plant pesticide.) The product was not approved for human consumption because in the judgment of the EPA (but not that of the company) the extensive tests conducted on the CRY9C protein could not rule out its potential allergenicity. However, in 1999 it was determined (first by a nongovernmental organization (NGO) and subsequently confirmed by government testing) that the human food chain had been inadvertently contaminated with Starlink maize. In the course of extensive investigations, the EPA Science Advisory Panel (consisting of external scientists) concluded that there remained a "medium likelihood" that the CRY9C protein is an allergen, but it had a "low probability to sensitize some individuals" in the United States because of the short duration of exposure, the low concentration of CRY9C in the overall maize supply (due to mixing with other varieties), the processing methods used, and the very low dietary intakes of maize products in the United States (EPA 2000b).

To underscore the latter point, the 95th percentile for dietary intake of whole maize grain (equivalents) in the United States is estimated to be 62 grams per day (EPA 2000a). Even for the segment of the population with the highest level of maize consumption (Hispanics) the 95th percentile is only 88 grams per day. These upper levels of intake are a mere fraction of the intakes common in the southern African region,[2] and the processing methods used in that region are unlikely to denature and degrade the proteins to the same extent as those used in the U.S. context.

The important point about these calculations is *not* that Starlink maize, or the food aid shipments in 2002, were necessarily unsafe for human consumption in the region. Rather the Starlink case is offered as a dramatic example of the need for scientists, policymakers, and NGOs in the region to carefully examine the assumptions made in the safety assessments conducted by the United States in light of specific knowledge of how contextual features of the region differ from those of the United States. This is underscored by statements in a U.S. Department of State fact sheet issued on January 17, 2003, which made no mention of the Starlink episode, the limited methods available for assessing allergenicity, or the potentially dramatic differences in maize consumption levels and processing methods between U.S. populations and those in southern Africa:

> To-date, scientific evidence demonstrates that these commercially available bio-engineered commodities and processed foods are as safe as their

> conventional counterparts. The food safety assessments were conducted to evaluate potential risks for the multi-ethnic U.S. population, and the United States is not aware of any reason to suggest that these foods would be unsafe for populations in other countries. . . . While these assessments were conducted to evaluate potential food safety and environmental impacts in the United States, it is expected that the issues are similar in Southern Africa. (U.S. Department of State 2003, p. 2)

Health and Nutritional Status in Southern Africa

An obvious difference between populations in the United States and in the southern African region is that the latter suffer from high levels of infectious disease morbidity, protein-energy and micronutrient malnutrition, and compromised immune systems due to HIV during drought and nondrought periods. A search of the scientific literature did not identify any empirical studies examining whether any of these health and nutritional conditions may affect the safety of GM foods, nor did it identify any systematic exploration of the potential mechanisms by which these conditions may increase or decrease the potential for food safety problems. Taking allergenicity as an example, it is possible that food allergens may more easily pass the mucosal barrier in the gastrointestinal (GI) tract if the GI tract has been compromised by parasites and diarrheal disease, thereby triggering an immune response (IgE) in previously sensitized individuals that may not be seen in healthy populations. On the other hand, individuals with compromised immune status due to HIV may be less likely to exhibit the pronounced IgE immune response that is characteristic in food allergies. Although empirical studies will ultimately be required to examine these issues, it would be valuable to conduct a systematic inventory of the possible or plausible biological mechanisms (or hypotheses) related to interactions between GM foods and the health and nutritional problems found in the southern African region.

The Potential Benefits of GM Agriculture and GM Food

Finally, although widespread morbidity and malnutrition have been presented as important contextual factors that may have a bearing on the safety of GM foods for the people of southern Africa, it is important to recognize that these also are major problems in their own right, which GM agriculture may help to address. Although, as noted, it is not the purpose of this chapter to describe these potential benefits and critically analyze the conditions under which they may be achieved, these clearly are major considerations that must be addressed in evaluating policy options and trade-offs, a subject taken up in the next section.

Policy Options and Trade-offs

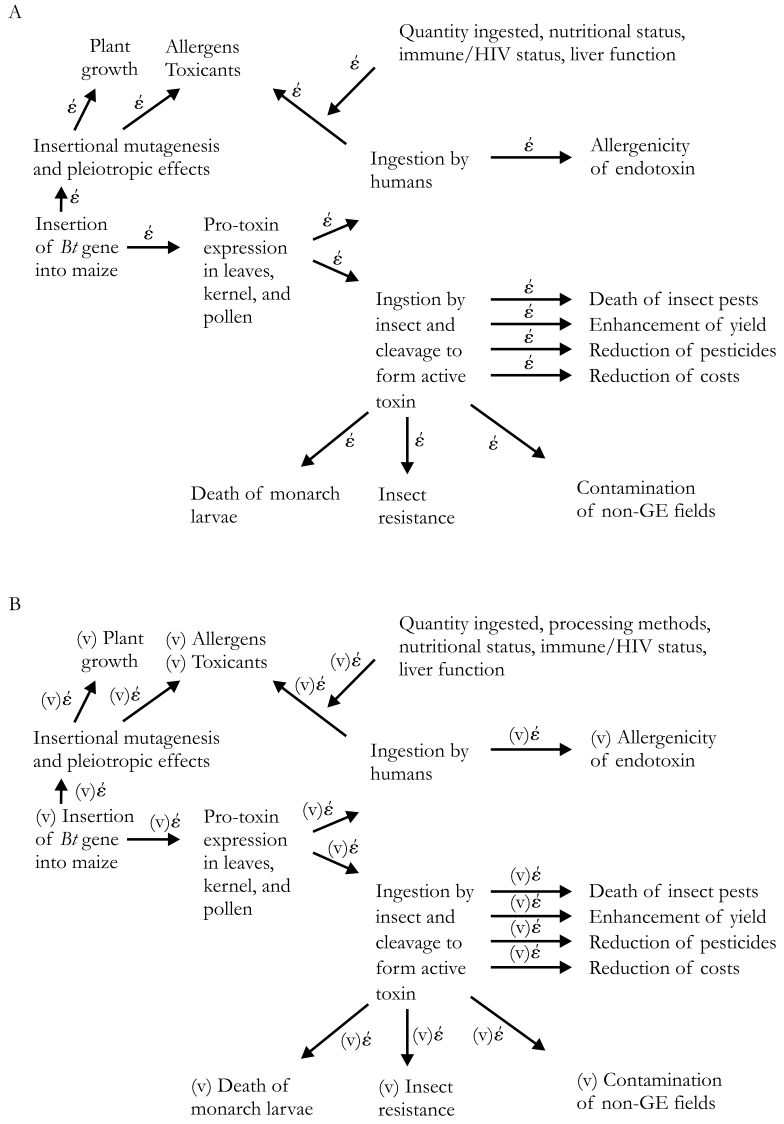
A Basic Framework of Science and Values

The pervasive and growing importance of science and the new technologies, and the potentially profound social changes they can engender, has raised fundamental questions about how new technologies should be governed in democratic societies and in a world community that espouses democratic principles. Whereas the dominant pattern in the last century has been to employ scientific institutions, such as scientific advisory committees, to provide guidance based on positive theories, there has been a growing recognition of the need to incorporate broader considerations into the deliberative process based on normative theories. Positive theories seek to explain "what is" and are the usual domain of the natural and social sciences, while normative theories seek to describe the way things ought to be and are the usual domain of the humanities, especially ethics and political philosophy. Normally scholars in these two traditions do not consider how their ideas relate to each other (Brunner and Ascher 1992). However, insights from both traditions are becoming increasingly integrated as regulatory agencies, stakeholders, and communities seek to develop more productive and appropriate methods for regulating the risks and benefits of new technologies (Renn, Webler, and Wiedemann 1995; NRC 1996; Coglianese 1997; Stirling and Mayer 1999; Beierle and Konisky 2000; Fischer 2000; Beierle 2002; Klinke and Renn 2002).

In most cases of new technology, collective (public) decisions must be made in the face of great scientific uncertainty. In addition, the affected individuals differ in their susceptibilities, in their circumstances, and in the values they attach to their autonomy, lifestyles, and potential risks and benefits. The central question is this: what role should science and politics play in relation to these collective or public decisions? From a positive theory perspective, "politics" refers to a wide range of processes that influence how diverse values are currently allocated in society. From a normative theory perspective, "good politics" refers to procedures that citizens would feel are fair and appropriate because they have characteristics such as openness, transparency, inclusiveness, and accountability.

A simplified schema for better understanding these relationships is shown in Figure 4.1, which builds on the cause and effect relationships that are at the core of positive scientific inquiry and rationality. The case of *Bt* maize is chosen for illustration, although conceptually similar diagrams and principles apply to the second-generation GM crops. Panel A depicts a variety of cause and effect relationships, each of which has a certain degree of uncertainty associated with it ($\acute{\epsilon}$). Within a strictly scientific paradigm each of the relationships shown here, and others not shown, would be of equal interest and vigorously pursued. The strictly scientific

Figure 4.1 Cause and effect relationships involved in the introduction of *Bacillus thuringiensis* maize as a food for a human population



Source: Compiled by the author.

Note: Panel A represents cause and effect relationships as studied by science, with uncertainties (έ); panel B represents these cause and effect relationships with social values included (v); *Bt* = *Bacillus thuringiensis.*

goal would be to test the existence and form of these relationships and understand the mechanisms and contextual factors (effect modifiers) that influence these relationships. This would amount to reducing the uncertainty associated with individual linkages and with the entire causal system.

The relationships among science, politics, and public values can be illustrated very simply through some modifications to this diagram. As shown in panel B, this is accomplished by attaching social values (v) to several elements of this diagram to indicate that different people and groups in society attach different meanings and importance to each of these elements. Although the addition of social values to this diagram appears simple and modest, it has profound implications for the relationship between science and politics in regulatory decisions.

This figure suggests that there are several ways in which GM foods may engender conflicts in social values. These relate to (a) the technology itself, (b) the various outcomes, (c) the uncertainties involved, and (d) boundaries and contexts. In much of the debate concerning GM foods insufficient attention is given to the distinctions among these four categories of values, with the implicit assumption that GM proponents and GM opponents have irreconcilable differences about the value of the technology as a whole. Such a limited view of the normative (or values) dimension of GM increases the chances of polarization, reduces the scope for mutual understanding, and obscures some common interests among various parties that could form the basis for dialogue and policy agreements. For this reason, the nature and implications of these values are explored in the following paragraphs, with an emphasis on the roles of positive theories (scientific knowledge) versus the roles of normative considerations (related to values) in reconciling value differences.

Values regarding technologies. Some people and groups vary in terms of the values they attach to GM as an entire class of technologies. These include intrinsic values regarding the creation of life forms that would not normally exist in nature, as well as extrinsic values related to the possibility that non-GE approaches may be more appropriate for addressing problems related to agriculture, the environment, food security, health, and the structure and ownership of the food system. Scientific knowledge and arguments can shape and inform one's views regarding intrinsic values but ultimately cannot resolve differences that may still exist.

Values regarding outcomes. People and groups vary in the importance they attach to various outcomes, including adverse outcomes (to health, the environment, and agriculture) and beneficial outcomes (to farmers and the environment through reduced losses, costs, and pesticide use). The role of science in such a situation is to estimate, to the best extent possible, the likelihood and magnitude of each of these

outcomes and devise ways to enhance the positive ones and minimize the negative ones. However, even with perfect information regarding the various outcomes of using *Bt* corn, there is no scientific method for resolving the value differences among people and groups (Arrow 1963). Moreover, it is inappropriate for scientists or scientific institutions to impose solutions to value-laden issues because, despite their specialized knowledge, "[scientists] remain no better equipped (or mandated) to decide upon profound general questions of values and interests than are any other assemblage of citizens." (Stirling and Mayer 1999, p. 10). The latter point applies equally well to NGOs, despite their claims that they represent the broader "public interest."

The use of market mechanisms is widely recognized as an efficient approach for resolving value differences among individuals, because each person can choose products based on his or her own values. However, the FDA's decision not to impose mandatory labeling of GM foods eliminated this powerful option, and, moreover, some of the outcomes (e.g., environmental ones) involve externalities that are not well addressed through market mechanisms alone. Thus the need remains for collective decisionmaking mechanisms other than science and other than markets to resolve these value differences.

Values regarding uncertainty. People and groups vary in their views of and reactions to uncertainties, and, as shown, uncertainties are pervasive in this causal system. As in the case of outcomes, the appropriate role of scientists, especially those working in public research institutions, is to reduce the degree of uncertainty through research and to improve the methods used to test for allergenicity, toxicity, and other adverse outcomes. As noted, research of this type has been seriously neglected in the GM case, reflecting the lower value placed on unintended consequences by researchers, their institutions, and funding agencies. However, as in the case of outcomes, it is not the role of science or scientists to decide how much and what type of uncertainty should be tolerated by different groups in society. Nor is it the role of science (or of regulators or politicians) to discount or misrepresent these uncertainties in communications with the public, as has been the case with GE.

Insofar as residual uncertainties always will remain, it is notable that three powerful mechanisms exist for managing uncertainty, and especially interindividual differences in risk taking or risk aversion. One efficient mechanism, again, is to permit individual choice in the marketplace. A second is to place legal liability with producers, as the FDA's adulteration clause does in principle. A third risk management method involves insurance markets. As one crude indication of the value Americans place on managing uncertainty, the insurance industry reported sales of $466 billion in the United States in 1998 (WEFA 2000). However, all three of

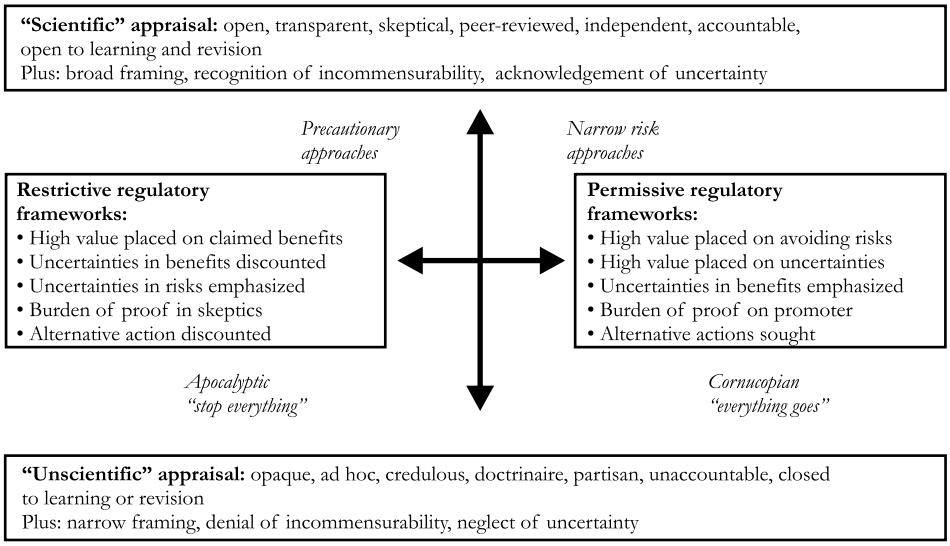
these policy instruments were rendered ineffective in the GM case because the FDA did not impose mandatory labeling and because of the lack of any systematic market surveillance system. This inaction removed the option of consumer choice and made it effectively impossible to establish links between GM foods and any adverse outcomes that might arise. Thus, while labeling and market surveillance might have partially compensated for the scientific uncertainties regarding unintended consequences, the FDA policy precluded even those second-best options.

Values regarding boundaries and context. People and groups differ in the boundaries they place on the breadth and scope of the "causal system" under consideration and on the contextual factors they either include or exclude in their analysis. A forceful example relates to the significant differences in population health and nutrition status that may affect the toxicity or allergenicity of the *Bt* endotoxin and any unintended compositional changes. These contextual or boundary differences were not acknowledged by the FDA or the Department of State.

Finally, as complex as Figure 4.1 and these examples are, they still represent only a small part of the causal system related to GM agriculture. A more complete representation of the causal system would include intellectual property rights; ownership and control of seed stocks and seed companies; long-term effects on ecological systems and on the structure and concentration of agriculture; potential long-term benefits and risks in developing countries; the influence of corporations on politics, regulations, and research funding; the role of the media in promoting the views of GM proponents or critics; public trust or mistrust of government, industry, and scientists and the historic reasons for that; the incentives causing public universities and research centers to do extensive research related to potential benefits and to neglect research related to risks; and so on. Despite the efforts of some GM proponents to limit the boundaries to only those causes and effects shown in Figure 4.1, these broader issues are intimately connected to the GM controversy. Science can play a role in estimating, assessing, and clarifying the nature of these relationships, but it is not the role of science to judge where to set the boundaries.

Science and values in regulatory regimes. Figure 4.2 attempts to integrate these considerations in a way that clarifies the scientific and normative dimensions of the debates over GM foods and other technologies. "Scientific" is defined here in terms of a basic orientation to acquiring knowledge, a broad framing of problems and causal systems, the need for open and accountable social processes such as peer review to verify and challenge accumulating knowledge, and the need to remain open to revision over time. By contrast, "unscientific" approaches are characterized by their lack of openness to challenge, their lack of transparency, their tendency to

Figure 4.2 The relationship between scientific and normative (unscientific) dimensions of regulatory frameworks



Source: Adapted from Stirling and Mayer 1999.

adopt a narrow view of problems and causal systems, their use of doctrinaire and partisan statements and positions, and their resistance to revision over time. Although many parties, notably the GM proponents inside and outside government, claim to be using "sound science," the evidence reveals that this tends to be backed up more through appeals to institutional authority (the NAS, Biotechnology Science Coordinating Committee (BSCC), FDA, and NIH and the broad scientific community) than by adherence to the characteristics of science shown in this figure.

The figure shows that this scientific dimension can coexist either with permissive or with restrictive regulatory frameworks. These latter concepts are characterized by a basic orientation to technologies and how they should be managed in society, and differences along this dimension also are readily discernible among various parties in the GM debates. It is significant, however, that the four quadrants suggested in this figure are not clearly distinguished in the public discourse, nor are they in the FDA's policy statement and scientific reports from the NAS and other bodies. Instead the overwhelming tendency is to conflate the scientific and normative dimensions and to use the authority of science to support or refute various regulatory approaches (Levidow and Carr 1997). Figure 4.2 demonstrates that a

precautionary view, far from being antiscientific, antitechnology, elitist, or immoral, as has been alleged, reflects a broader view of the causal system under consideration and a greater skepticism concerning the state of knowledge related to the actual benefits and actual risks of GE (Auberson-Huang 2002). In addition, proponents of precaution often favor more open, transparent, inclusive, and accountable procedures for deliberating the science and the normative dimensions of GE (Raffensperger and Barrett 2001), while many regulators and scientists in the United States express deep reservations about such approaches (Miller and Conko 2001).

This section reveals the pervasive nature of social values, and thus "politics" in the broadest sense, in both the science and the regulation of GM foods. It also reveals that it is not only industry proponents and activist critics who are engaged in politics over GM foods. Statements or actions that support GE, discount its uncertainties, or set boundaries on the causal system, whether made by scientists, research centers, universities, or scientific institutions (like the NAS and professional societies), are all powerful value statements that explicitly or implicitly promote GM technology even when those parties assert that such statements are purely science-based.

Framing the Policy Goals, Options, and Trade-offs

The previous section suggests that the policy roundtable in southern Africa should help clarify several issues, some of which are covered in the terms of reference for the chapters of this book and some of which are not:

1. what is known about outcomes, that is, the likelihood, frequency, magnitude, and distribution of various outcomes from GM agriculture, based on the best available scientific knowledge and knowledge of local contextual features;

2. the social values attached to each of these outcomes by various groups in society and the policy options for reducing the negative outcomes and enhancing the positive ones;

3. the level of uncertainty associated with various outcomes, the social values attached to that uncertainty, and the policy options for reducing or coping with uncertainty;

4. the relevant boundaries on the issue, which will define which issues are "on the table" for discussion and which are not, and the social values that should guide these decisions; and

5. the nature of the "authorizing institutions" that will be making these decisions as well as the final decisions, the appropriateness of procedures for informing their decisions (e.g., how are social values to be identified—who speaks for whom?), and the methods necessary to ensure openness, inclusiveness, transparency, and accountability in these procedures and decisions.

It is beyond the scope of this chapter to address all of these issues, but the following paragraphs pose contrasting ways to frame the policy questions, outline some distinct policy options, and provide some of the information needed to begin addressing the trade-offs.

There are at least two ways to frame the policy questions related to food safety for this roundtable. They are reflected in the following two sets of questions:

1. Can GM agriculture contribute meaningfully to improving food security and nutrition in southern Africa without creating an unacceptable risk to food safety?

2. What is the relative importance of improving (a) household food security; (b) population nutritional status, especially that of vulnerable groups such as women and children; and (c) morbidity related to food safety? What GM-inclusive policy options and non-GM policy options exist for achieving each of these goals? And what is the full range of potential benefits, risks, and costs associated with each policy option?

Clearly the second set represents a much broader framing of the policy questions and opens the discussion to a much wider set of potentially relevant goals, values, and policy options. While there are some merits to adopting the first question, in that it appears more tractable, the broader goals and social values left "off the table" by that question are problematic and likely will fail to address some of the strongest concerns held by some stakeholders. This section attempts to identify policy options and trade-offs related only to malnutrition, food insecurity, and food safety, recognizing that further options and trade-offs are treated in greater detail in other chapters.[3]

Comparison of problems and uncertainties. Despite the enormous uncertainties implied by the second set of questions, Table 4.5 presents some of the information relevant for addressing those questions. The table suggests that malnutrition and food insecurity are highly prevalent and highly certain problems in the region. By

Table 4.5 Outcomes and uncertainties of genetic modification under GM and non-GM policy options

	Outcomes		
Uncertainties	**Malnutrition**	**Food insecurity**	**Allergens or toxicants**
Onset	Chronic and acute	Chronic and acute	Chronic and acute
Prevalence	10–80% all forms	20–80%	Depends on the nature of the allergen or toxin, individual sensitivity, how widely a commodity is consumed, and the quantitites consumed
Protein-energy	10–50% protein energy	N/A	
Iron deficiency	up to 80% iron deficiency	N/A	
Vitamin A	0–30% vitamin A deficiency	N/A	
Zinc, folate, etc.	5–30% zinc, folate deficiency	N/A	
Probability of occurrence	100%	100%	Uncertain but low
Targets for policy change	Non-GM (current): Food security Diet diversification Supplements Supplemental feeding Fortification Breastfeeding promotion Growth promotion Community-based primary health care Water, sanitation, hygiene Female education Child spacing	Non-GM (current): Agricultural intensification Agricultural diversification Export of agricultural products Nonagricultural income Postharvest technology Market infrastructure Trade Targeted food subsidies Food aid (peace, rule of law, good governance, equity, human rights, international support)	GM (new): Strengthened premarket testing Mandatory standardized profiling methods Context-relevant Export-relevant Public access Public comment Liability incentives Use of test markets Labeling, traceability, segregation Country choice Consumer choice
Marginal impact of GM agriculture on these policy targets	As yet uncertain	As yet uncertain	Not applicable
Issues/questions to be addressed in estimating the potential impact of policy change in these areas	Technical feasibility Efficacy Coverage rates Distribution Acceptance Contextual factors (dietary interactions, parasites, malaria, child feeding practices, etc.)	Technical feasibility Efficacy Variability Adoption rates Distribution Contextual factors (seed markets, performance in local varieties, local agronomy conditions, etc.)	

Source: Compiled by the author.

contrast, problems associated with allergens and toxicants from current and future GM foods are rated here as having a high degree of uncertainty; if they do occur, their prevalence could range from very low to very high (in my judgment).

The basis for this latter judgment is that, in the case of allergens, all known allergens affect only a small proportion of the population and their effects are sufficiently acute and immediate that the offending foods can be quickly identified and avoided. In the case of toxicants, the high end estimate is a worst-case scenario that would occur only if a previously unknown toxicant in a new GM food were toxic to a majority of humans (e.g., lectins in legumes and cyanoglycosides in cassava); were not removed or detoxified through the methods of processing used in a given context; did not affect the taste of the food, the growth and appearance of plants, or other properties that historically have helped to screen out toxic foods; and would escape detection by current premarket testing procedures (which generally focus on known toxicants and have limited ability to screen for unintended and previously unknown toxicants).

GM and non-GM policy options. The second portion of Table 4.5 provides a very brief list of some of the current policy options for addressing malnutrition and food insecurity and for strengthening the safety of GM foods. With respect to malnutrition and food insecurity, the view prior to the advent of GM foods was that these policy options have the demonstrated potential to reduce malnutrition and food insecurity if they are chosen and designed in light of the national and local contexts, are well managed and implemented, and receive the requisite levels of political, institutional, and economic support. In addition, there are some "transboundary" conditions, such as peace, rule of law, good governance, respect for human rights, equity in development, and supportive international institutions that have a powerful bearing on a country's ability to improve the nutrition and food security of its people.

A common concern expressed by critics of GM agriculture is that a technological solution is being advanced for problems that are fundamentally social and political in character, that is, that the more basic policies and changes shown here are required and may be neglected. As suggested in the table, at the present stage of development the marginal impact of GM agriculture might be considered "as yet uncertain." This is due to remaining questions regarding the technical feasibility of developing complex traits such as drought resistance and nutritional improvements and, more important, to questions concerning the efficacy of these changes in light of the diverse national and local contexts in which they might be introduced. It is likely that the ultimate impact of GM agriculture on malnutrition and food insecurity will require continued and even expanded attention to the current policy

options. For instance, iron and pro–vitamin A (beta carotene) in plants has very low bioavailability, such that enhanced levels of these nutrients in GM foods may have little or no impact unless the quality of the overall diets also is improved. As another example, enhanced household food security via GM (if achieved) will not reduce child malnutrition unless attention also is given to child health, child care, and child feeding, all of which are constrained by women's health, nutritional status, knowledge, and time demands.

The net effect of these considerations is to suggest that the marginal impact of GM foods on food security and nutrition will depend on simultaneous reduction or elimination of many of the underlying causes of these problems. In addition, these considerations increase the level of uncertainty about the actual effects to be expected from GM foods.

These considerations suggest that a more constructive policy question might be posed as follows: if the success of GM agriculture in improving food security and nutrition requires simultaneous attention to other contextual factors, and if the failure to address these other factors is one of the strong values-based objections to GM agriculture, should the decisions to pursue GM agriculture be tightly linked to firmer commitments to address these contextual factors? Or, put another way, if there are no firm commitments to address the underlying contextual factors, should GM agriculture be pursued?

Strengthening the regulation of GM foods. In the event that GM agriculture is pursued, Table 4.5 suggests a number of ways in which policies could be strengthened to reduce the potential food safety risks of GM foods. These suggestions apply equally to developed and developing countries if problems related to trade are to be avoided. The measures include mandatory (rather than voluntary) premarket testing of new products, greater standardization of testing methods and decision criteria, and the use of newly emerging broad-spectrum profiling techniques to detect unintended compositional changes (Kuiper et al. 2001). In addition, procedures for developing, testing, labeling, and exporting or importing GM foods should recognize the diverse contexts in which a given GM product may be consumed (and recognize that a food safe in one context may not be safe in another), or the distribution of these foods should be limited to the contexts for which they were intended.

The FDA already has expressed an intent to provide oversight for GM foods developed in other countries and bound for the United States (FDA 2001), but it has not expressed an intent to oversee the export of U.S.-developed GM products to other developed or developing countries. The tacit assumption either is that foods deemed safe in the United States are also safe for other contexts (which can be

questioned in light of the contextual factors identified here) or that this oversight is the responsibility of importing countries. In either case, developing countries would need to become very knowledgeable of the testing procedures and results in other countries and be capable of examining them in light of the conditions prevailing in their own contexts.

In addition to issues related to testing and premarket approval, Table 4.5 suggests some procedural and legal changes that would strengthen the incentives for developers to apply rigorous testing methods. These include making the testing protocols and data accessible to the public (already underway at the FDA), providing the opportunity for the public to comment on test results prior to commercialization, and ensuring that the legal liabilities for unintended harm are incentive-appropriate. Mandatory labeling, traceability, and segregation are important for enforcing legal liability, in addition to being important for ensuring consumer choice.

Finally, the use of test markets and monitoring in those markets may be appropriate for some products for several reasons, including (a) the wide variety of products now under consideration and development; (b) the more complex genetic, metabolic, and compositional changes expected in these products; (c) the wide range of contextual factors that may affect their safety; and (d) the increasing knowledge of genetic variation within human populations. This approach would give greater meaning to the claims that "GM foods have been used for years in the United States with no evidence of safety problems" and is consistent with the requirements placed on some producers when controversial or questionable food additives have been introduced in the past.

Summary

Consideration of the relative magnitudes and uncertainties related to the effects of GM agriculture on malnutrition, food security, and food safety suggests that discussions, decisions, and effects related to GM agriculture might be more productive if (a) the development of GM agriculture were tightly linked to firmer commitments to address the underlying causes of these problems and (b) policies were strengthened in relation to the testing, labeling, and marketing of GM foods along the lines suggested here. More fundamentally, this chapter suggests a need for more authentic mechanisms by which governments, stakeholders, and citizens in the southern African region might engage with the scientific and normative dimensions of these issues and develop policies appropriate to the situations, values, and democratic aspirations of the southern African context.

The key food risk concerns identified in this chapter are toxicity and allergenicity. The rDNA techniques used for plant breeding are not simply an accelerated

version of traditional plant breeding. There are theoretical reasons to expect a higher degree of unpredictability using these techniques, and this is relevant to the potential for toxicity and allergenicity. Very little empirical experimental work has been done on the safety of GMOs. Policymakers in southern Africa may be tempted to piggyback on the regulatory decisions of developed countries, thinking, "If it is permitted in the United States, we will permit it here." This may not be warranted for two reasons. First, the regulatory framework used in the United States has been based on an imperfect understanding of the science underlying biotechnology, and that regulatory framework is in the process of being modified. Second, the dietary habits in the United States and southern Africa are so different that a product that is "safe" in the U.S. diet is not necessarily safe in the diets of southern Africans.

Notes

1. FDCA, CFR 21 U.S.C. 301 et seq.

2. Assuming an energy intake of 2000 kcal/d, 60 percent of which comes from maize (with an energy content of 350 kcal/100 grams), the typical intake of maize meal in southern Africa would be approximately 340 grams per day.

3. It should be emphasized that the terms of reference for this chapter did not include identifying the policy options to address malnutrition and food insecurity. However, the most common actions to address these problems are presented in Table 4.5, because the analysis of trade-offs with GM food safety concerns could not proceed without them.

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